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

OFFICE OF
CHEMICAL SAFETY AND
POLLUTION PREVENTION

MEMORANDUM

Date: December 21, 2015

SUBJECT: **Tetrachlorvinphos (TCVP)** Human Health Draft Risk Assessment (DRA) for Registration Review

PC Code: 083701, 083702
Petition No.: NA
Risk Assessment Type: Single Chemical Aggregate
TXR No.: NA
MRID No.: NA

DP Barcode: D411095
Registration Nos.: NA
Regulatory Action: Registration Review
Case No.: 1321
CAS No.: 22248-79-9
40 CFR: §180.252

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Attached is HED's human health risk assessment in support of the registration review of the insecticide tetrachlorvinphos.

1.0 Executive Summary

The insecticide tetrachlorvinphos (TCVP) [(Z)-2-chloro-1-(2,4,5-trichlorophenyl) vinyl dimethyl phosphate] is a member of the organophosphate (OP) class of pesticides. TCVP is used as a dermal or oral treatment to livestock (i.e., cattle, swine, poultry and horses) and their premises, in kennels, outdoors as a perimeter treatment, and as a flea treatment on cats and dogs. Formulations for pet use include collars, dusts/powders, and pump and trigger sprays. The other uses include dusts (D), emulsifiable concentrates (EC), feed through (solid and liquid food additives), feed blocks, and wettable powders (WP). Human exposure to TCVP in food may occur as a result of consuming residues in animal commodities. Exposure may also occur from drinking water that may contain TCVP residues as a result of some use patterns. Residential exposures may occur as a result of applying flea products to pets (cats and dogs) or contacting treated pets. Occupational exposures may occur during application of TCVP to livestock or their premises, or during outdoor perimeter or kennel treatments. Occupational exposures may also occur to veterinarians and pet groomers. Exposure via spray drift is not anticipated based on the current use patterns.

The most recent risk assessment for TCVP was a residential pet use assessment completed in November 2014 (W. Britton, 11/05/14, D420283)[1]. The current TCVP human health risk assessment takes into account, where appropriate, arguments presented in the Natural Resources Defense Council, Inc.'s (NRDC) Aug. 5, 2015 Opening Brief in *NRDC v. EPA*, Case No. 15-70025 (9th Cir.) (Opening Brief), which was filed as a result of the 2014 residential pet product assessment and EPA's subsequent denial of NRDC's 2009 petition to cancel all TCVP pet products. (The EPA point-by-point response to NRDC comments can be found in D430589[2].) The current TCVP human health risk assessment reflects the following changes since the 2014 residential assessment:

- Inclusion of the 10X FQPA safety factor/uncertainty factor.
- There is no non-cancer dermal hazard for TCVP.
- A female-specific body weight, 69 kg, is used for assessment of adult (inhalation) exposures instead of the average adult body weight of 80 kg.
- Use of newer pet residue data for pet collars that result in more conservative estimates of residue transfer and exposure than the data used in the 2014 risk assessment. Residential post-application assessments for TCVP pet collar uses are performed using data from two recently submitted pet collar residue transfer studies (an amitraz pet collar study[3] (herein referred to as "the amitraz study") and a literature study using TCVP pet collars (Davis, 2008[4], herein referred to as "the Davis study").

[1] W. Britton, 11/05/14, D420283, *Residential Exposure Assessment in Response to the Natural Resources Defense Council Petition to Cancel All Pet Uses for Tetrachlorvinphos.*

[2] W. Britton, 12/21/15, D430589, Tetrachlorvinphos (TCVP): Responses to Arguments Presented in the Natural Resources Defense Council, Inc.'s (NRDC) Aug. 5, 2015 Opening Brief in *NRDC v. EPA*, Case No. 15-70025 (9th Cir.)

[3] MRID 49468801: *Determination of Transferable Residues of Amitraz from the Hair of Dogs Following the Application of the Preventic® Collar*.

[4] Davis, M. et. al., *Assessing Intermittent Pesticide Exposure from Flea Control Collars Containing the Organophosphorus Insecticide Tetrachlorvinphos*. Journal of Exposure Science and Environmental Epidemiology. (2008) 18, 564-57)

- Because it cannot be confirmed at this time if TCVP pet collar products are manufactured as liquid or solid formulations, the exposures to TCVP pet collar products are assessed 1) assuming all collars may be a liquid formulation and 2) assuming all collars may be a solid (dust) formulation.

Hazard

TCVP is a member of the OP class of pesticides. For TCVP, like other OPs, the initiating event in the adverse outcome pathway/mode of action (AOP/MOA) involves inhibition of the enzyme acetylcholinesterase (AChE) *via* phosphorylation of the serine residue at the active site of the enzyme. This inhibition leads to accumulation of acetylcholine and ultimately to neurotoxicity in the central and/or peripheral nervous system. For TCVP, AChE inhibition is the most sensitive endpoint in the toxicology database in multiple species, durations, lifestages, and routes. TCVP does not require metabolic activation to an oxon to inhibit AChE; *i.e.*, the parent compound is the active form inhibiting AChE. OPs also exhibit a phenomenon known as steady state AChE inhibition. After repeated dosing at the same dose level, the degree of inhibition comes into equilibrium with the production of new, uninhibited enzyme. OP AChE studies of 2-3 weeks generally show the same degree of inhibition as those of longer duration (*i.e.*, up to 2 years of exposure). Therefore, a steady state assessment based on 21 days of exposure may be conducted in place of the traditional chronic or long-term assessments. The steady state point of departure is protective of any exposure duration longer than 21-days, including chronic exposure, since cholinesterase inhibition does not increase after reaching maximum inhibition or steady state.

The toxicology database for TCVP is complete for risk assessment. TCVP has cholinesterase data across multiple lifestages, durations, and routes for both red blood cell (RBC) and brain cholinesterase inhibition. There are acceptable studies available for toxicity endpoint and point of departure (POD) selection. For TCVP, RBC AChE inhibition is the most sensitive endpoint and is the endpoint from which the PODs for all TCVP exposure routes and durations were selected.

There is no evidence of quantitative or qualitative sensitivity in the developmental rat and rabbit study or in the gestational (fetus) or juvenile (postnatal day; PND11) components of the comparative cholinesterase assay (CCA) study. In the acute and repeated comparative cholinesterase assays, juvenile rats (PND 11 and PND 21), pregnant dams, fetuses, and non-pregnant females show similar results in both RBC and brain AChE activity. At the lowest tested dose of 75 mg/kg/day in the acute CCA study, there was little difference in RBC or brain AChE inhibition between the PND11, PND21, or young adult (PND42). Similarly, the PND11 and PND21 rats in the CCA study are similarly sensitive as adult rats exposed to a single dose of 50 mg/kg from a separate peak inhibition study. The repeat dosing phase of the CCA also demonstrates the lack of sensitivity in AChE inhibition in the juvenile (PND11) rats. Furthermore, the fetus is not more sensitive than the pregnant dam. Therefore, points of departure that are based on adult AChE data are also protective of the postnatal and gestational lifestages.

High quality AChE data for the dermal and inhalation routes are also available and allow for route specific evaluation. RBC AChE inhibition was observed in both sexes in the inhalation study (brain AChE was not assessed), while no inhibition of RBC or brain AChE was observed in the dermal

study up to the limit dose. A non-cancer dermal assessment is not required for TCVP; however, a cancer dermal assessment is required.

TCVP is classified as a Group C possible human carcinogen (based on statistically significant increases in combined hepatocellular adenoma/carcinoma in female mice) with a linear low-dose approach for quantification of risk using the oral slope factor (Q1*) of 1.83×10^{-3} $(mg/kg/day)^{-1}$. Whereas parent compound TCVP is the residue of concern for AChE inhibition, TCVP plus metabolites containing the 2,4,5 trichlorobenzene moiety are the residues of concern for cancer assessment.

Uncertainty Factors

For TCVP, as for other OPs, the FQPA safety factor (SF) of 10X has been retained for infants, children, youths, and women of childbearing age for all exposure scenarios due to uncertainty in the human dose-response relationship for neurodevelopmental effects (see Section 4.4).

For the acute and steady state dietary assessments, a total uncertainty factor of 1000X is appropriate for infants, children, youths and females of childbearing age (10X to account for interspecies extrapolation and 10X for intraspecies variation and the 10X FQPA SF). The only population subgroup for dietary exposure scenarios for which the FQPA SF is not retained is adults 50-99 years of age; therefore, the total uncertainty factor for that population is 100X.

A total uncertainty factor of 1000X is appropriate for residential incidental oral exposures (10X for interspecies extrapolation, 10X for intraspecies variation, and a 10X FQPA SF). A total uncertainty factor of 300X is appropriate for all inhalation exposures (3X for interspecies extrapolation, 10X for intraspecies variation, and a 10X FQPA SF for residential assessments or a 10X database uncertainty factor for occupational assessments to protect potentially pregnant female workers due to uncertainty in the human dose-response relationship for neurodevelopmental effects (see Section 4.4)).

Tolerance/ MRL

Tolerances for residues of TCVP are established under 40 CFR §180.252 for livestock commodities based on oral feed-through and direct dermal uses on livestock (cattle, swine, and poultry). The residues of concern for tolerance enforcement are tetrachlorvinphos, des-O-methyl tetrachlorvinphos, 1-(2,4,5-trichlorophenyl)ethanol (free and conjugated forms), 2,4,5-trichloroacetophenone, and 1-(2,4,5-trichlorophenyl)ethanediol (frequently abbreviated as TCVP, TCVPdeme, TCPEol , TCPEone, and TCPEdiol, respectively). The current tolerance expression under 40 CFR §180.252 includes all of these residues except des-O-methyl tetrachlorvinphos; this metabolite should be included in the tolerance expression. The current tolerance levels should be updated in the 40 CFR as discussed in Section 2.2.3.

There are no Codex maximum residue limits (MRLs) established or proposed for residues of TCVP. Canada has established MRLs for plant (apple and grape) and livestock commodities. The differences in U.S. and Canadian residue definitions prohibit harmonization.

Dietary Risk Assessment

Acute (TCVP), steady state (TCVP), and cancer (TCVP plus metabolites containing the 2,4,5 trichlorobenzene moiety) dietary (food and drinking water) exposure and risk assessments were conducted using the DEEM-FCID v3.16 model. The dietary exposure analyses for TCVP are mostly refined. The only food forms included in the analyses are based on animal commodities. The food residues were based upon U. S. Department of Agriculture's Pesticide Data Program (USDA PDP) monitoring data except in a couple of instances where no appropriate PDP data were available (i.e., high-end residues from poultry direct dermal application studies were used for poultry fat and poultry skin). The Biological and Economic Analysis Division (BEAD) of OPP provided percent livestock treated information. Model-derived estimated drinking water concentrations (EDWCs) were provided by the Environmental Fate and Effect Division (EFED). For acute and cancer dietary analyses, the EDWCs were included as single point estimates. For the steady state analysis, the entire distribution of 21-day average water concentrations from a thirty year simulation was used; this refinement was done for the purpose of aggregating the steady state residential and dietary exposures.

The acute and steady state dietary (food and drinking water) exposure estimates are below HED's level of concern (<100 % of the acute population adjusted dose (aPAD) or the steady state population adjusted dose (ssPAD)) for the U.S. population and all population subgroups. The most highly exposed population subgroup was children (3-5 years old) at 73% of the aPAD and 43% of the ssPAD.

The cancer dietary (food and drinking water) risk estimate for adults from lifetime exposure to TCVP and its metabolites containing the 2,4,5 trichlorobenzene moiety is 1×10^{-6} .

Residential Risk Assessment

Residential exposures (handler and post-application) are anticipated from the use of TCVP pet products for dogs and cats (collars, dusts/powders, and pump/trigger sprays). Exposures are assessed for adults who apply TCVP products to their pets and from post-application exposures to adults and children who may contact previously treated pets. The lifestages selected for each residential scenario [i.e., adults (using female body weight) and children 1 to < 2 years old] are health protective for the exposures and risk estimates for any other potentially exposed lifestage.

<u>Handler</u>
Dust/Powder and Pump/Trigger Spray: All residential handler (adults) non-cancer (steady state) inhalation risks estimated for the TCVP pet dust/powder and pump/trigger spray formulations are not of concern (i.e., all MOEs are > 300; LOC=300). Residential handler estimated cancer risks (combined dermal and inhalation) for TCVP dusts/powders range from 10^{-8} to 10^{-7}, and for pump/trigger sprays range from 10^{-9} to 10^{-8}.

Pet Collars: All residential handler (adults) non-cancer (steady state) inhalation risks estimated for the TCVP pet collars (whether assessed as liquid or dust formulations) are not of concern (i.e., all MOEs are > 300; LOC=300).

Residential handler cancer risks (inhalation and dermal combined) estimated for TCVP pet collars are all in the 10^{-8} range when assuming a liquid formulation and are all in the 10^{-7} range when assuming a dust formulation.

Post-Application

Since there is no non-cancer dermal hazard for TCVP and post-application inhalation exposures to treated pets are negligible, a quantitative non-cancer post-application exposure assessment was not performed for adults; there are no residential non-cancer risk estimates of concern for adults contacting pets treated with TCVP products.

Dust/Powder and Pump/Trigger Spray: Residential post-application non-cancer child (incidental oral) exposures to pets treated with TCVP pump/trigger sprays do not result in risk estimates of concern (i.e., MOEs are > 1,000; LOC=1000). However, child incidental oral exposures to pets treated with TCVP dust/powder products are estimated to be of concern for 14 of the 17 total exposure scenarios assessed (i.e., MOEs are < 1,000; LOC =1000). Residential post-application (adult) cancer risks estimated for TCVP pump/trigger sprays range from 10^{-7} to 10^{-6} and, for TCVP dust/powder products estimated cancer risks are 10^{-7}.

Pet Collars: The post-application assessments for the TCVP pet collars were performed assuming pet collars could be either liquid or solid (dust) formulations, and using residue transfer data from two available collar studies (the amitraz study and the Davis study). Data from both studies have been included because the Davis study has not yet undergone review by the Human Studies Review Board (HSRB); the study is scheduled for review at the next HSRB meeting in January 2016. Until the Davis study undergoes a complete review by the HSRB, any assumptions, risk estimates or conclusions using the Davis study are considered preliminary. The post-application exposure and risk estimates for the various pet collar assumptions are provided below:

> *Liquid formulation/Amitraz study assumption:* Post-application child non-cancer incidental oral risk estimates are not of concern (i.e., MOEs are > 1,000; LOC=1000). Estimated adult post-application cancer risks range from 10^{-7} to 10^{-6}.
>
> *Liquid formulation/Davis study assumption:* One of the 23 scenarios assessed for post-application child non-cancer incidental oral risk is of concern (MOE = 650; LOC=1000). Estimated adult post-application cancer risks range from 10^{-6} to 10^{-5}.
>
> *Solid (Dust) formulation/Amitraz study assumption:* Post-application child non-cancer incidental oral risk estimates are of concern for all of the TCVP pet collar exposure scenarios assessed (i.e., MOEs are < 1,000; LOC=1000). All estimated adult post-application cancer risks are estimated to be 10^{-5}.
>
> *Solid (Dust) formulation/Davis study assumption:* Quantitative assessments were not performed assuming collars are dust formulations and using the Davis study since the mean residue transfer measured in the Davis study was greater than that in the amitraz study; therefore, post-application exposures from TCVP pet collars would be greater, and

MOEs lower, when using the Davis study than those resulting from using the amitraz study (which are of concern for children).

Spray Drift

A quantitative spray drift assessment was not conducted because the use of TCVP for direct animal treatment to livestock and their premises, in kennels, outdoors as a perimeter treatment, and as a flea treatment on cats and dogs are either 1) not applied via aircraft, groundboom, or airblast equipment or 2) for applications to poultry buildings with groundboom equipment, the use is indoors and not anticipated to be a significant source of spray drift.

Aggregate Risk Assessment

Acute

The acute aggregate risk assessment includes only dietary (food and drinking water) exposures. There are no acute aggregate risk estimates of concern.

Steady State

The steady state aggregate risk assessment combines steady state exposures from food, drinking water, and residential uses. The TCVP steady state aggregate assessment was performed for adult handlers (applying pet collars, dust/powders, and pump/trigger sprays) and children post-application activities (contacting treated pets). All pet collar products were assessed as both a liquid formulation and as a solid (dust) formulation.

Handler: Residential handler (adult) steady state aggregate (food, water, residential) risk estimates for all TCVP pet product scenarios (collars, dust/powders, and pump/trigger sprays) are not of concern (Aggregate Risk Index (ARI) ≥ 1).

Post-application: For the TCVP dust/powder pet products, the steady state post-application aggregate assessments result in 16 of the 17 scenarios with risk estimates of concern (MOEs < 1000) for children. For all TCVP pump/trigger spray product scenarios, steady state post-application aggregate risk estimates are not of concern. Residential post-application (children) steady state aggregate risk estimates for all TCVP pet collar scenarios are not of concern (MOEs > 1000) when assuming collars are liquid formulations and using data from the amitraz study. Assuming liquid formulation and using the Davis study, 8 of the 23 collar scenarios resulted in aggregate MOEs of concern. Assuming collars are solid (dust) formulations and using the amitraz study, all 23 scenarios resulted in aggregate MOEs of concern. Quantitative assessments were not performed assuming collars are dust formulation and using the Davis study; those MOEs would be even lower than for the dust/amitraz assessments (which are of concern).

Cancer

The cancer aggregate risk assessment combines residential and dietary (food and drinking water) expected lifetime exposures for adults. For TCVP, a cancer aggregate assessment was performed for adult handlers (applying TCVP pet products) and adult post-application activities (contacting treated pets). Pet collar products were assessed as both a liquid formulation and as a solid (dust)

formulation.

> *Handler:* For the handler cancer aggregate, all registered pet product scenarios (collars, dust/powders, and pump/trigger sprays) result in residential handler cancer aggregate (residential and dietary) risk estimates in the 10^{-6} range.
>
> *Post-application:* All registered dust/powder and pump/trigger spray products result in residential post-application cancer aggregate (residential and dietary) risk estimates in the 10^{-6} range. Assuming liquid formulation of pet collars, aggregate risk estimates are in the 10^{-6} range using the amitraz study and are in the 10^{-5} to 10^{-6} range when using the Davis study. For the dust collar assumption, only the amitraz data were used and those cancer aggregate risk estimates are in the 10^{-5} range (cancer aggregate risk estimate values would be lower if using the Davis data).

Occupational Risk Assessment

Non-cancer (steady state) and cancer exposures and risks were calculated for occupational handlers of TCVP for all registered uses. Generic, surrogate handler data were used except in the case of a WP high pressure hand wand scenario; that scenario used chemical specific data in addition to the generic data.

Steady state inhalation exposure and risk estimates were calculated for occupational handlers of TCVP for a variety of exposure scenarios at differing levels of respiratory personal protection including engineering controls. Steady state dermal exposures were not quantitatively assessed as there is no non-cancer dermal hazard.

Of the 172 total occupational handler exposure scenarios assessed, the majority (152) are not of concern (i.e., steady state inhalation MOEs are ≥ 300) with currently required personal protective equipment (PPE) (i.e., respiratory protection). Of the remaining 20 handler exposure scenarios, an additional 16 are not of concern with consideration of increasing levels of respiratory protection (i.e., four occupational handler exposure scenarios result in estimated risks of concern despite the addition of respiratory protection or engineering controls). These four handler scenarios are all dust formulations (mixing/loading/applying TCVP by rotary duster, self-treating dust bag, or shaker can).

Occupational cancer (combined inhalation and dermal) risks were estimated for both private/farmer and contract/commercial handlers. Cancer risks range from 10^{-10} to 10^{-5} for private/farmer handlers and from 10^{-10} to 10^{-4} for contract/commercial handlers with currently required PPE.

Occupational post-application exposures are not expected as reentry activities are not anticipated for the registered TCVP uses. There are no risk concerns for occupational post-application exposures to TCVP.

Human Studies Review

This risk assessment relies in part on data from studies in which adult human subjects were intentionally exposed to a pesticide or other chemical. These data, which include studies from PHED 1.1; the AHETF database; the Outdoor Residential Exposure Task Force (ORETF) database; the ARTF database; the Residential SOPs (Treated Pets); as well as a TCVP dust/powder applicator exposure study (MRID 45519601), and TCVP dust and pump spray study (MRID 45485501) and an amitraz pet collar residue transfer study (MRID 49468801**)** (1) subject to ethics review pursuant to 40 CFR Part 26, (2) have received that review, and (3) are compliant with applicable ethics requirements. For certain studies, the ethics review may have included review by the Human Studies Review Board (HSRB). Descriptions of data sources, as well as guidance on their use, can be found at the agency website[5].

Data were also used from a literature study using TCVP pet collars (Davis, M. et. al., 2008). That study has undergone internal EPA science and ethics review and will also undergo review by the HSRB (the next scheduled HSRB meeting is January 2016).

2.0 HED Recommendations

2.1 Data Deficiencies

None.

2.2 Tolerance Considerations

2.2.1 Enforcement Analytical Method

A gas liquid chromatography (GLC) method for the determination of TCVP *per se* in livestock commodities is described in the Pesticide Analytical Method (PAM), Vol. II, as Method I.

The registrant has submitted a method (14020.6106) for the determination of tetrachlorvinphos and its metabolites (TCVPdeme, TCPEdiol, TCPEone and TCPEol) in livestock commodities, which uses QuEChERS and LC/MS/MS methods. The test data for method 14020.6106 are classified as scientifically acceptable for use as an analytical method for ruminant and poultry commodities.

The submitted multiresidue method testing data are acceptable and indicate that FDA multiresidue methods are not suitable for analysis of the TCVP metabolites TCPEdiol and TCVPdeme. However, the metabolites TCPEol and TCPEone were recoverable under Protocol F, although fortified recoveries were small (<50%).

It should be noted that the FDA PESTDATA database dated 8/93 (PAM Vol. I, Appendix II) indicates that parent compound TCVP is completely recovered (>80%) using FDA multiresidue

[5] http://www.epa.gov/pesticides/science/handler-exposure-data.html and http://www.epa.gov/pesticides/science/post-app-exposure-data.html

method protocol D (section 232.4) but is not recovered using protocol E (Sections 211.1/231.1 and 212.1/232.1, fatty and nonfatty matrices).

2.2.2 International Harmonization

There are no Codex maximum residue limits (MRLs) established or proposed for residues of TCVP. Canada has established MRLs for plant (apple and grape) and livestock commodities. The U.S. tolerances are for livestock commodities; there are no registered crop uses. Canada's residue definition is 2-chloro-1-(2,4,5-trichlorophenyl) vinyl dimethyl phosphate (TCVP) and its low melting isomer as opposed to the U.S. definition which includes the parent compound TCVP plus the four metabolites of concern. The differences in U.S. and Canadian residue definitions prohibit harmonization. HED has not examined the Canadian registrations; different use patterns may also be a factor in achieving harmonization. A summary of U.S. and international tolerances and maximum residue limits is presented in Appendix E.

2.2.3 Recommended Tolerances

Tolerances for residues of TCVP are established under 40 CFR §180.252. The current tolerance expression is for the combined residues of tetrachlorvinphos [(Z)-2-chloro-1-(2,4,5-trichlorophenyl)vinyl dimethyl phosphate] and its metabolites, 1-(2,4,5-trichlorophenyl)-ethanol (free and conjugated forms), 2,4,5-trichloroacetophenone, and 1-(2,4,5-trichlorophenyl)-ethanediol.

Time limited TCVP tolerances are established for the animal commodities under 40 CFR §180.252 and were based on the available metabolism data. In the 2006 RED (USEPA, July 2006, Reregistration Eligibility Decision (RED)), time-limited tolerances were recommended to allow time for the registrant to submit new magnitude of residue studies. Sufficient residue data have been submitted in order to determine the appropriate tolerances for residues of TCVP on livestock commodities.

The HED Metabolism Committee has determined that the residues of concern for tolerance enforcement are tetrachlorvinphos, des-O-methyl tetrachlorvinphos, 1-(2,4,5-trichlorophenyl)ethanol (free and conjugated forms), 2,4,5-trichloroacetophenone, and 1-(2,4,5-trichlorophenyl)ethanediol. The current tolerance expression under 40 CFR §180.252 includes all of these residues *except des-O-methyl tetrachlorvinphos*; this metabolite should be included in the tolerance expression. To allow separate risk assessments for 1) cholinesterase inhibition (parent TCVP only) and 2) carcinogenicity (parent plus metabolites), the tolerances for each livestock commodity also specify the maximum residues of TCVP *per se* from the total residues. The tolerance definition should be modified as follows, to be consistent with the Tolerance Expression Guidance issued 5/27/09 (S. Knizner).

> Tolerances are established for residues of the insecticide tetrachlorvinphos, including its metabolites and degradates, in or on the commodities in the table below. Compliance with the tolerance levels specified below is to be determined by measuring only the sum of tetrachlorvinphos [(Z)-2-chloro-1-(2,4,5-trichlorophenyl)vinyl dimethyl phosphate) and its metabolites chloro- 1 -(2,4,5-

trichlorophenyl)-vinylmonomethyl phosphate, 1-(2,4,5-trichlorophenyl)-ethanol (free and conjugated forms), 2,4,5-trichloroacetophenone, and 1-(2,4,5-trichlorophenyl)-ethanediol, calculated as the stoichiometric equivalent of tetrachlorvinphos, in or on the commodity.

Table 2.2.3. Tolerance Reassessment Summary for Tetrachlorvinphos.

Commodity	Established Tolerance [1] (ppm)	Maximum Residues [2] (ppm)	Reassessed Tolerance [3,4] (ppm)	Comments; *Correct Commodity Definition*
Cattle, fat (of which no more than 0.1 ppm is tetrachlorvinphos *per se*)	0.2	0.84 (0.56) subcutaneous fat; 0.75 (0.34) peritoneal fat	1.0	*Cattle, fat (of which no more than 0.6 ppm is tetrachlorvinphos per se)*
Cattle, kidney (of which no more than 0.05 ppm is tetrachlorvinphos *per se*)	1.0	--	Remove	See cattle, meat byproducts
Cattle, liver (of which no more than 0.05 ppm is tetrachlorvinphos *per se*)	0.5	--	Remove	
Cattle, meat (of which no more than 2.0 ppm is tetrachlorvinphos *per se*)	2.0	0.27 (0.21) muscle	0.3	*Cattle, meat (of which no more than 0.2 ppm is tetrachlorvinphos per se)*
Cattle, meat by products, except kidney and liver	1.0	--	Remove	See cattle, meat byproducts
Cattle, meat by products	None	0.16 (<0.01) liver; 0.28 (0.015) kidney; 0.84 (0.56) subcutaneous fat; 0.75 (0.34) peritoneal fat; 0.27 (0.21) muscle	1.0	*Cattle, meat byproducts (of which no more than 0.6 ppm is tetrachlorvinphos per se)* [5]
Egg (of which no more than 0.05 ppm is tetrachlorvinphos *per se*)	0.2	0.288 (0.026)	0.3	*Egg (of which no more than 0.03 ppm is tetrachlorvinphos per se)*
Hog, fat (of which no more than 0.1 ppm is tetrachlorvinphos *per se*)	0.2	0.84 (0.56) subcutaneous fat; 0.75 (0.34) peritoneal fat	1.0	*Hog, fat (of which no more than 0.6 ppm is tetrachlorvinphos per se)*
Hog, kidney (of which no more than 0.05 ppm is tetrachlorvinphos *per se*)	1.0	--	Remove	See hog, meat byproducts
Hog, liver (of which no more than 0.05 ppm is tetrachlorvinphos *per se*)	0.5	--	Remove	
Hog, meat (of which no more than 2.0 ppm is tetrachlorvinphos *per se*)	2.0	0.27 (0.21) muscle	0.3	*Hog, meat (of which no more than 0.2 ppm is tetrachlorvinphos per se)*
Hog, meat byproducts, except kidney and liver	1.0	--	Remove	See hog, meat byproducts

Table 2.2.3. Tolerance Reassessment Summary for Tetrachlorvinphos.				
Commodity	Established Tolerance [1] (ppm)	Maximum Residues [2] (ppm)	Reassessed Tolerance [3,4] (ppm)	Comments; *Correct Commodity Definition*
Hog, meat by products	None	0.16 (<0.01) liver; 0.28 (0.015) kidney; 0.84 (0.56) subcutaneous fat; 0.75 (0.34) peritoneal fat; 0.27 (0.21) muscle	1.0	*Hog, meat byproducts (of which no more than 0.6 ppm is tetrachlorvinphos per se)* [5]
Milk, fat (reflecting negligible residues in whole milk and of which no more than 0.05 ppm is tetrachlorvinphos *per se*)	0.05	0.072 (0.036) for milk; 0.078 (<0.01) for cream	0.1	*Milk (of which no more than 0.04 ppm is tetrachlorvinphos per se)*
Poultry, fat (of which no more than 7.0 ppm is tetrachlorvinphos *per se*)	7.0	1.298 (0.099) abdominal fat	1.4	*Poultry, fat (of which no more than 0.1 ppm is tetrachlorvinphos per se)*
Poultry, liver (of which no more than 0.05 ppm is tetrachlorvinphos *per se*)	2.0		Remove	See poultry, meat byproducts
Poultry, meat (of which no more than 3.0 ppm is tetrachlorvinphos *per se*)	3.0	0.40 (0.082) muscle	0.4	*Poultry, meat (of which no more than 0.1 ppm is tetrachlorvinphos per se)*
Poultry, meat byproducts, except liver	2.0	--	Remove	See poultry, meat byproducts
Poultry, meat byproducts	None	0.52 (0.016) liver; 0.58 (0.022) kidney; 0.40 (0.082) muscle; 19.41 (6.03) skin with fat; 1.30 (0.099) abdominal fat	20	*Poultry, meat byproducts (of which no more than 6.0 ppm is tetrachlorvinphos per se)* [5]

[1] Time-limited tolerances; current tolerance expression is for the combined residues of tetrachlorvinphos [(Z)-2-chloro-1-(2,4,5-trichlorophenyl)vinyl dimethyl phosphate] and its metabolites, 1-(2,4,5-trichlorophenyl)-ethanol (free and conjugated forms), 2,4,5-trichloroacetophenone, and 1-(2,4,5-trichlorophenyl)-ethanediol; expression should also include des-O-methyl tetrachlorvinphos.

[2] Total residues of tetrachlorvinphos and its metabolites, TCVP-deme, TCPEone, TCPEol (free and conjugated forms), and TCPEdiol (free and conjugated), expressed in terms of parent equivalents; the value in parentheses represents the maximum residues of the parent tetrachlorvinphos.

[3] Reassessed tolerance is based on the maximum residue from the respective magnitude of the residue study; the maximum residues of the parent tetrachlorvinphos are reported in the corrected commodity definition.

[4] The residue data for cattle can be used to set tolerances for hog commodities since residues in hog tissues are not likely to be greater than those in cattle tissues.

[5] According to the 18 July 2007 Minutes of the HED ChemSAC meeting, the guidance document will be revised to include language detailing the use of the highest residue data for any tissue (liver, kidney, fat, skin or muscle) to determine the tolerance for meat byproducts. A single tolerance on "meat byproducts" will be recommended based on that highest residue, and individual tolerances will no longer be set on liver, kidney, or meat byproducts (except liver and kidney).

2.3 Label Recommendations

2.3.1 Recommendations from Residue Reviews

The following label revisions are recommended based on the application methods and rates used in the tetrachlorvinphos magnitude of the residue studies, which were used to determine the appropriate tolerance levels in livestock commodities (GLN 860.1200 Directions for Use):

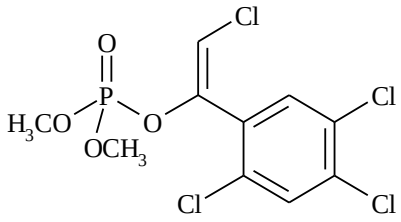
- Based on the magnitude of the residue study on cattle, the product labels with direct animal spray uses on cattle (EPA Reg. Nos. 61483-43 and 61483-50) should be amended to specify a maximum of three applications, with two-week retreatment intervals, at 19 g ai/animal/dose. The product label for Ravap (EPA Reg. No. 61483-50) should also be amended to provide conversion factors to allow calculation of direct animal spray treatment rate in terms of g ai/animal.

- Based on the magnitude of the residue study on poultry, the product labels with direct animal spray uses on poultry (EPA Reg. Nos. 61483-43 and 61483-50) should be amended to specify a maximum of seven applications (with two-week retreatment intervals) at 0.18 g ai/hen/application. Note that the label should specify the weight or volume of the product to be applied.

3.0 Introduction

3.1 Chemical Identity

Table 3.1. Tetrachlorvinphos Nomenclature.

Compound	
Common name	Tetrachlorvinphos
Company experimental name	TCVP
IUPAC name	(Z)-2-chloro-1-(2,4,5-trichlorophenyl) vinyl dimethyl phosphate
CAS registry number	22248-79-9
End-use products registered to KMG Bernuth, Inc.	Rabon 50 WP Insecticide (EPA Reg. No. 61483-43, 50% WP); Rabon 3% Insecticide Dust EPA Reg. No. 61483-45, 3% D); Rabon 97.3 Oral Larvicide (EPA Reg. No. 61483-47, 97.3% G); Rabon 7.76 Oral Larvicide Premix (EPA Reg. No. 61483-48, 7.76% G); and Ravap EC Livestock, Poultry & Premise Insecticide Spray (EPA Reg. No. 61483-50, 23% EC)

See Appendices C and D for nomenclature and physical/chemical properties of TCVP and metabolites (TCVPdeme, TCPEdiol, TCPEone and TCPEol, TCCEol, TCBA).

3.2 Physical/Chemical Characteristics

Technical tetrachlorvinphos is a tan to brown crystalline solid with a melting point of 93-98 °C. TCVP is not expected to volatilize significantly due to a low vapor pressure of 2.6×10^{-7} torr (25°C). The solubility of tetrachlorvinphos in water at 25°C is 11.6 mg/L. TCVP has limited solubility in most aromatic hydrocarbons. TCVP is hydrophobic, with an octanol-water partition coefficient of 3350 (Log K_{ow} of 3.53).

3.3 Pesticide Use Pattern

TCVP is used as a direct animal treatment to livestock (i.e., cattle, horses, poultry and swine) and their premises, in kennels, outdoors as a perimeter treatment, and as a flea treatment on cats and dogs. There are 42 end-use product labels currently registered with TCVP as the active ingredient (ai). The TCVP livestock and perimeter treatment uses are formulated as follows: dusts (D), emulsifiable concentrates (EC), feed through (solid and liquid food additives), feed blocks, and wettable powders (WP). TCVP can be applied by a variety of means/equipment types including: backrubber/facerubber; backpack; cup; groundboom; handheld fogger; manually-pressurized handwand; mechanically-pressurized handwand; open pour (dust and liquid formulations); paint (airless sprayer or brush/roller); pet collar; plunger; rotary duster; shaker can; spoon; stationary fogger; and trigger spray. For a complete list of registered uses, including maximum use rates, see Appendix L of this document.

3.4 Anticipated Exposure Pathways

Humans may be exposed to TCVP residues in food since TCVP may be directly applied to, or fed to, livestock which may result in residues in animal commodities. TCVP may reach surface and ground water sources of drinking water through the outdoor usage on poultry droppings, garbage and manure piles, and kennels and corrals. Residential exposures (handler and post-application) may occur as a result of the application to dogs and cats as dust/powders, sprays, or collars. In an occupational setting, applicators may be exposed while handling the pesticide prior to application, as well as during application. Occupational post-application exposures are not expected as reentry activities are not anticipated for the registered TCVP uses.

3.5 Consideration 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," http://www.epa.gov/compliance/environmentaljustice/resources/policy/exec_order_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 USDA under the National Health and Nutrition 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. Further considerations are currently in development as OPP has committed resources and expertise to the development of specialized software and models that consider exposure to bystanders and farm workers as well as lifestyle and traditional dietary patterns among specific subgroups.

4.0 Hazard Characterization and Dose-Response Assessment

TCVP is a member of the organophosphate class of pesticides. Like other OPs, the initiating event in the adverse outcome pathway/mode of action (AOP/MOA) for TCVP involves inhibition of the enzyme AChE *via* phosphorylation of the serine residue at the active site of the enzyme. This inhibition leads to accumulation of acetylcholine and ultimately to neurotoxicity in the central and/or peripheral nervous system (see Figure 1). For TCVP, AChE inhibition is the most sensitive endpoint in the toxicology database in multiple species, durations, lifestages, and routes. AChE inhibition is the focus of this hazard characterization; the availability of reliable AChE inhibition dose response data is one of the key determinants in evaluating this toxicology database.

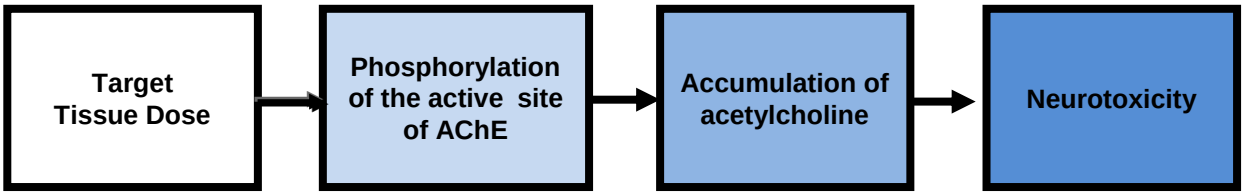


Figure 1. Adverse outcome pathway for OPs

4.1 Toxicology Studies Available for Analysis

The toxicology database for TCVP is complete for risk assessment. There are acceptable studies available for toxicity endpoint selection; they include:

- subchronic oral toxicity studies in rats
- chronic oral toxicity studies in rats and dogs
- carcinogenicity studies in rats and mice
- developmental studies in rats and rabbits
- reproduction study in rats
- acute and subchronic neurotoxicity studies in rats
- developmental neurotoxicity (DNT) study in rats
- acute and repeated comparative (CCA) cholinesterase (ChE) studies in juvenile and adult rats
- repeated, gestational ChE study in pregnant rat and fetuses
- delayed neurotoxicity study in hens
- subchronic dermal toxicity study in rats

- repeated dosing inhalation toxicity study in rats
- immunotoxicity study in mice
- complete mutagenicity study battery
- metabolism study in rats

4.2 Absorption, Distribution, Metabolism, & Excretion (ADME)

TCVP, unlike some other OPs, does not require metabolic activation to the oxon metabolite to inhibit AChE. In a rat metabolism study, TCVP was almost completely metabolized, and most of the radiolabel was excreted in the urine (46%-60%) and feces (38%-56%) within 48 hours of dosing. Only minor amounts (>0.5%) were found in the tissues. Very little un-metabolized parent compound was recovered. The major metabolite in feces was trichlorophenylethanol, with lesser amounts of trichlorophenylethandiol. The major metabolite in urine was trichloromandelic acid, with lesser amounts of desmethyl tetrachlorvinphos. There is no evidence of bioaccumulation. Some differences in metabolism were noted between the sexes; *e.g.*, males excreted more trichloromandelic acid, a more completely metabolized form of TCVP, whereas females excreted more of the desmethyl TCVP, which could be derived from TCVP with only a single metabolic step.

4.2.1 Dermal Absorption

A dermal absorption factor (DAF) of 9.6% was used to evaluate dermal exposures in the cancer risk assessment. Since there was no dermal hazard identified for non-cancer endpoints, a quantitative dermal assessment was not performed (see Section 4.6.1).

4.3 Toxicological Effects

AChE inhibition is the well-established cholinergic mode of action for OPs and is typically used as the critical effect in hazard characterization for members of this class of pesticides. TCVP inhibits cholinesterase activity in various species including rats, mice, rabbits, and dogs. TCVP has cholinesterase data across multiple lifestages, durations, and routes for both red blood cell (RBC) and brain cholinesterase inhibition. Cholinesterase inhibition is the most sensitive effect for TCVP, however, TCVP data demonstrate a shallow dose-response curve for AChE inhibition across many of the studies in the database resulting in varying magnitudes of response across the database. Large increases in administered dose result in only small changes in AChE inhibition. For example, in the 11-day repeat adult CCA study, 5 mg/kg and 10 mg/kg resulted in about 10% RBC inhibition, 50 mg/kg from 30-40% RBC inhibition, and 200 mg/kg only 40-60% inhibition. A similar response was observed in brain AChE with no inhibition at 5 mg/kg, 7-12% at 10 mg/kg, 15-40% at 50 mg/kg, and only 18-57% at 200 mg/kg. In the 21-day repeat toxicity study, 20 mg/kg resulted in approximately 30% RBC inhibition while the highest dose of 50 mg/kg resulted in only 30-40% inhibition.

Many of the toxicological studies for TCVP have been considered for benchmark dose (BMD) modeling (Bever/Holman; 5/20/14; TXR# 0056970 and Appendix B). However, a number of datasets were not amenable to BMD modeling due to the shallow dose response described above. Some studies in the database, however, were amenable to BMD modeling and provided a robust

evaluation of the RBC and brain AChE activity. In general, RBC and brain cholinesterase inhibition were similarly inhibited across the database. It should be noted that is some cases RBC data provided a more robust dose-response and, therefore, more reliable BMD estimates. Male and female adult rats were also generally affected similarly across the various studies; although sporadically, one sex appears more sensitive; there is no consistent pattern. For example, in the repeat oral subchronic study, adult females were more sensitive (RBC and brain) than adult males, while in the single dose study (MRID 45570601), males were more sensitive (brain) than adult females. High quality AChE data for the dermal and inhalation routes are also available and allow for route specific evaluation. RBC AChE inhibition was observed in both sexes in the inhalation study (brain AChE was not assessed), while no inhibition of RBC or brain AChE was observed in the dermal study up to the limit dose.

Transient clinical signs [gait alterations, constricted pupils, tremors (fore- and hindlimb), body cool to the touch, decreased defecation, red material on forelimbs, around eyes, nose, mouth] characteristic of cholinergic toxicity were observed at the high dose (650 mg/kg) in the acute neurotoxicity rat study, and tremors were observed in pregnant rats in the developmental toxicity study at dose levels 5X higher than those eliciting AChE inhibition.

There is no evidence of quantitative or qualitative sensitivity in the developmental rat and rabbit study or in the gestational (fetus) or juvenile (PND11) components of the CCA study. In the acute and repeated comparative cholinesterase assays, juvenile rats (PND 11 and PND 21), pregnant dams, fetuses, and non-pregnant females show similar results in both RBC and brain AChE activity. At the lowest tested dose of 75 mg/kg/day in the acute CCA study, there was little difference in RBC or brain AChE inhibition between the PND11, PND21, or young adult (PND42). Similarly, the PND11 and PND21 rats in the CCA study are similarly sensitive as adult rats exposed to a single dose of 50 mg/kg from a separate peak inhibition study. The repeat dosing phase of the CCA also demonstrates the lack of sensitivity in AChE inhibition in the juvenile (PND11) rats. Furthermore, the fetus is not more sensitive than the pregnant dam. Therefore, points of departure that are based on adult AChE data are also protective of the postnatal and gestational lifestages.

In the rat developmental toxicity study, no developmental effects were observed in the fetus at dose levels where minimal effects (decreased body weight gains) were observed in the dams. Developmental toxicity (increased early resorptions, post-implantation loss, and decreased number of live fetuses) was observed in the rabbit developmental toxicity study at the same dose level where significant toxicity (mortality, abortion) was observed in the maternal rabbit. No reproductive or offspring toxicity was observed in the 2-generation reproductive rat study, but increased adrenal weights were observed in the parental rats.

In the developmental neurotoxicity study (DNT), quantitative susceptibility was only observed in pups (decreased pup weight, decreased relative brain weight/measurements) at the high dose of 200 mg/kg/day. However, a 200 mg/kg/day dose to juvenile rats is 10-fold higher than doses reflecting approximately 10% inhibition in juvenile pups in the CCA study and 25-fold higher than the point of departure. Therefore, when considered in combination with the results from the CCA, sensitivity occurring at doses relevant for risk assessment was not observed in the database. Thus,

data from adult animals are protective of any effects in the young. Additionally, BMD results using cholinesterase inhibition are protective for the effects observed in pups in the DNT study.

TCVP is classified as a Group C possible human carcinogen with a linear low-dose approach for quantification of risk using the oral slope factor (Q1*) of 1.83×10^{-3}.

In acute lethality studies, TCVP has low acute toxicity by the oral, dermal, and inhalation routes of exposure. It is a slight dermal irritant, a moderate eye irritant, and a dermal sensitizer.

4.3.2 Critical Durations of Exposure

One of the key elements in risk assessment is the appropriate integration of temporality between the exposure and hazard assessments. One advantage of an AOP understanding is that human health risk assessments can be refined and focused on the most relevant durations of exposure. The following text provides an analysis of the temporal pattern of AChE inhibition from repeated dosing studies in laboratory animals for TCVP. This analysis provides the basis for determining which exposure durations are appropriate for assessing the human health risk. Table 4.3.2.1 provides a summary of the representative results from experimental toxicology studies with TCVP for female adult rats.

Table 4.3.2.1. TCVP BMD_{10} Results (mg/kg/day) for RBC and Brain AChE Inhibition Over Time in Female Adult Rats

MRID (study)	Days of Dosing	% inhibition at LOAEL (mg/kg) or the BMD_{10} [1]
		RBC
MRID 45570601 (single dose)	1 day	37% at 50
MRID 48773401 (repeat CCA)	11 days	10% at 8.7 (BMD_{10})
MRID 45570601 (21-day oral)	21 days	10% at 9.9 (BMD_{10})
MRID 43371201 (90-day oral)	90 days	10% at 10.5 (BMD_{10})
MRID 42980901 (chronic oral)	365 days	29% at 63
		Brain
MRID 45570601 (single dose)	1 day	23% at 50
MRID 48294601 (acute CCA)	1 day	10% at 11.3 (BMD_{10})
MRID 48773401 (repeat CCA)	11 days	10% at 7.2 (BMD_{10})
MRID 45570601 (21-day oral)	21 days	10% at 14.7 (BMD_{10})
MRID 43371201 (90-day oral)	90 days	12% at 6.7
MRID 42980901 (chronic oral)	365 days	14% at 63

[1]The BMD, not the BMDL, estimates are shown when available in Table 4.3.2.1. According to the BMD guidance, the central estimate (i.e., the BMD) is used for purposes of comparison. The LOAEL and percent inhibition is presented when a BMD estimate is not available.

In adults, OPs generally exhibit a phenomenon known as steady state cholinesterase inhibition. After repeated dosing at the same dose, the degree of inhibition comes into equilibrium with the production of new, uninhibited enzyme. At this point, the amount of AChE inhibition at a given dose remains consistent across duration. In general, OPs reach steady state within 2-3 weeks but this can vary among OPs. This pattern is observed for most OPs, but not every OP, like TCVP, which shows no difference in response across duration.

In the specific case for TCVP, this OP exhibits a shallow dose-response curve for cholinesterase inhibition and little change in response across duration. In other words, large increases in administered dose result in only small changes in AChE inhibition, and increasing duration does not result in more inhibition as is typical for most OPs. This shallow dose response leads to variability in the AChE data and a relatively broad range of BMD_{10}/$BMDL_{10}$ values from 6.8 to 61.6 mg/kg/day BMD_{10} / 3.6 to 26.3 mg/kg/day $BMDL_{10}$ (Appendix B). Moreover, when evaluating the data cross the database, the magnitude of the AChE inhibition varies across different studies at comparable dose levels.

A single dose rat study (MRID 45570601) resulted in no RBC or brain AChE inhibition at 8 mg/kg while in males 12 mg/kg resulted in 29% RBC inhibition and only 46% at 50 mg/kg; in other words in the single dose adult rat study, a 4-fold dose spread led to only 16% increased response. Similarly, the acute CCA study (MRID 48294601) shows a shallow dose response: 75 mg/kg resulted in 14-35% RBC inhibition with 15-35% inhibition at 150 mg/kg and 20-47% at 300 mg/kg. Similar RBC AChE inhibition was observed from these two acute studies and across the 12 mg/kg to 300 mg/kg combined dose range.

In the chronic rat toxicity study, increasing the dose 2-fold only leads to changes in female RBC AChE inhibition of less than 10%. In the same study at a dose of 125 mg/kg/day, females displayed 17-25% RBC AChE inhibition, whereas males displayed no RBC AChE inhibition at 88 mg/kg/day. Similarly, in the gestational CCA study, pregnant dams did not exhibit any RBC AChE inhibition at a dose of 75 mg/kg/day, whereas in the 21-day subchronic oral study, non-pregnant female rats showed approximately 40% RBC AChE inhibition at a dose of 50 mg/kg/day.

All of these studies support the shallow dose-response across 10-fold or greater doses as well as the lack of increased inhibition with repeat exposure. For example, the single dose study in adults demonstrates a NOAEL of 8 mg/kg for both brain and RBC AChE; the RBC $BMDL_{10}$ from the 90-day subchronic toxicity rat study being used as the POD is 8 mg/kg/day. A single dose of 50 to 75 mg/kg resulted in 14- 46% RBC AChE while in the 11-day repeat CCA study a dose of 75 mg/kg/day resulted in similar RBC AChE inhibition of 13-40%. The 21-day toxicity study (MRID 45570601) evaluated doses of 8, 12, 20 and 50, which resulted in RBC NOAELs of 8 mg/kg/day after 21 days and NOAEL of 12 mg/kg/day in females for brain AChE. No RBC inhibition was observed at 6 mg/kg/day in the 90-day toxicity study while RBC was 30-80% inhibited at 142 mg/kg/day. The chronic toxicity study also demonstrated lack of RBC AChE inhibition at 5.9 mg/kg/day and approximately 30% RBC AChE inhibition at 63 mg/kg/day. Therefore, the lack of inhibition at 6 and 8 mg/kg/day across the acute and repeat dosing studies suggests the lack of increased inhibition with duration.

Although the durations of the toxicity and exposure assessments may differ among the OPs, an exact match is not necessary and would suggest a level of precision that the toxicity data do not support. Given this, the 21-day and longer exposure assessment is scientifically supportable and also provides consistency with the OP cumulative risk assessment (OP Cumulative Risk Assessment (CRA); 2002, 2006) and across the single chemical risk assessment for the OPs. As such, the single chemical OP assessments will evaluate steady state (a 21-day assessment) instead of the typical chronic duration dietary assessment. The steady state point of departure is protective of any exposure duration longer than 21-days, including chronic exposure, since cholinesterase inhibition does not increase after reaching maximum inhibition or steady state.

4.4 Literature Review on Neurodevelopment Effects

For the OPs, historically the agency has used inhibition of AChE as the POD for human health risk assessment; at present time, this policy continues. This science policy is based on decades of work which shows that AChE inhibition is the initial event in the pathway to acute cholinergic neurotoxicity. The use of AChE inhibition data for deriving PODs was supported by the FIFRA SAP (2008, 2012) for chlorpyrifos as the most robust source of dose-response data for extrapolating risk and is the source of data for PODs for TCVP. A detailed review of the epidemiological studies used in this review can be found either in the 2014 chlorpyrifos revised draft human health risk assessment ((D424485, D. Drew et al., 12/29/2014) or in the 2015 literature review for other organophosphates (OPP/USEPA; D331251; 9/15/15).

Newer lines of research on OPs in the areas of potential AOPs, *in vivo* animal studies, and notably epidemiological studies in mothers and children, have raised some uncertainty about the agency's risk assessment approach with regard to the potential for neurodevelopmental effects in fetuses and children. Many of these studies have been the subject of review by the agency over the last several years as part of efforts to develop a risk assessment for chlorpyrifos (D424485, D. Drew et al., 12/29/2014). Initially, the agency focused on studies from three US cohorts: 1) The Mothers and Newborn Study of North Manhattan and South Bronx performed by the Columbia Children's Center for Environmental Health (CCCEH) at Columbia University; 2) the Mt. Sinai Inner-City Toxicants, Child Growth and Development Study or the "Mt. Sinai Child Growth and Development Study;" and 3) the Center for Health Assessment of Mothers and Children of Salinas Valley (CHAMACOS) conducted by researchers at University of California Berkeley. The agency has evaluated these studies and sought external peer review (FIFRA SAP reviews in 2008 and 2012; federal panel, 2013[6]) and concludes they are of high quality. In the three US epidemiology cohort studies, mother-infant pairs were recruited for the purpose of studying the potential health effects of environmental exposures during pregnancy on subsequent child development. Each of these cohorts evaluated the association between prenatal chlorpyrifos and/or OP exposure (with adverse neurodevelopmental outcomes in children through age 7 years. For the 2014 chlorpyrifos revised human health risk assessment (D424485, D. Drew et al., 12/29/2014), EPA included epidemiologic research results from these three US prospective birth cohort studies but primarily focused on the results of CCCEH since this cohort has published studies on the association between cord blood levels of chlorpyrifos and

[6] http://www.regulations.gov/#!documentDetail;D=EPA-HQ-OPP-2008-0850-0170

neurodevelopmental outcomes. The agency retained the FQPA 10X Safety Factor (SF) in the 2014 chlorpyrifos revised risk assessment, in large part, based on the findings of these studies.

In the 2015 updated literature review (OPP/USEPA; D331251; 9/15/15), the agency conducted a systematic review expanding the scope of the 2012/2014 review focused on US cohort studies with particular emphasis on chlorpyrifos. The expanded 2015 review includes consideration of the epidemiological data on any OP pesticide, study designs beyond prospective cohort studies, and non-U.S. based studies. The updated literature review identified seven studies which were relevant (Bouchard et al., 2010; Fortenberry et al., 2014; Furlong et al., 2014; Guodong et al., 2012; Oulhote and Bouchard, 2013; Zhang et al., 2014; Shelton et al., 2014). These seven studies have been evaluated in context with studies from the 2012/2014 review (D424485, D. Drew et al., 12/29/2014). Only a brief summary is provided below.

The OP exposure being assessed in many of these studies used concentrations of urinary dialkyl phosphate metabolites (DAPs) as the urinary biomarker. Total DAPs is a non-specific measure of OP exposure and is the sum of six separate molecules - three dimethyl alkylphosphate (DMAP) molecules of DMP, DMTP, DMDTP, and three diethyl alkylphosphate (DEAP) molecules of DEP, DETP, and DEDTP. Each metabolite is a breakdown product from multiple OPs (Table 4.4.-1; CDC, 2008)[7]. Specifically, DMP, DMTP, and DMDTP are associated with 18, 13, and 5 OPs, whereas DEP, DETP, and DEDTP are associated with 10, 10, and 4 OPs, respectively. Thus, using urinary DAPs alone as an exposure measure, it is not possible to separate the exposure and associated effects for single, specific OPs.

Table 4.4.1. CDC Table of organophosphate pesticides and their dialkyl phosphate metabolites (2008)

Pesticide	DMP	DMTP	DMDTP	DEP	DETP	DEDTP
Azinphos methyl	X	X	X			
Chlorethoxyphos				X	X	
Chlorpyrifos				X	X	
Chlorpyrifos methyl	X	X				
Coumaphos				X	X	
Dichlorvos (DDVP)	X					
Diazinon				X	X	
Dicrotophos	X					
Dimethoate	X	X	X			
Disulfoton				X	X	X
Ethion				X	X	X
Fenitrothion	X	X				
Fenthion	X	X				
Isazaphos-methyl	X	X				
Malathion	X	X	X			
Methidathion	X	X	X			
Methyl parathion	X	X				
Naled	X					
Oxydemeton-methyl	X	X				

[7] http://www.cdc.gov/nchs/data/nhanes/nhanes_03_04/l26opd_c_met_organophosphorus_pesticides.pdf

Parathion				X	X	
Phorate				X	X	X
Phosmet	X	X	X			
Pirimiphos-methyl	X	X				
Sulfotepp				X	X	
Temephos	X	X				
Terbufos				X	X	X
Tetrachlorvinphos	X					
Trichlorfon	X					

DMP = dimethylphosphate; DEP = diethylphosphate; DMTP = dimethylthiophosphate; DMDTP = dimethyldithiophosphate; DETP = diethylthiophosphate; DEDTP = diethyldithiophosphate.

For studies which measured urinary 3,5,6-trichloro-2-pyridinol (TCPy) (e.g., Fortenberry et al., 2014; Eskenazi et al., 2007; Whyatt et al., 2009), this metabolite can be derived from chlorpyrifos, chlorpyrifos-methyl, and the herbicide triclopyr. TCPy is also the primary environmental degradate of chlorpyrifos, chlorpyrifos-methyl, and triclopyr; thus exposure can be found directly on food treated with these pesticides. CCCEH studies have largely used chlorpyrifos measured in cord blood as the specific biomarker (e.g., Lovasi et al., 2010; Whyatt et al., 2004; Rauh et al., 2011). The CHARGE study (Shelton et al., 2015) did not measure biomarkers but instead used geospatial analysis to focus on the residential proximity to OP exposure using data from the California Department of Pesticide Regulation, with five OPs accounting for a total of 73% of the pesticide applied near residential settings (chlorpyrifos, acephate, diazinon, bensulide, and dimethoate).

Similarly, DAPs can be found directly on food following OP applications (Zhang et al., 2008; Chen et al., 2012). Specifically, studies have shown that DAPs may form as environmental degradates from abiotic hydrolysis, photolysis, and plant metabolism (Zhang et al., 2008; Chen et al., 2012; Racke et al., 1994). Furthermore, since these DAPs are excreted more rapidly and extensively than the parent OPs (Zhang et al., 2008; Forsberg et al., 2008), direct exposure to DAPs may lead to an overestimate of OP exposure when using urinary DAPs as a biomarker of OP exposure. The agency recognizes that this is a source of uncertainty when using DAPs for assessing OP exposure and will continue to monitor this issue in future assessments.

With respect to neurological effects near birth, the CHAMACOS and Mt. Sinai cohorts measured neurological effects at birth, and observed a putative association with total DEAP, total DMAP, and total DAP exposure (Engel et al., 2007; Young et al., 2005). Similarly, a Chinese study (Zhang et al., 2014) reported statistically significant associations between for total DEAPs, total DMAPs, and total DAPs from prenatal OP pesticide exposure and neonatal neurodevelopment assessed 3 days after birth. However, another cross-sectional Chinese study, Guodong et al. (2012), observed no association with urinary DAPs and a developmental quotient score for 23-25 month old children.

The 3 US cohorts (CCCEH, Mt. Sinai, CHAMACOS) each reported evidence of impaired mental and psychomotor development, albeit not consistent by age at time of testing (ranging from 6 month to 36 months across the three cohorts). Attentional problems and ADHD were reported by three prospective cohorts [Rauh et al., 2006; Eskenazi et al., 2007; Marks et al., 2010; and Fortenberry et al. (2014)] investigators with additional support from a case control study,

Bouchard et al. (2010). The exposure metric varied among these studies. Specifically, Fortenberry et al. (2014) found suggestive evidence of an association with TCPy and ADHD in boys, whereas statistically significant associations were observed by Rauh et al. (2006) with chlorpyrifos exposure and ADHD. Eskenazi et al. (2007) reported associations with total DMAPs and total DAPs and ADHD; Marks et al. (2010) reported associations with total DEAP, DMAP, and total DAP exposure and ADHD. In a national cross-sectional study of Canadian children, using 2007-2009 data for children age 6-11 years (Oulhote and Bouchard, 2013), there were no overall statistically significant associations observed between child urinary DEAP, DMAP, or total DAP metabolite levels and parentally reported behavioral problems. In contrast, Bouchard et al. (2010), looking at U.S. children age 8-15 years in the 2000-2004 National Health and Nutrition Examination Survey (NHANES), observed a positive association between attention and behavior problems and total DAPs and DMAPs, but not DEAPs. As part of their analysis, Oulhote and Bouchard (2013) noted that their outcome assessment for behavioral problems may not have been as sensitive as Bouchard et al. (2010), which may in part account for the difference in the observed results from these studies.

In addition, the three US cohorts and the CHARGE study have reported suggestive or positive associations between OP exposure and autism spectrum disorders (Rauh et al., 2006; Shelton et al., 2014; Eskenazi et al., 2007; Furlong et al., 2014). Specifically, Furlong et al. (2014) documented suggestive evidence of an association between total DEAP exposure and reciprocal social responsiveness among blacks and boys. Eskenazi et al. (2007) reported a statistically significant association between pervasive developmental disorder (PDD) and total DAP exposure, whereas Eskenazi et al. (2010) reported non-significant, but suggestive, increased odds of PDD of 2.0 (0.8 to 5.1; p=0.14). Rauh et al. (2006) documented a significant association between PDD and specifically chlorpyrifos exposure. Both PDD and reciprocal social responsiveness are related to the autism spectrum disorder. Using a different exposure assessment method (geospatial analysis and residential proximity to total OP exposure), Shelton et al. (2014) also showed statistically significant associations between total OP exposure and ASD. While these studies vary in the magnitude of the overall strength of association, they have consistently observed a positive association between OP exposure and ASD. Finally, CCCEH, Mt. Sinai, CHAMACOS have reported an inverse relation between the respective prenatal measures of chlorpyrifos and intelligence measures at age 7 years (Rauh et al. ,2011; Engel et al., 2011; Bouchard et al., 2011).

Across the epidemiology database of studies, the maternal urine, cord blood, and other (meconium) measures provide evidence that exposure did occur to the fetus during gestation but the actual level of such exposure during the critical window(s) of susceptibility is not known. While significant uncertainties remain about the actual exposure levels experienced by mothers and infant participants in the children's health cohorts, it is unlikely that these exposures resulted in AChE inhibition. As part of the CHAMACOS study, Eskenazi et al. (2004) measured AChE activity and showed that no differences in AChE activity were observed. The biomarker data (chlorpyrifos) from the Columbia University studies are supported by the agency's dose reconstruction analysis using the PBPK-PD model (D424485, D. Drew et al., 12/29/2014). Following the recommendation of the FIFRA SAP (2012), the agency conducted a dose reconstruction analysis of residential uses available prior to 2000 for pregnant women and young children inside the home. The PBPK-PD model results indicate for the highest exposure

considered (i.e., indoor broadcast use of a 1% chlorpyrifos formulation) <1% RBC AChE inhibition was produced in pregnant women. While uncertainty exists as to actual OP exposure at (unknown) critical windows of exposure, EPA believes it is unlikely individuals in the epidemiology studies experienced RBC AChE inhibition.

A review of the scientific literature on potential modes of action/adverse outcome pathways (MOA/AOP)[8] leading to effects on the developing brain was conducted for the 2012 FIFRA SAP meeting (USEPA, 2012) and updated for the December 2014 chlorpyrifos revised risk assessment (D424485, D. Drew et al., 12/29/2014). In short, multiple biologically plausible hypotheses and pathways are being pursued by researchers that include targets other than AChE inhibition, including cholinergic and non-cholinergic systems, signaling pathways, proteins, and others. However, no one pathway has sufficient data to be considered more credible than the others. The fact that there are, however, sparse AOP data to support the *in vitro* to *in vivo* extrapolation, or the extrapolation from biological perturbation to adverse consequence significantly limits their quantitative use in risk assessment. The SAP concurred with the agency in 2008 and 2012 about the lack of definable key events in a MOA/AOP leading to developmental neurobehavioral effects. However, since the 2014 literature review, there are no substantive changes in the ability to define and quantitate steps in an MOA/AOP leading from exposure to effects on the developing brain. Published and submitted guideline DNT laboratory animal studies have been reviewed for OPs as part of the 2012/2014 review (D424485, D. Drew et al., 12/29/2014) and the updated 2015 review (OPP/USEPA; D331251; 9/15/15). Neurobehavioral alterations in laboratory animals were often reported, albeit at AChE inhibiting doses, but there was generally a lack of consistency in terms of pattern, timing, or dose-response for these effects, and a number of studies were of lower quality. However, this information does provide evidence of long-lasting neurodevelopmental disorders in rats and mice following gestational exposure.

At this time, a MOA(s)/AOP(s) has/have not been established for neurodevelopmental outcomes. This growing body of literature does demonstrate, however, that OPs are biologically active on a number of processes that affect the developing brain. Moreover, there is a large body of *in vivo* laboratory studies which show long-term behavioral effects from early life exposure, albeit at doses which cause AChE inhibition. EPA considers the results of the toxicological studies relevant to the human population, as qualitatively supported by the results of epidemiology studies. The agency acknowledges the lack of established MOA/AOP pathway and uncertainties associated with the lack of ability to make strong causal linkages and unknown window(s) of susceptibility. These uncertainties do not undermine or reduce the confidence in the findings of the epidemiology studies. The epidemiology studies reviewed in the 2012/2014 and 2015 literature reviews represent different investigators, locations, points in time, exposure assessment procedures, and outcome measurements. Despite all these differences in study design, with the exception of two negative studies in the 2015 literature review (Guodong et al., 2012; Oulhote and Bouchard, 2013), authors have identified associations with neurodevelopmental outcomes associated with OP exposure across four cohorts and twelve study citations. Specifically, there is evidence of delays in mental development in infants (24-36 months), attention problems and autism spectrum disorder in early childhood, and intelligence decrements in school age children

[8] Mode of action (MOA) and adverse outcome pathways (AOPs) describe a set of measureable key events that make up the biological processes leading to an adverse outcome and the causal linkages between such events.

who were exposed to OPs during gestation. Investigators reported strong measures of statistical association across several of these evaluations (odds ratios 2-4 fold increased in some instances), and observed evidence of exposures-response trends in some instances, *e.g.*, intelligence measures.

As section 408(b)(2)(C) of the FFDCA instructs EPA, in making its "reasonable certainty of no harm" finding, that in "the case of threshold effects, an additional tenfold margin of safety for the pesticide chemical residue and other sources of exposure shall be applied for infants and children to take into account potential pre- and postnatal toxicity and completeness of data with respect to exposure and toxicity to infants and children." Section 408 (b)(2)(C) further states that "the Administrator may use a different margin of safety for the pesticide chemical residue only if, on the basis of reliable data, such margin will be safe for infants and children." Given the totality of the evidence, there is sufficient uncertainty in the human dose-response relationship for neurodevelopmental effects which prevents the agency from reducing or removing the statutory 10X FQPA Safety Factor. For the TCVP DRA, a value of 10X has been applied. Similarly, a database uncertainty factor of 10X will be retained for occupational risk assessments. The agency will continue to evaluate the epidemiology studies and pursue approaches for quantitative or semi-quantitative comparisons between doses which elicit AChE inhibition and those which are associated with neurodevelopmental outcomes prior to a revised human health risk assessment.

4.5 Safety Factor for Infants and Children (FQPA Safety Factor)

No increased susceptibility was observed in the developmental and reproductive toxicity studies, and there was no evidence that the young animal is more sensitive to cholinesterase inhibition than the adult animal in the comparative cholinesterase assays (CCA). The quantitative susceptibility observed in pups at the high dose of 200 mg/kg/day in the DNT occurred at a dose 10-fold higher than doses reflecting 10% inhibition in juvenile pups in the CCA study and 25-fold higher than the point of departure. Therefore, quantitative sensitivity occurring at doses relevant for risk assessment was not observed in the TCVP database.

As noted above, the lack of an established MOA/AOP makes quantitative use of the epidemiology studies in risk assessment challenging, particularly with respect to determining dose-response, critical duration of exposure, and window(s) of susceptibility. However, exposure levels in the range measured in the epidemiology studies are likely low enough that they are unlikely to result in AChE inhibition. Epidemiology studies consistently identified associations with neurodevelopmental outcomes associated with OP exposure such as delays in mental development in infants (24-36 months), attention problems and autism spectrum disorder in early childhood, and intelligence decrements in school age children. Therefore, there is a need to protect children from exposures that may cause these effects; this need prevents the agency from reducing or removing the statutory FQPA Safety Factor. **Thus, the FQPA 10X Safety Factor will be retained for TCVP for the population subgroups that include infants, children, youths, and women of childbearing age for all exposure scenarios.**

4.5.1 Completeness of the Toxicology Database

The database of toxicology studies for TCVP is complete and includes developmental toxicity studies in the rat and rabbit, a reproductive toxicity study in the rat, acute and subchronic neurotoxicity studies in the rat, a developmental neurotoxicity study in the rat, a comparative cholinesterase study in the rat with three components (acute, repeat, and gestational exposure).

As discussed in Section 4.4, there is uncertainty in the human dose-response relationship for neurodevelopmental effects and this warrants retention of the FQPA Safety Factor for the population subgroups that include infants, children, youths, and women of childbearing age for all exposure scenarios.

4.5.2 Evidence of Neurotoxicity

TCVP is an organophosphate insecticide with an established neurotoxic AOP; neurotoxicity is the most sensitive effect in all species, routes, and lifestages and is being used to derive points of departure (PODs).

4.5.3 Evidence of Sensitivity/Susceptibility in the Developing or Young Animal

The concern for susceptibility is low based on the lack of susceptibility following *in utero* exposure to TCVP in either the rat or rabbit developmental toxicity study or following *in utero* and/or pre-/post-natal exposure to TCVP in the 2-generation reproduction rat study. The quantitative susceptibility observed in pups at the high dose of 200 mg/kg/day in the DNT occurred at a dose 10-fold higher than doses reflecting 10% inhibition in juvenile pups in the CCA study and 25-fold higher than the point of departure. Additionally, the maternal animal in the DNT was likely experiencing significant AChE inhibition at the dose level where developmental toxicity was observed. In the comparative cholinesterase studies following both acute and repeat exposure, as well as gestational exposure, there was no evidence that the young animal is more sensitive to cholinesterase inhibition than the adult animal.

As discussed in Section 4.4, there is uncertainty in the human dose-response relationship for neurodevelopmental effects and this warrants retention of the FQPA Safety Factor for the population subgroups that include infants, children, youths, and women of childbearing age for all exposure scenarios.

4.5.4 Residual Uncertainty in the Exposure Database

There are no residual uncertainties in the exposure database. The mostly refined dietary risk assessment uses food residues levels from monitoring data and from empirical studies, percent livestock treated data and model-estimated drinking water concentrations from maximum application rates. Residential exposure assessments use data from surrogate and chemical-specific sources. The exposure assumptions will not underestimate risks.

4.6 Toxicology Endpoint and Point of Departure Selections

4.6.1 Dose-Response Assessment

Table 4.6.4.1 summarizes the TCVP toxicity endpoints and points of departure (PODs) selected from an evaluation of the database. This endpoint selection was based on a weight of the evidence evaluation using the following considerations:

- *Relative sensitivity of the brain and RBC compartments*: For TCVP, the brain and RBC compartments were generally similarly inhibited, as discussed in the toxicological effects section. AChE data were evaluated across several durations and studies (Table A.3.1 in Appendix A). However, based upon the robustness of the AChE data and dose-response across the dose selection in the 90-day toxicity rat study, the RBC AChE data from female rats were selected as the endpoint for deriving the acute and steady state POD for risk assessment. In this study the female RBC data were more robust than in males.

- *Potentially susceptible populations (fetuses, juveniles, pregnant dams*): The available AChE data across multiple lifestages (adults, pregnant females, fetuses, juveniles) from the acute and repeat CCA studies demonstrate no lifestage sensitivity for either RBC or brain AChE. The lowest dose in the acute CCA study was 75 mg/kg. Similar RBC AChE inhibition (20-40%) was observed at this dose in PND11 and PND21 juvenile pups as well as in the young adult. The gestational CCA component also demonstrate the lack of sensitivity of the fetus with derived a LOAEL of 75 mg/kg. A NOAEL from the CCA study was not identified and, hypothetically, a LOAEL to NOAEL factor would result in a 7.5 mg/kg derived NOAEL, similar to the $BMDL_{10}$ of 8 mg/kg/day. Therefore, reliance of adult female AChE data for risk assessment is protective of all lifestages.

- *Route of exposure:* It is preferred to match, to the degree possible, the route of exposure in the toxicity study with the exposure scenario(s) of interest. In the case of TCVP, there are oral, dermal, and inhalation studies that contain measurements of AChE inhibition.

- *Duration of exposure:* It is preferred to match, to the degree possible, the duration of toxicity study with the exposure duration of interest. In the case of TCVP, there are single day and steady state/repeat exposure oral studies and steady state dermal and inhalation studies. The oral AChE data, as discussed in section 4.3.2, show the magnitude of AChE inhibition does not significantly increase with dose such that AChE inhibition from a single oral dose was comparable to inhibition after repeated oral exposure. For example, the single dose study in adult rats demonstrates a NOAEL of 8 mg/kg for both brain and RBC AChE, and the RBC $BMDL_{10}$ from the 90-day subchronic toxicity rat study is 8 mg/kg/day. As such, the same POD is being used for oral exposure across all durations.

- *Consistency across studies:* In cases where multiple datasets are available for a single duration, it is important to evaluate the extent to which data are consistent (or not) across studies. As discussed, the database shows a consistent shallow dose response across studies and durations demonstrating that TCVP is less potent than many organophosphates. However, the POD relied upon by the agency is conservative and health protective.

Descriptions of the primary toxicity studies used for selecting toxicity endpoints and points of departure for various exposure scenarios are presented in Appendix A of this document. Summary tables of BMD analyses can be found in Appendix B and the technical details of the analysis can be found in the BMD memo (J. Bever; TXR No. 0056970; D420286).

Consistent with risk assessments for other AChE-inhibiting compounds, OPP has used a benchmark response (BMR) level of 10% and has thus calculated BMD_{10}s and $BMDL_{10}$s. The BMD_{10} is the estimated dose where AChE is inhibited by 10% compared to background AChE activity. The $BMDL_{10}$ is the lower confidence bound on the BMD_{10} value. As a matter of science policy, the agency uses the BMDL, not the BMD, for use as the PoD (USEPA, 2012). All BMD/BMDL modeling was completed using USEPA BMD Software, version 2.4; an exponential model was used to fit the data.

Acute Dietary

As presented earlier in Section 4.3.2 of the hazard assessment, the AChE data suggest lack of toxicity or greater inhibition with repeated exposure. Several lines of evidence suggest a NOAEL of 8 mg/kg/day is protective for both acute and steady state assessments. The single dose study in adults demonstrates a NOAEL of 8 mg/kg for both brain and RBC AChE. The acute CCA study (juveniles, gestation, and young adult) provides a LOAEL of 75 mg/kg (lowest dose tested) and hypothetically the use of a 10x LOAEL to NOAEL UF would result in a 7.5 mg/kg POD. Likewise, the RBC $BMDL_{10}$ from the 90-day subchronic toxicity rat study is 8 mg/kg/day. Therefore, a POD for the acute dietary (all populations) exposure scenario was derived based on the RBC AChE inhibition from the oral 90-day subchronic toxicity rat study (MRID 43371201). This 90-day rat study was selected since it provided the most robust dose-response RBC AChE data from doses relevant to risk assessment. The female $BMDL_{10}$ of 8.0 mg/kg/day associated with RBC ChE inhibition in both sexes in the subchronic oral study was selected as the most protective and suitable POD for the acute dietary (all populations) exposure scenario. The corresponding BMD_{10} was 10.5 mg/kg/day.

The FQPA SF (10X) will be retained for infants, children, youths, and women of childbearing age due to uncertainty in the human dose-response relationship for neurodevelopmental effects (see Section 4.4). The acute population adjusted dose (aPAD) for these lifestages is 0.008 mg/kg/day (includes a total uncertainty factor of 1000X: 10X to account for interspecies extrapolation and 10X for intraspecies variation and the 10X FQPA SF). The only population subgroup for dietary exposure scenarios that the FQPA SF is not retained for is adults 50-99 years of age; therefore, the aPAD for this population subgroup is 0.08 mg/kg/day.

Steady-State Dietary

The steady state dietary endpoint was selected from an oral subchronic toxicity rat study conducted in which RBC AChE inhibition was observed. The duration of this study is considered appropriate for this exposure scenario since AChE data across the database demonstrate that there is no progression of AChE inhibition over duration with TCVP and that steady state inhibition occurs essentially after a single dose and within 21 days for other OPs, and a longer-term exposure would not be expected to result in a lower POD. The female $BMDL_{10}$ of 8.0

mg/kg/day associated with RBC AChE inhibition in both sexes was selected as a suitable POD for the steady state dietary (all populations) exposure scenario. The steady state point of departure is protective of any exposure duration longer than 21-days, including chronic exposure, since cholinesterase inhibition does not increase after reaching maximum inhibition or steady state.

The FQPA SF (10X) will be retained for infants, children, youths, and women of childbearing age due to uncertainty in the human dose-response relationship for neurodevelopmental effects (see Section 4.4). The steady state population adjusted dose (ssPAD) for these lifestages is 0.008 mg/kg/day (includes a total uncertainty factor of 1000X: 10X to account for interspecies extrapolation and 10X for intraspecies variation and the 10X FQPA SF). The only population subgroup for dietary exposure scenarios that the FQPA SF is not retained for is adults 50-99 years of age; therefore, the ssPAD for this population subgroup is 0.08 mg/kg/day.

Incidental Oral, Steady State

For the purpose of assessing potential risk associated with incidental oral exposure from steady state durations, OPP selected the POD and endpoint from an oral subchronic toxicity study conducted in adult rats in which RBC cholinesterase inhibition was observed. This study is appropriate for a childrens assessment since the acute and repeat CCA studies did not demonstrate sensitivity of juvenile pups compared to adults. Therefore, quantitation of incidental oral risks was performed using the female $BMDL_{10}$ value of 8.0 mg/kg/day, based on RBC AChE inhibition and the BMD_{10} of 10.5 mg/kg. The selected study is protective of all populations since there is no concern for increased quantitative susceptibility in acute and repeated dosing CCA studies.

A total uncertainty factor of 1000X is appropriate for incidental oral exposures (10X for interspecies extrapolation, 10X for intraspecies variation, and a 10X FQPA SF due to uncertainty in the human dose-response relationship for neurodevelopmental effects (see Section 4.4)).

Dermal, Steady State

No quantification of dermal non-cancer risk is required for TCVP. There were (1) no treatment related effects (no clinical signs) at doses up to and including the limit dose in the dermal toxicity study; (2) both RBC and brain cholinesterase activity were assessed in the dermal study and neither compartment was affected at the limit dose; (3) there is no concern for quantitative susceptibility for juvenile or gestational lifestages based on results of the developmental, reproductive, or CCA toxicity studies; and (4) the effects observed in pups from the DNT were 10-fold above the 10% inhibition level with a dermal equivalent dose necessary to produce an effect well above the limit dose.

Inhalation, Steady State

The steady state inhalation POD was selected from a 4-week inhalation toxicity study (MRID 48803501) in rats, based on an increase in RBC cholinesterase inhibition in both sexes. Females had slightly lower modeled values ($BMDL_{10}$ of 0.022 mg/L/day: BMD_{10} of 0.12 mg/L/day). The duration of this study is considered appropriate for the steady state exposure scenario since steady state occurs within 21 days, as demonstrated for other OPs, and a longer-term exposure would not be expected to result in a lower POD. The methods and dosimetry equations described in the agency's reference concentration (RfC) guidance are suited for calculating human equivalent

concentrations (HECs) based on the inhalation toxicity POD obtained in rats exposed for 6 hr/day for an average of 5.5 days/week. The regional deposited dose ratio (RDDR), which accounts for the particulate diameter (mass median aerodynamic diameter [MMAD] and geometric standard deviation [GSD] of aerosols) can be used to estimate the different dose fractions deposited along the respiratory tract surface areas. Thus, the RDDR can be used to adjust an observed inhalation particulate exposure of an animal to the predicted inhalation exposure for a human. For the subchronic inhalation toxicity study with TCVP, a RDDR of 2.525 was estimated based on extrarespiratory effects (RBC AChE inhibition) in Sprague Dawley rats (bodyweight = 267g). The MMAD and GSD of 2.57 and 3.785 µm, respectively, at 0.05 mg/L were used to derive the RDDR.

The HECs are summarized in Table 4.6.1.1, as well as human equivalent doses (HEDs) calculated for residential and occupational handler scenarios. For residential handler scenarios, a HED was calculated using a breathing rate of 16.7 L/min. For occupational handler scenarios, HEDs were calculated for breathing rates of 8.3, 16.7, and 29 L/min to account for different occupational activities. The standard interspecies extrapolation uncertainty factor can be reduced from 10X to 3X due to the HEC calculation accounting for pharmacokinetic (not pharmacodynamic) interspecies differences. The intraspecies uncertainty factor remains at 10X.

Table 4.6.1.1 Estimated Human Equivalent Concentration (HEC)/Human Equivalent Dose (HED)

Population	HEC (mg/L)	HED (mg/kg/day)
Residential Handler	0.05555	1.590
Residential Bystander	0.00992	-
Occupational -8.3 L/min breathing rate -16.7 L/min breathing rate -29 L/min breathing rats	0.04166	 2.371 4.771 8.285

RDDR = 2.525 (extrarespiratory) based on MMAD±GSD of 2.57±3.785 observed at 0.05 mg/L in Sprague-Dawley rats using 267g default bodyweight (MRID 48803501).

A total uncertainty factor of 300X is appropriate for inhalation exposures (3X for interspecies extrapolation, 10X for intraspecies variation, and a 10X FQPA SF for residential assessments or a 10X database uncertainty factor in occupational assessments due to uncertainty in the human dose-response relationship for neurodevelopmental effects (see Section 4.4)).

4.6.2 Recommendations for Combining Routes of Exposure for Risk Assessment

PODs for the oral, dermal, and inhalation routes are all derived from RBC cholinesterase inhibition. The data do not support any differences in response across different lifestages or sexes. Thus, all routes can be combined.

4.6.3 Cancer Classification and Risk Assessment Recommendation

TCVP is classified as a Group C, possible human carcinogen, based on statistically significant increases in combined hepatocellular adenoma/carcinoma (primarily carcinomas) in the female B6C3F1 mouse, suggestive evidence of thyroid c-cell adenomas, and adrenal pheochromocytomas in the rat, as well as mutagenicity concerns. A cancer potency factor (Q_1 *) of 1.83×10^{-3} $(mg/kg/day)^{-1}$ was estimated using the Weibull 83 time-to-tumor model. A 3/4 body weight scaling factor was used to convert from mouse to human equivalents.

4.6.4 Summary of Points of Departure and Toxicity Endpoints Used in Human Risk Assessment

See Table 4.6.4.1 below.

Table 4.6.4.1. Summary of Toxicological Doses and Endpoints for TCVP for Use in Dietary and Non-Occupational Human Health Risk Assessments				
Exposure/ Scenario	**Point of Departure**	**Uncertainty Factors***	**Level of Concern for Risk Assessment**	**Study and Toxicological Effects**
Acute Dietary (all populations, except adults 50-99)	$BMDL_{10}$ = 8.0 mg/kg/day	UF_A= 10x UF_H=10x FQPA SF = 10x	Acute RfD = 0.08 mg/kg/day aPAD = 0.008 mg/kg/day	Subchronic Oral Toxicity Study (MRID 43371201) – Rat BMD_{10} = 10.49 mg/kg/day, based on female RBC AChE inhibition
Acute Dietary (Adults 50-99)	$BMDL_{10}$ = 8.0 mg/kg/day	UF_A= 10x UF_H=10x FQPA SF = 1x	Acute RfD = 0.08 mg/kg/day aPAD = 0.08 mg/kg/day	Subchronic Oral Toxicity Study (MRID 43371201) - Rat BMD_{10} = 10.49 mg/kg/day, based on female RBC AChE inhibition
Steady State Dietary (all populations, except adults 50-99)	$BMDL_{10}$ = 8.0 mg/kg/day	UF_A= 10x UF_H=10x FQPA SF = 10x	Steady State RfD = 0.08 mg/kg/day ssPAD = 0.008 mg/kg/day	Subchronic Oral Toxicity Study (MRID 43371201) – Rat BMD_{10} = 10.49 mg/kg/day, based on female RBC AChE inhibition
Steady State Dietary (Adults 50-99)	$BMDL_{10}$ = 8.0 mg/kg/day	UF_A= 10x UF_H=10x FQPA SF = 1x	Steady State RfD = 0.08 mg/kg/day ssPAD = 0.08 mg/kg/day	Subchronic Oral Toxicity Study (MRID 43371201) – Rat BMD_{10} = 10.49 mg/kg/day, based on female RBC AChE inhibition
Incidental Oral (steady state)	$BMDL_{10}$ = 8.0 mg/kg/day	UF_A= 10x UF_H=10x FQPA SF = 10x	Residential LOC for MOE = 1000	Subchronic Oral Toxicity Study (MRID 43371201) – Rat BMD_{10} = 10.49 mg/kg/day, based on female RBC AChE inhibition
Dermal (steady state)	No potential hazard *via* the dermal route, based on the lack of treatment-related effects, including the lack of RBC and brain cholinesterase inhibition following repeat dermal exposure of rats at dose levels up to 1000 mg/kg/day and no concern for quantitative susceptibility.			
Inhalation (steady state)	$BMDL_{10}$=0.022 mg/L/day (males)	UF_A= 3x UF_H=10x FQPA SF = 10X	Residential LOC for MOE = 300	Subchronic Inhalation Toxicity Study (MRID 48803501) – Rat BMD_{10} = 0.12 mg/L/day, based on RBC AChE inhibition in both sexes
Cancer (oral, dermal, inhalation)	Classification: A possible human (Group C) carcinogen. Q_1^* = 1.83 x 10^{-3} $(mg/kg/day)^{-1}$			

[1] **Explanation of Abbreviations:** Point of Departure (POD) = A data point or an estimated point that is derived from observed dose-response data and used to mark the beginning of extrapolation to determine risk associated with lower environmentally relevant human exposures. NOAEL = no observed adverse effect level. LOAEL = lowest observed adverse effect level. UF = uncertainty factor. UFA = extrapolation from animal to human (interspecies). UFH = potential variation in sensitivity among members of the human population (intraspecies); MOE = margin of exposure. LOC = level of concern. RBC = red blood cell. $BMDL_{10}$= benchmark dose lower limit for 10% response. PAD = population adjusted dose. (a = acute. ss = steady state or maximal AChE inhibition which occurs around 2-3 weeks for OPs and is a specific exposure assessment conducted for OPs instead of the traditional short, intermediate, or chronic assessments. The SS assessment is protective of longer durations including chronic).
*The 10X FQPA SF is retained for infants, children, youths, and women of childbearing age for all exposure scenarios due to uncertainty in the human dose-response relationship for neurodevelopmental effects (see Section 4.4). This includes all exposure scenarios, except the dietary exposure scenarios for the population subgroup adults 50-99 for which the FQPA SF has been reduced to 1X.

Table 4.6.4.2 Summary of Toxicological Doses and Endpoints for TCVP for Use in Occupational Human Health Risk Assessments

Exposure/ Scenario	Point of Departure	Uncertainty Factors	Level of Concern for Risk Assessment	Study and Toxicological Effects
Dermal (steady state)	No potential hazard *via* the dermal route, based on the lack of treatment-related effects, including the lack of RBC and brain cholinesterase inhibition following repeat dermal exposure of rats at dose levels up to 1000 mg/kg/day and no concern for quantitative susceptibility.			
Inhalation (steady state)	$BMDL_{10}$=0.022 mg/L/day (males)	UF_A= 3x UF_H=10x UF_{DB}= 10x*	Occupational LOC for MOE = 300	Subchronic Inhalation Toxicity Study (MRID 48803501) - Rat BMD_{10} = 0.12 mg/L/day, based on RBC AChE inhibition in both sexes
Cancer (oral, dermal, inhalation)	Classification: A possible human (Group C) carcinogen. Q_1* = 1.83 x 10^{-3} $(mg/kg/day)^{-1}$			

[1] **Explanation of Abbreviations:** Point of Departure (POD) = A data point or an estimated point that is derived from observed dose-response data and used to mark the beginning of extrapolation to determine risk associated with lower environmentally relevant human exposures. NOAEL = no observed adverse effect level. LOAEL = lowest observed adverse effect level. UF = uncertainty factor. UFA = extrapolation from animal to human (interspecies). UFH = potential variation in sensitivity among members of the human population (intraspecies); UF_{DB} = database uncertainty factor; MOE = margin of exposure. LOC = level of concern. RBC = red blood cell. $BMDL_{10}$= benchmark dose lower limit for 10% response. SS = steady state or maximal AChE inhibition which occurs around 2-3 weeks for OPs and is a specific exposure assessment conducted for OPs instead of the traditional short, intermediate, or chronic assessments. The SS assessment is protective of longer durations including chronic.
*The 10X database uncertainty factor applies to occupational worker assessment to account for potentially pregnant workers due to uncertainty in the human dose-response relationship for neurodevelopmental effects (see Section 4.4).

4.7 Endocrine Disruption

As required by FIFRA and FFDCA, EPA reviews numerous studies to assess potential adverse outcomes from exposure to chemicals. Collectively, these studies include acute, subchronic and chronic toxicity, including assessments of carcinogenicity, neurotoxicity, developmental, reproductive, and general or systemic toxicity. These studies include endpoints which may be susceptible to endocrine influence, including effects on endocrine target organ histopathology, organ weights, estrus cyclicity, sexual maturation, fertility, pregnancy rates, reproductive loss, and sex ratios in offspring. For ecological hazard assessments, EPA evaluates acute tests and chronic studies that assess growth, developmental and reproductive effects in different taxonomic groups. As part of its reregistration decision for TCVP, EPA reviewed these data and selected the most sensitive endpoints for relevant risk assessment scenarios from the existing hazard database. However, as required by FFDCA section 408(p), TCVP is subject to the endocrine screening part of the Endocrine Disruptor Screening Program (EDSP).

EPA has developed the EDSP to determine whether certain substances (including pesticide active and other ingredients) may have an effect in humans or wildlife similar to an effect produced by a "naturally occurring estrogen, or other such endocrine effects as the Administrator may designate." The EDSP employs a two-tiered approach to making the statutorily required determinations. Tier 1 consists of a battery of 11 screening assays to identify the potential of a chemical substance to interact with the estrogen, androgen, or thyroid (E, A, or T) hormonal systems. Chemicals that go through Tier 1 screening and are found to have the potential to interact with E, A, or T hormonal systems will proceed to the next stage of the EDSP where EPA will determine which, if any, of the Tier 2 tests are necessary based on the available data. Tier 2 testing is designed to identify any adverse endocrine-related effects caused by the substance, and establish a dose-response relationship between the dose and the E, A, or T effect.

Under FFDCA section 408(p), the agency must screen all pesticide chemicals. Between October 2009 and February 2010, EPA issued test orders/data call-ins for the first group of 67 chemicals, which contains 58 pesticide active ingredients and 9 inert ingredients. A second list of chemicals identified for EDSP screening was published on June 14, 2013[9] and includes some pesticides scheduled for registration review and chemicals found in water. Neither of these lists should be construed as a list of known or likely endocrine disruptors. TCVP is on List 1 for which EPA has received all the required Tier 1 assay data. The agency has reviewed all of the assay data received for the appropriate List 1 chemicals and the conclusions of those reviews are available in the chemical-specific public dockets (http://www2.epa.gov/sites/production/files/2015-06/documents/tetrachlorvinphos-083701_2015-06-29_txr0057147.pdf). For further information on the status of the EDSP, the policies and procedures, the lists of chemicals, future lists, the test guidelines and the Tier 1 screening battery, please visit our website[10].

[9] See http://www.regulations.gov/#!documentDetail;D=EPA-HQ-OPPT-2009-0477-0074 for the final second list of chemicals.

[10] http://www.epa.gov/endo/

5.0 Dietary Exposure and Risk Assessment

5.1 Metabolite/Degradate Residue Profile

5.1.1 Summary of Plant and Animal Metabolism Studies

Residue Chemistry Memo: DP# 243528, 3/11/98, D. Miller
Residue Chemistry Memo: DP# 206721, 9/21/94, D. Miller (Addendum to RED)
Residue Chemistry Chapter to Tetrachlorvinphos RED (DP# 199644, 7/6/94, F. Suhre)
Residue Chemistry Memo: J. Abbotts, No DP#, 4/93, Results of Metabolism Committee Meeting

There are no registrations or tolerances for plant commodities, so plant metabolism studies are not required for TCVP. The qualitative nature of the residue in ruminants following oral or dermal dosing, and in poultry following dermal application, is adequately understood based on previously submitted studies. The HED Metabolism Committee (9/8/93 Meeting) has determined that the residues of concern for tolerance enforcement and for risk assessment for carcinogenicity are the parent compound and four metabolites: tetrachlorvinphos, des-O-methyl tetrachlorvinphos, 1-(2,4,5-trichlorophenyl)ethanol (free and conjugated forms), 2,4,5-trichloroacetophenone, and 1-(2,4,5-trichlorophenyl)ethanediol. For the non-cancer risk assessment for cholinesterase inhibition, tetrachlorvinphos is the only residue of concern.

5.1.2 Summary of Environmental Degradation

Drinking Water Assessment Memo (EFED): DP# 419448, 11/6/14, C. Peck

TCVP is moderately mobile in soil and not stable in terrestrial or aquatic environments. The TCVP degradates appear to be as mobile, and in most cases more mobile, than the parent. TCVP is soluble in water at up to 11.6 mg/L, and is not expected to volatilize significantly due to a low vapor pressure of 2.6×10^{-7} torr (25°C). The compound is hydrophobic (Log K_{ow} of 3.53). TCVP hydrolyzes in water at a pH-dependent rate. Hydrolysis is relatively rapid in alkaline water (half-life of 10.3 days at pH 9). In neutral to acidic water (pH 5 to 7), TCVP hydrolyzes with slower half-lives of 30 to 57 days. A major degradate of hydrolysis found in the aqueous solution at pH 9 was des-O-methyl tetrachlorvinphos (28% at Day 21). Hydrolysis rates for the TCVP TRC could not be calculated, as not all degradates in the study extracts were identified; therefore, TCVP TRC was considered stable to hydrolysis. Photolysis studies of TCVP have not been submitted (not required for residential outdoor use).

TCVP isomer mixture (50:50, Z:E) readily biodegraded in aerobic soils, with a half-life of approximately 9 days. However, the rate of biodegradation for the mixed isomer of the parent TCVP was slightly reduced as concentrations decreased, which may indicate that one isomer degrades more rapidly than the other. Major soil degradates include TCPEol, TCCEol, TCPEone and TCBA. The TCVP TRC that were identified in the aerobic soils biodegraded with half-lives of from 53 to 200 days.

5.1.3 Comparison of Metabolic Pathways

Metabolism in ruminants (dermal and oral administration; tissue), poultry (oral; tissue) and rats (oral; excreta) is similar, generally resulting in parent TCVP and the four metabolites of concern (TCVPdeme, TCPEdiol, TCPEone and TCPEol). However, the metabolite TCPEone was not

found in detectable levels in the rat metabolism study and the metabolite TCPEdiol was not detected in the goat studies. Unchanged parent TCVP was found in the goat dermal study, but was not detected in the goat oral study.

5.1.4 Residues of Concern Summary and Rationale

The HED Metabolism Committee (9/8/93 Meeting) has determined that the total residues of concern (TRC) for carcinogenicity are the parent compound tetrachlorvinphos and metabolites which, like tetrachlorvinphos, contain the 2,4,5 trichlorobenzene ring. For livestock commodities, the total residues of concern for carcinogenicity are tetrachlorvinphos [TCVP] plus the following four metabolites: des-O-methyl tetrachlorvinphos [TCVPdeme]; 1-(2,4,5-trichlorophenyl)ethanol (free and conjugated forms) [TCPEol]; 2,4,5-trichloroacetophenone [TCPEone]; and 1-(2,4,5-trichlorophenyl)ethanediol [TCPEdiol]. For drinking water carcinogenicity assessment, the total residues of concern include the four aforementioned metabolites for livestock plus 2 additional degradates: l-(2,4,5-trichlorophenyl)-2-chloroethanol [TCCEol], and 2,4,5-trichlorobenzoic acid [TCBA].

For the non-cancer risk assessment for cholinesterase inhibition, TCVP is the only residue of concern. For tolerance enforcement the residues of concern include TCVP plus, TCVPdeme, TCPEdiol, TCPEone and TCPEol.

See Appendix D for a table of parent and metabolite structures and chemical properties.

Table 5.1.4 Summary of Metabolites and Degradates to be included in the Risk Assessment and Tolerance Expression

Matrix		**Residues included in Risk Assessment (Cholinesterase Inhibition)**	**Residues included in Risk Assessment (Carcinogenicity)**	**Residues included in Tolerance Expression**
Plants	Primary Crop	NA	NA	NA
	Rotational Crop	NA	NA	NA
Livestock	Ruminant	TCVP	TCVP, TCVPdeme, TCPEdiol, TCPEone and TCPEol	TCVP, TCVPdeme, TCPEdiol, TCPEone and TCPEol
	Poultry	TCVP	TCVP, TCVPdeme, TCPEdiol, TCPEone and TCPEol	TCVP, TCVPdeme, TCPEdiol, TCPEone and TCPEol
Drinking Water		TCVP	TCVP, TCVPdeme, TCPEdiol, TCPEone and TCPEol, TCCEol, TCBA	NA

NA= not applicable
TCVP= tetrachlorvinphos
TCVPdeme,= des-O-methyl tetrachlorvinphos
TCPEol= 1-(2,4,5-trichlorophenyl)ethanol (free and conjugated forms)
TCPEone= 2,4,5-trichloroacetophenone
TCPEdiol= 1-(2,4,5-trichlorophenyl)ethanediol
TCCEol =l-(2,4,5-trichlorophenyl)-2-chloroethanol

TCBA =2,4,5-Trichlorobenzoic acid

5.2 Residue Chemistry and Food Residue Profile

Residue Chemistry Memo: DP# 243528, 3/11/98, D. Miller
Dietary Assessment Memo: DP#426985, 10/29/15, D.Drew

Residue Chemistry

Tolerances are established for residues of TCVP in animal commodities since residues may occur in milk, eggs, meat, fat, or meat byproducts as a result of the registered uses on livestock (oral and dermal uses) and around livestock premises. There are no registered uses on plant (including feedstuffs) commodities. This section provides the background and current status of residue chemistry requirements for TCVP and includes residue data submitted and reviewed since the 1994 Residue Chemistry Chapter of the TCVP RED and the 2006 TCVP RED.

The 1994 Residue Chemistry Chapter cited the need for the following magnitude of the residue studies: *New magnitude of the residue studies reflecting oral and dermal exposure of beef cattle, dairy cattle, and hogs, and dermal exposure of poultry to tetrachlorvinphos are required. All residues of concern should be analyzed in cattle, hogs, and poultry using validated analytical methods.*

Subsequent to the TCVP RED, in 2007, residue studies on cattle (dermal and oral treatments; MRID 47193001) and poultry (dermal treatment; MRID 47193001) were submitted, as was a companion storage stability study (MRID 47193001) and a residue analytical method (MRID 47369201). Those studies were reviewed under DP #s D320848, D320858, D320859, and D381350 (C. Olinger, 10/7/10, *Tetrachlorvinphos. Cattle Oral/Dermal and Poultry Dermal Studies. Summary of Residue Data Submitted in Support of Reregistration*). The submitted magnitude of the residue studies on cattle and poultry were determined to be inadequate, but upgradeable pending submission of supporting storage stability data. The companion storage stability study was determined to be unacceptable because of study design. Additional information was also requested regarding the maximum storage duration of all samples collected from both the cattle and poultry studies. In 2011, additional information (MRIDs 486378101 and 48319001) pertaining to the storage stability deficiencies was submitted and reviewed (C. Olinger, 3/25/11, D385359 and D386954, *Tetrachlorvinphos. Response to Comment on Storage Stability Residue Data Deficiencies)*. The poultry and cattle residue data (860.1480) deficiencies are now fulfilled and no further data are being required.

In response to the data requirement for a residue study in hogs, a waiver request was submitted and granted in 2011 (C. Olinger, 4/25/11, D320857, *Tetrachlorvinphos. Request for Waiver of a Swine Magnitude of Residue Study).* It was determined that TCVP residues in swine tissues are not likely to be higher than the residues in ruminants and that ruminant data may be translated to swine. The conclusion was based on the poor oral and dermal absorption of TCVP in livestock and the fact that residence time in swine intestines is significantly shorter relative to that in a ruminant. No additional residue data (860.1480) on hogs are being required.

In response to a TCVP Generic Data Call-In (GDCI) issued 12/29/09, data were submitted evaluating TCVP metabolites using the FDA Multiresidue Methods Test guidelines in Pesticide Analytical Manual (PAM) Vol. I (MRID 48655201) and were reviewed 7/5/12 (D. Drew,

D396833, *Tetrachlorvinphos (TCVP). Multiresidue Methods (MRM) Study of the Metabolites of TCVP*). The data requirement for MRM testing (860.1360) has been fulfilled.

The registrant submitted a proposed method SCR/006 for tolerance enforcement of livestock commodities that includes detection of TCVP and the metabolites TCVPdeme, TCPEol, TCPEone and TCPEdiol (MRID 47369201, 2007). The HED review (D320848, D320858, D320859, and D381350) determined that the method was adequate, but that an independent laboratory validation (ILV) trial remained outstanding. A Generic Data Call-In (GDCI) for an ILV was originally issued December 29, 2009. A different proposed method (Method 14020.6106) and an associated ILV study (Method 14020.6107) were subsequently submitted to the agency (MRID 49419301, 2015). Because the proposed Method 14020.6106 monitors only a single ion transition for each analyte, alternative confirmatory procedures are necessary; the previously submitted method SCR/006 (MRID 47369201) is considered acceptable as a confirmatory method. The analytical method test data for 14020.6106 are classified as scientifically acceptable for use as an analytical method for ruminant and poultry commodities.

Food Residue Profile
The available magnitude of the residue study for dairy cattle reflect a combination of two treatments: oral administration of tetrachlorvinphos for 29-31 days at actual rates of 1.512-1.555 and 4.630 g ai/750 kg BW per day (6.3-6.5x and 19.3x, respectively, the maximum registered rate of 0.24 g ai/750 kg BW for feed-through treatment) and dermal spray treatments on three occasions, at ~14 day intervals, at actual rates of 10.111 and 19.166-19.493 g ai per animal per dose (~0.5 and 1.0x, respectively, the maximum registered rate of 18.9 g ai/animal for direct animal spray treatment). At the combined treatment regime (6.5x dermal spray plus 1x oral treatment), the maximum total residues of concern (with the maximum residues of the parent in parentheses) were: 0.072 (0.036) ppm for milk, 0.078 (<0.01) ppm for cream, 0.158 (<0.01) ppm for liver, 0.278 (0.015) ppm for kidney, 0.272 (0.212) ppm for muscle, 0.842 (0.558) ppm for subcutaneous fat, and 0.747 (0.340) ppm for peritoneal fat.

The available magnitude of the residue study for poultry reflects 6-7 dermal spray treatments of laying hens with an EC formulation, made at two-week retreatment intervals, at 0.0908, 0.1816, or 0.5448 g ai/hen/application. These application rates, respectively, correspond to ~0.5x, 1.0x, or 2.9x the maximum registered direct spray treatment rate of 0.19 g ai/bird daily. At ~1.0x, the maximum total residues of concern (with the maximum residues of the parent in parentheses) were: 0.288 (0.026) ppm for egg, 0.517 (0.016) ppm for liver, 0.583 (0.022) ppm for kidney, 0.396 (0.082) ppm for muscle, 19.405 (6.030) ppm for skin with fat, and 1.298 (0.099) ppm for abdominal fat.

There were no detectable residues of parent TCVP in the most recent USDA PDP monitoring data for beef meat, liver, or fat, or for milk and cream; nor were there detectable residues in pork fat. There were no detectable residues in chicken meat or liver. There was one detectable residue in egg just above the method limit of detection (LOD; 742 samples). PDP did not analyze chicken fat or skin for TCVP. The TCVP metabolites of concern for cancer assessment were not measured by PDP.

5.3 Water Residue Profile

Drinking Water Assessment Memo (EFED): DP# 419448, 11/6/14, C. Peck

The Surface Water Concentration Calculator (SWCC) computer model was used to generate surface water Estimated Drinking Water Concentrations (EDWCs) for use in the human health dietary risk assessment, while the PRZM-GW and SCI-GROW models were used to generate groundwater EDWCs. The residues of concern for acute and steady state dietary exposure included cholinesterase-inhibiting compounds, which were determined to be TCVP parent only. For carcinogenicity, (total) residues of concern (TRC) included TCVP and the following metabolites which, like TCVP, contain the 2,4,5 trichlorobenzene ring: des-O-methyl tetrachlorvinphos,1-(2,4,5-trichlorophenyl)ethanediol, TCPEol (1-(2,4,5-trichlorophenyl)ethanol), TCPEone (2,4,5-trichloroacetophenone), TCCEol (l-(2,4,5-trichlorophenyl)-2-chloroethanol), and TCBA (2,4,5-trichlorobenzoic acid).

Maximum EDWCs (based on maximum labeled usage for kennels, poultry droppings, garbage and manure piles, and corrals) for TCVP residues in surface water and groundwater for dietary assessment are presented in Table 5.3. Daily time series outputs for the thirty year simulation were also provided to HED for use in dietary exposure modeling.

This dietary assessment used the maximum total residues of concern (TRC) EDWC of 22.4 ug/L for the cancer analysis, input as a single point estimate. For the acute analysis, the conservative highest acute EDWC of 4.03 ug/L (TCVP only) was used as a single point estimate. For the steady state analysis, the entire distribution of 21-day averages from a thirty year simulation was used.

Table 5.3 Summary of Estimated Surface Water and Groundwater Concentrations for Tetrachlorvinphos

DRINKING WATER SOURCE (MODEL USED)	MAXIMUM ESTIMATED DRINKING WATER CONCENTRATION (EDWC)	
	Acute (µg/L) (TCVP only)	Cancer (µg/L) (TRC)
Surface water (SWCC)	**4.03**	4.11
Groundwater (PRZM-GW)	8.54×10^{-5}	**22.4**
Groundwater (SCI-GROW)	5.61×10^{-3}	7.36×10^{-2}

* EDWCs based on maximum labeled usage for kennels, poultry droppings, garbage and manure piles, and corrals.

5.4 Dietary Risk Assessment

5.4.1 Description of Residue Data Used in Dietary Assessment

HED has conducted acute, steady state, and cancer dietary (food and drinking water) exposure and risk assessments using DEEM version 3.16 for TCVP. OPs exhibit a phenomenon known as steady state AChE inhibition. After repeated dosing at the same dose level, the degree of inhibition comes into equilibrium with the production of new, uninhibited enzyme. OP AChE studies of 2-3 weeks generally show the same degree of inhibition as those of longer duration (*i.e.*, up to 2 years of exposure). Therefore, a steady state assessment based on 21 days of exposure may be conducted in place of the traditional chronic assessment.

For steady state dietary assessments for OP pesticides, the DEEM acute module may be used to conduct two-day average assessments which uses two-day average food and water consumptions along with the steady state POD. These two-day average assessments provide an estimate of 21-day (steady state) average daily food and drinking water exposures. For the two-day average assessments, using a 21-day forward-rolling average water distribution file provides an accurate overall estimate of the 21-day ("steady-state") average daily exposures at the per-capita 95th percentile for drinking water, to the extent that predicted drinking water concentrations for any 21-day duration is known for any given year. For food alone, the two-day average assessments reflect an average daily exposure for a two-day exposure duration rather than a 21-day exposure duration. Since the DEEM two-day average assessment does not capture day to day variation in food residues, it will generally result in higher food-only exposure estimates than a model that calculates 21-day rolling averages for food. Although the DEEM two-day average assessment for TCVP may result in higher exposure estimates for both water and food than would a 21-day average model, the assessment provides an acceptable estimate of steady state exposure for food and drinking water for use in risk assessment and will not underestimate the risk.

TCVP dietary risk assessments were performed for the following population groups: the general U.S. population, all infants (<1 year old), children 1-2, children 3-5, children 6-12, youth 13-19, adults 20-49, females 13-49, and adults 50-99 years old. The lifestage relevant to TCVP cancer assessment is adults and the reported population for the cancer dietary assessment is the general U.S. population.

The dietary exposure analyses for TCVP are refined. The only food forms included in the analyses are based on animal commodities. The food residues were based upon U. S. Department of Agriculture's Pesticide Data Program (USDA PDP) monitoring data except in a couple of instances where no appropriate PDP data were available (i.e., high-end residues from poultry dermal studies were used for poultry fat and poultry skin). The Biological and Economic Analysis Division (BEAD) of OPP provided percent livestock treated information. Model-derived estimated drinking water concentrations (EDWCs) were provided by the Environmental Fate and Effect Division (EFED). EDWCs were based on spot applications to kennels, poultry droppings, garbage and manure piles, and corrals and were directly incorporated into the assessments as described in Section 5.3 above.

Since the PDP only analyzed for residues of TCVP (and not for TCVP metabolites) a factor was applied to the PDP residues in order to account for all the metabolites of concern for the cancer assessment. The factor was calculated by determining the ratio of parent TCVP to total residues of concern in the livestock residue studies (see Table 2, D426985).

5.4.2 Percent Crop Treated Used in Dietary Assessment

For the acute and steady state analyses, the maximum estimated percent livestock treated of 3% was used for cattle and swine and the estimated maximum of 11% was used for poultry.

For the cancer analysis, the following estimated average percent livestock treated was used: 1% for dairy cattle, 2% for beef cattle and swine, and 6% for poultry.

5.4.3 Acute Dietary Risk Assessment

The acute dietary risk estimates are below HED's level of concern (<100 % of the acute population adjusted dose (aPAD)) for all population subgroups. Combined dietary exposure from food and drinking water at the 99.9th percentile of exposure is 73% of the aPAD for children (3-5 years old), the most highly exposed population subgroup (Table 5.4.3 below). Acute exposures to TCVP from food consumption are higher than those from drinking water. Most of the exposure from food is due to the high-end residue on chicken skin from poultry dermal studies (residue on uncooked chicken skin from direct dermal spray applications at maximum labeled rates with a 0-day pre-slaughter interval).

Table 5.4.3. Results of Acute Dietary Exposure Analysis for TCVP Food only, Drinking Water only, and Food plus Drinking Water

Population Subgroup	aPAD (mg/kg/day)[1]	Food only		Drinking Water only		Food plus Drinking Water	
		99.9th Percentile		99.9th Percentile		99.9th Percentile	
		Exposure (mg/kg/day)	% aPAD	Exposure (mg/kg/day)	% aPAD	Exposure (mg/kg/day)	% aPAD
General U.S. Population	0.008	0.002873	36	0.000688	8.6	0.002954	37
All Infants (<1 year old)	0.008	0.002749	34	0.001366	17	0.003017	38
Children 1-2 years old	0.008	0.004902	61	0.001257	16	0.004896	61
Children 3-5 years old	0.008	0.005585	70	0.000676	8.4	**0.005841**	**73**
Children 6-12 years old	0.008	0.004134	52	0.000531	6.6	0.004260	53
Youth 13-19 years old	0.008	0.003378	42	0.000455	5.7	0.003412	43
Adults 20-49 years old	0.008	0.002657	33	0.000468	5.8	0.002777	35
Females 13-49 years old	0.008	0.002348	29	0.000452	5.6	0.002416	30
Adults 50-99 years old	0.08	0.001749	2.2	0.000460	<1	0.001826	2.3

*Population with the greatest exposure is in bold.

5.4.4 Steady State Dietary Risk Assessment

The steady state dietary exposure estimates are below HED's level of concern (<100% of the steady state population adjusted dose (ssPAD)) for all population subgroups. Combined dietary exposure from food and drinking water at the 99.9th percentile of exposure is 43% of the ssPAD for children (3-5 years old), the most highly exposed population subgroup (Table 5.4.4 below). Steady state exposures to TCVP from food consumption are higher than those from drinking water. Most of the exposure from food is due to the high-end residue on chicken skin from poultry dermal studies.

Table 5.4.4. Results of Steady State Dietary Exposure Analysis for TCVP Food only, Drinking Water only, and Food plus Drinking Water							
Population Subgroup	ssPAD (mg/kg/day)[1]	Food only		Drinking Water only		Food plus Drinking Water	
		99.9th Percentile		99.9th Percentile		99.9th Percentile	
		Exposure (mg/kg/day)	% ssPAD	Exposure (mg/kg/day)	% ssPAD	Exposure (mg/kg/day)	% ssPAD
General U.S. Population	0.008	0.002041	26	0.000096	1.2	0.002046	26
All Infants (<1 year old)	0.008	0.001850	23	0.000300	3.8	0.001875	23
Children 1-2 years old	0.008	0.003242	40	0.000143	1.8	0.003274	41
Children 3-5 years old	0.008	0.003468	43	0.000114	1.4	**0.003459**	**43**
Children 6-12 years old	0.008	0.003020	38	0.000085	1.1	0.003005	38
Youth 13-19 years old	0.008	0.002170	27	0.000075	1.0	0.002188	27
Adults 20-49 years old	0.008	0.001983	25	0.000094	1.2	0.001989	25
Females 13-49 years old	0.008	0.001571	20	0.000095	1.2	0.001557	19
Adults 50-99 years old	0.08	0.001128	1.4	0.000087	<1	0.001132	1.4

*Population with the greatest exposure is in bold.

5.4.5 Cancer Dietary Risk Assessment

The estimated cancer dietary (food and drinking water) exposure of the general U.S. population to TCVP and its metabolites containing the 2,4,5 trichlorobenzene moiety is 0.000566 mg/kg/day. Applying the Q_1* of 0.00183 $(mg/kg/day)^{-1}$ to the exposure value results in a cancer risk estimate of 1×10^{-6} (Table 5.4.5 below). Drinking water is the major contributor to the cancer dietary exposure.

Table 5.4.5. Results of Cancer Dietary Exposure Analysis for TCVP and Metabolites for Food only, Drinking Water only, and Food plus Drinking Water							
Population Subgroup	Q* $(mg/kg/day)^{-1}$	Food only		Drinking Water only		Food plus Drinking Water	
		Exposure (mg/kg/day)	Risk	Exposure (mg/kg/day)	Risk	Exposure (mg/kg/day)	Risk
General U.S. Population (Adults)	0.00183	0.000097	2×10^{-7}	0.000469	9×10^{-7}	0.000566	1×10^{-6}

5.4.6 Summary of Dietary (Food and Drinking water) Exposure and Risk Assessment

Table 5.4.6. Summary of Dietary (Food and Drinking Water) Exposure and Risk for Tetrachlorvinphos						
Population Subgroup[1]	**Acute Dietary (99.9th Percentile)**		**Steady State (99.9th Percentile)**		**Cancer**	
	Dietary Exposure (mg/kg/day)	**% aPAD**	**Dietary Exposure (mg/kg/day)**	**% ssPAD**	**Dietary Exposure (mg/kg/day)**	**Risk**
General U.S. Population	0.002954	37	0.002046	26	0.000566	1×10^{-6}
All Infants (<1 year old)	0.003017	38	0.001875	23	NA	
Children 1-2 years old	0.004896	61	0.003274	41		
Children 3-5 years old	**0.005841**	**73**	**0.003459**	**43**		
Children 6-12 years old	0.004260	53	0.003005	38		
Youth 13-19 years old	0.003412	43	0.002188	27		
Adults 20-49 years old	0.002777	35	0.001989	25		
Females 13-49 years old	0.002416	30	0.001557	19		
Adults 50-99 years old	0.001826	2.3	0.001132	1.4		

*Population with the greatest exposure is in bold.

6.0 Residential and Non-Occupational Exposure/Risk Characterization

Occupational and Residential Exposure Memo: D426984, 12/21/15, W. Britton.

Residential exposures (handler and post-application) are anticipated from the use of TCVP pet products for dogs and cats (collars, dusts/powders, and pump/trigger sprays). Exposures are expected for adults who apply TCVP products to their pets and from post-application exposures for adults and children who may contact previously treated pets.

Updates to the Residential Assessment: The most recent residential risk assessment for TCVP was completed in November 2014 (W. Britton, 11/05/14, D420283). The current TCVP human health risk assessment takes into account, where appropriate, comments from NRDC in their August 5, 2015 Opening Brief to the U.S. Court of Appeals of the 9th Circuit, which was filed as a result of the 2014 residential assessment and EPA's subsequent denial of the NRDC petition to cancel all TCVP pet products. The current assessment also reflects the following changes from the 2014 residential assessment:

- LOCs for incidental oral and inhalation exposures have been revised to reflect inclusion of the 10X FQPA safety factor.
- There is no non-cancer dermal hazard for TCVP.
- A female-specific body weight, 69 kg, is used for assessment of adult exposures instead of the average adult body weight of 80 kg (more detailed information provided below).
- Use of newer pet residue transfer data for pet collars that result in more conservative estimates of residue transfer/exposure than the data used in the 2014 risk assessment.

Residential assessments are performed using data from two recently submitted pet collar residue transfer studies (the amitraz study and the Davis study; more detailed information provided below).

- The exposures to TCVP pet collar products are assessed assuming collars may be a liquid formulation or a dust formulation (more detailed information provided below).

Body Weight Assumptions: For adults, when an endpoint is not sex-specific (i.e., the endpoints are based on developmental or fetal effects) a body weight of 80 kg is typically used in risk assessment. However, for the OP chemical class, a female-specific body weight of 69 kg is now assumed for adults. While the endpoint of concern, RBC AChE inhibition, is not sex-specific, the female body weight is used in the TCVP residential assessments, as for the other OP assessments, for adults due to concerns for potentially pregnant women. A body weight of 11 kg was assumed for children (1 to < 2 years old). The lifestages selected for each residential scenario (i.e., adults (female body weight) and children 1 to < 2 years old) are health protective for the exposures and risk estimates for any other potentially exposed lifestage.

Residue Data Assumptions: Several sources of data were used in the current residential assessment. Similar to the 2014 assessment, these include the 2012 Residential SOPs (Treated Pets), a TCVP dust/powder applicator exposure study (MRID 45519601), and a TCVP dust and pump spray study (MRID 45485501). For assessment of post-application exposure to pet collars, different pet fur residue transfer studies have been used in the current assessment compared to the 2014 assessment. In the 2014 assessment, a propoxur pet collar study (MRID 448589901) was used; however, in the current assessment, both an amitraz pet collar residue transfer study (MRID 49468801), and a literature study using TCVP pet collars (the Davis study)[11] were used. These studies have been chosen for use in the current risk assessment as they provide higher estimates of residue transfer resulting in a more conservative exposure assessment.

Exposure/risk estimates are provided using residue transfer data from both the amitraz and Davis pet collar studies since the Davis has yet to undergo review by the HSRB. The EPA intends to present the Davis study at the next meeting of the HSRB, which is scheduled for January 12-13, 2016. If the HSRB concludes that the Davis study does not constitute a human study and is scientifically valid, then EPA can rely on these data for regulatory risk decision making. Alternatively, if HSRB concludes the Davis study constitutes a human study, then under 40 CFR §26.1706, OPP is required to provide an opportunity for public comment and publish a full explanation of its decision to rely on the otherwise unacceptable data, including a thorough review of the ethical deficiencies of the underlying research and the full rationale for finding that reliance on the data is crucial to imposing a more stringent regulatory restriction. Until such time that these data have undergone HSRB review, post-application risk estimates for exposures to pet collar treated pets are to be considered preliminary and are presented for purposes of comparison only.

[11] Davis, M. et. al., Assessing Intermittent Pesticide Exposure from Flea Control Collars Containing the Organophosphorus Insecticide Tetrachlorvinphos. Journal of Exposure Science and Environmental Epidemiology. (2008) 18, 564-57)

EPA has conducted an ethics and science review of the Davis study. The OPP-internal review of the applicable human ethical standards (as outlined in 40 CFR Part 26, Subpart Q) has been conducted and concluded that "there is no clear or convincing evidence that the conduct of the Davis study was fundamentally unethical; that is, the research was not intended to harm the participants and did not fail to obtain informed consent. Similarly, the conduct of the study was not deficient relative to the ethical standards prevailing at the time the research was conducted; the studies did not place participants at increased risk of harm (based on knowledge available at the time the study was conducted) or impair their informed consent." [12] The ethics review also states that, "OPP wishes to rely on the TCVP glove residue data generated. The data may be crucial to a potential EPA decision to improve public health protection by imposing a more stringent regulatory restriction than could be justified without the data. If EPA proceeds under §26.1706, EPA needs to obtain the views of the Human Studies Review Board, provide an opportunity for public comment, and publish a full explanation of its decision to rely on the data, including a thorough discussion of the ethical deficiencies of the underlying research and the full rationale for finding that EPA met the standard in 40 CFR §26.1706 (c) (i.e., that the research is essential to a more stringent regulatory action to improve protection of public health)."

The OPP-internal science review for the Davis study[13] has concluded that the methods used for conduct of the collection of transferable TCVP residues from petting/rubbing of the dogs treated with TCVP pet collars are scientifically valid. In addition to the transferable residue data, the Davis study also includes 1) plasma cholinesterase (ChE) from treated dogs 2) T-shirt samples collected from children exposed to TCVP treated dogs and 3) urinary biomonitoring for adults and children exposure to TCVP treated dogs. For purposes of the TCVP risk assessment, EPA may rely only on the transferable residue data as these are the only data from the study that result in the potential for greater risks, are applicable to human exposures (in the case of the dog plasma ChE measures), or in the case of the urinary biomonitoring data, are useful given current scientific limitations (i.e., a physiologically based pharmacokinetic (PBPK) model applicable to TCVP).

Table 6.1 below provides a summary of the studies considered for the residue transfer input.

Table 6.1. Summary of Pet Collar Residue Transfer Studies and Assumptions for use in TCVP Residential Assessment

Residue Transfer Study	Used in Current Risk Assessment	Methodology	Non-Cancer Residue Transfer Assumption	Cancer Residue Transfer Assumption
Propoxur pet collar[1]	No (used in 2014)	Twenty petting simulations to treated dogs. Each simulation consisted of three strokes (60 strokes total) conducted using a mannequin hand fitted with cotton gloves over top of a nitrile glove	0.072% (mean Day 0)	0.013% (mean over 28 days)
Amitraz pet collar[2]	Yes		0.14% (mean Day 0)	0.047% (mean over 28 days)
Davis pet collar[3]	Yes	Dogs were petted by volunteers continuously for a 5 minute period with use of cotton glove in	0.40% (mean Day 12)	0.3% (mean over 112 days)

[12] M. Lydon. Ethics Review of Davis et al Research on Flea Collars with TCVP. 12/15/2015.
[13] W. Britton. Science Review of "Davis et al., 2008. Assessing Intermittent Pesticide Exposure from Flea Control Collars Containing the Organophosphorus Insecticide Tetrachlorvinphos" for HSRB Consideration. D430707. 12/16/2015.

Table 6.1. Summary of Pet Collar Residue Transfer Studies and Assumptions for use in TCVP Residential Assessment				
Residue Transfer Study	**Used in Current Risk Assessment**	**Methodology**	**Non-Cancer Residue Transfer Assumption**	**Cancer Residue Transfer Assumption**
		following with a defined rubbing protocol		

1. MRID 448589901: Determination of Transferable Residues of Propoxur from the Hair of Dogs Wearing collars Impregnated with Propoxur – Final Report.
2. MRID 49468801: Determination of Transferable Residues of Amitraz from the Hair of Dogs Following the Application of the Preventic® Collar.
3. Davis, M. et. al., Assessing Intermittent Pesticide Exposure from Flea Control Collars Containing the Organophosphorus Insecticide Tetrachlorvinphos. Journal of Exposure Science and Environmental Epidemiology. (2008) 18, 564-57*)*

Pet Collar Formulation Assumptions: Per the 2012 Residential SOPs, Treated Pets, pet collar products have been categorized as a liquid formulation. This assertion was based on research conducted at the time of SOP development that supported that pet collars function by means of diffusion, transferring from the collar to the surrounding area. More specifically, the active ingredient, which is embedded in the collar matrix, diffuses slowly through the matrix, thus controlling the amount of the active ingredient at the collar's surface. The active ingredient available on the surface of the pet collar then "rubs off" or transfers from the collar to the animal's hair coat via embedded lubricants which function like transfer agents at the surface of the collar. However, the NRDC asserts that TCVP pet collars are a solid formulation since a TCVP collar product (EPA Reg. No. 2596-84) states that "as the collar begins to work, a fine white powder will appear on the surface." HED has confirmed this statement is present on the current labeling for the identified product and that an identical statement is also found on the following TCVP pet collar products (5 of 9 total pet collar products): EPA Reg. Nos. 2596-62, 2596-63, 2596-83, 2596-84, and 2596-139. Taking into account these label statements, and based upon further research which suggests that that some pet collars may act by extrusion of the active ingredient from the collar matrix as a fine dust, HED has reconsidered the position that the TCVP pet collars are all liquid formulated products. At this time, HED has not received confirmation from the TCVP pet product registrants regarding whether the pet collars are designed to release the active ingredient in a dust or liquid form. Because there remains uncertainty around whether the TCVP pet collars are liquid or solid formulations, the collar products are assessed here as both a liquid formulation and as a solid (dust) formulation. Until the formulation types of the registered TCVP pet collar products can be determined, any risk results or conclusions regarding exposures to the collars may be considered preliminary.

6.1 Residential Handler Exposure

HED uses the term "handlers" to describe those individuals who are involved in the pesticide application process. HED believes that there are distinct tasks related to applications and that exposures can vary depending on the specifics of each task. Residential handlers are assumed to complete all elements of an application without use of any protective equipment.

Residential handler exposures to TCVP pet products may occur via the dermal or inhalation routes while the product is placed on a cat or dog. Both non-cancer (steady state) and cancer residential handler exposure assessments were performed for adult homeowners applying TCVP pet collars, dusts/powders, and pump/trigger spray products to cats and dogs. Since there is no non-cancer dermal hazard for TCVP, the non-cancer handler assessment includes only inhalation exposures. For the cancer assessment, both dermal and inhalation exposures are

assessed.

For handlers, when assuming the TCVP pet collars are a liquid formulation, the liquid-specific unit exposure (UE) values (i.e., surrogate data from spot-on applicator study) from the 2012 Residential SOPs were used. When assuming the pet collars are a solid formulation, HED used the best available data, a TCVP dust/powder applicator exposure study (MRID 45519601).

TCVP-specific handler exposure data are not available for the dust/powder and pump/trigger spray formulations. Those handler scenarios are assessed using the 2012 Residential SOPs surrogate data.

Residential Handler Non-Cancer Exposure and Risk Estimates

The exposure data and assumptions that underlie the residential handler non-cancer risk estimates can be found in the occupational and residential exposure (ORE) memo (D426984) and the 2012 Residential SOPs. The algorithms used to estimate non-cancer exposure and dose for residential handlers can be found in Appendix D of D426984 and/or the 2012 Residential SOPs.

Summary of Residential Handler Non Cancer Exposure and Risk Estimates:

> *Dust/Powder and Pump/Trigger Spray:* All residential handler (adults) non-cancer (steady state) inhalation risks estimated for the TCVP pet dust/powder and pump/trigger spray formulations are not of concern (i.e., all MOEs are > 300; LOC=300).
>
> *Pet Collars:* Assuming that all TCVP pet collars are solid (dust) formulations, all residential handler (adults) non-cancer inhalation risks estimated are not of concern (i.e., all MOEs are > 300; LOC=300). Assuming that all TCVP pet collars are liquid formulations, the application of the collars are expected to result in negligible inhalation exposure; therefore, there are no non-cancer risks of concern for handlers applying TCVP collars as liquid formulations.

A summary of residential handler exposures and risks is presented in Appendix F.

Residential Handler Cancer Exposure and Risk Estimates

Cancer risk estimates were calculated using a linear low-dose extrapolation approach in which a Lifetime Average Daily Dose (LADD) is first calculated and then compared with a Q_1^* that has been calculated for TCVP based on dose response data in the appropriate toxicology study ($Q_1^* = 1.83 \times 10^{-3}$ $(mg/kg/day)^{-1}$). Absorbed average daily dose (ADD) levels were used as the basis for calculating the LADD values. Dermal and inhalation ADD values were first added together to obtain combined ADD values. LADD values were then calculated and compared to the Q_1^* to obtain cancer risk estimates.

The exposure data and assumptions that underlie the residential handler cancer risk estimates can be found in the ORE memo (D426984) and the 2012 Residential SOPs. The algorithms used to estimate the LADD and cancer risk for residential handlers can be found in Appendix D of D426984.

Summary of Residential Handler Cancer Exposure and Risk Estimates

Dust/Powder and Pump/Trigger Spray: Residential handler cancer risks (inhalation and dermal combined) estimated for TCVP dusts/powders range from 10^{-8} to 10^{-7}, and for pump/trigger sprays range from 10^{-9} to 10^{-8}.

Pet Collars: Residential handler cancer risks (inhalation and dermal combined) estimated for TCVP pet collars are all in the 10^{-8} range when assuming a liquid formulation and are all in the 10^{-7} range when assuming a dust formulation.

A summary of residential handler cancer exposures and risks is presented in Appendix G.

6.2 Residential Post-Application Exposure

There is the potential for post-application exposure for individuals exposed as a result of contacting a cat or dog previously treated with TCVP pet products (dusts/powders, pump/trigger sprays, pet collars). The quantitative exposure/risk assessment for residential post-application exposures is based on the following scenarios:

1) Post-application cancer dermal (adults) exposure from contacting cats and dogs treated with TCVP; and
2) Post-application non-cancer incidental oral (hand-to-mouth) exposure (children 1 to < 2 year olds) from contacting cats and dogs treated with TCVP.

Since there is no non-cancer dermal hazard for TCVP, the non-cancer post-application assessment would include only inhalation (adult and child) and incidental oral (child) exposures. However, a quantitative residential post-application inhalation exposure assessment was not performed as inhalation exposure is expected to be negligible from contact with treated pets. An inhalation exposure assessment was performed for occupational pet handlers (i.e., veterinarians, veterinary assistants, and groomers) and this exposure scenario is considered protective of any potential low-level post-application inhalation exposure that could result from these types of uses (see Section 8.0 below). For the adult cancer post-application assessment, only dermal exposures are quantitatively assessed.

Non-Cancer Post-application Assessment

Residential Non-Cancer Post-Application Exposure Data and Assumptions
A series of assumptions and exposure factors served as the basis for completing the residential cancer post-application risk assessment. More detailed information about the exposure data and assumptions that underlie the residential post-application cancer risk estimates can be found in D426984.

Residue Transfer Assumptions: Surrogate and chemical-specific residue transfer studies were used for assessment of non-cancer post-application exposures from registered TCVP pet products.

For dusts/powders and pump/trigger sprays, the maximum residue transfers of 0.048% and 0.81% respectively were used from a TCVP powder and pump spray study (MRID 45485501) was used. As described in the 2014 residential risk assessment, the TCVP powder and pump spray post-application exposure study was not conducted in a manner reflective of current standards that require a defined stroking procedure and greater number of petting simulations. In order to account for the differences between the TCVP powder and pump spray study and the currently recommended standard, the agency used the maximum observed percent residue transfer on the day of product application (Day 0) for both formulations for exposure and risk quantification. Typically, the agency assesses post-application risk with use of the mean percent residue transfer measured on Day 0; the use of the maximum value results in a more health protective risk assessment. Even though the post-application exposure study methods have evolved, the TCVP study employed a rigorous collection method and is not anticipated to underestimate exposure.

For pet collars, in conjunction with the 2012 SOPs, data from the amitraz study and the Davis study were used (see Table 6.1). For the non-cancer post-application assessment of TCVP collars, the mean residue transfers of 0.14% (amitraz study; day 0 mean) and 0.40% (Davis study; 12 day mean) were used. Typically, Day 0 residue transfer values are used for the assessment of risks occurring over short- or intermediate-term, or steady state durations; however, the Davis study presents only a 12 day mean transferable residue value. Until the Davis study has undergone HSRB review, post-application risk estimates for exposure to pet collar treated pets are considered to be preliminary. A full description of the amitraz and Davis studies can be found in Section 5.3 of the ORE memo (D426984). The non-cancer and cancer post-application assessments for the pet collars were performed assuming pet collars could be either a liquid or solid formulation, and using residue transfer data from the two available studies (the amitraz study and the Davis study).

Residential Non-Cancer Post-application Exposure and Risk Equations

The algorithms used to estimate non-cancer exposure and dose for residential post-application can be found in Appendix D of D426984 and the 2012 Residential SOPs.

Summary of Residential Post-Application Non-Cancer Exposure and Risk Estimates

Since there is no non-cancer dermal hazard for TCVP and post-application inhalation exposures to treated pets are negligible, a quantitative non-cancer post-application exposure assessment was not performed for adults; there are no residential non-cancer risk estimates of concern for adults contacting pets treated with TCVP products.

Dust/Powder and Pump/Trigger Spray: For children (child 1 to < 2 years old), residential post-application non-cancer incidental oral (hand-to-mouth) exposures to pets treated with TCVP pump/trigger sprays are not of concern (i.e., MOEs are > 1,000; LOC=1000). However, child incidental oral (hand-to-mouth) exposures to pets treated with TCVP dust/powder products are estimated to be of concern for 14 of 17 total exposure scenarios assessed (i.e., MOEs are < 1,000; LOC=1000).

Pet Collars: The post-application exposure and risk estimates for the various pet collar assumptions are provided below:

Liquid formulation/Amitraz study assumption: With use of the amitraz pet collar residue transfer study and SOP inputs specific for liquid formulation products, residential post-application child (1 to < 2 years) old incidental oral risk estimates for all TCVP pet collars are not of concern (i.e., MOEs are > 1,000; LOC=1000).

Liquid formulation/Davis study assumption: With use of the Davis study and assuming collars are liquid formulations, all but 1 of the exposure scenarios assessed, 22 of 23 total, are not of concern (EPA Reg. No. 2596-139; exposures to a small sized dog).

Solid formulation/Amitraz study assumption: With use of the amitraz pet collar study and SOP inputs specific for solid (dust) formulation products, residential post-application child (1 to < 2 years) old incidental oral risk estimates for all TCVP pet collars are of concern (i.e., MOEs are < 1,000; LOC=1000).

Solid formulation/Davis study assumption: A quantitative post-application child incidental oral assessment was not performed using the Davis study and assuming the collars are dust formulations since the mean residue transfer measured in the Davis study was greater than that in the amitraz study. MOEs would be lower using the Davis study than when using the amitraz study. When assuming the TCVP collars are solid (dust) formulations, whether the amitraz study or Davis study is used, post-application child incidental oral risk estimates for all TCVP pet collars are of concern (i.e., MOEs are < 1,000; LOC=1000).

A summary of residential post-application exposures and risks from TCVP pet products is presented in Appendix H.

Cancer Post-application Assessment

Residential Cancer Post-Application Exposure Data and Assumptions
A series of assumptions and exposure factors served as the basis for completing the residential cancer post-application risk assessment. All exposure data and assumptions that underlie the residential post-application cancer risk estimates can be found in D426984.

Residue Transfer Assumptions: For the cancer post-application assessment of TCVP dusts/powders and pump/trigger sprays, the maximum observed percent residue transfer for each day tested for calculation of cancer exposures/risks resulting in an F_{AR} of 0.022% and 0.18% for dusts/powders and pump sprays, respectively. Due to the reasons described above (under "Residential Non-Cancer Post-Application Exposure Data and Assumptions"), maximum residue values from the TCVP powder and pump spray study were used for cancer post-application assessment. For the cancer post-application assessment of TCVP collars, the mean residue transfers of 0.047% (amitraz study; 28 day mean) and 0.30% (Davis study; study 1 - 112 day mean) were used (see Table 6.1).

Residential Cancer Post-application Exposure and Risk Estimate Equations
As was done for residential handlers, cancer post-application risk estimates for adults were

calculated using a linear low-dose extrapolation approach in which a LADD is first calculated and then compared with a Q_1* that has been calculated for TCVP based on dose response data in the appropriate toxicology study (Q_1* = 1.83 x 10^{-3} $(mg/kg/day)^{-1}$). The algorithms used to estimate the LADD and cancer risk for residential post-application exposure can be found in Appendix D of D426984.

It should be noted that in the past, cancer risk assessments have assumed that children are no more sensitive than adults to carcinogens (i.e., no adjustment was made to children's exposure estimates in calculating a cumulative lifetime exposure). More recently, the agency's "Guidelines for Carcinogen Risk Assessment" (USEPA, 2005) and "Supplemental Guidance for Assessing Susceptibility from Early-Life Exposure to Carcinogens" (USEPA, 2005) proposed age-dependent adjustment factors to be applied to children's exposure. These age-dependent factors are applied only to carcinogens shown to have a mutagenic mode of action. In general, most carcinogenic pesticides have not been shown to act through a mutagenic mode of action, and thus separate assessment of children and adults is not warranted. Any pesticide found to be a carcinogen acting through a mutagenic mode of action should be dealt with on a case by case basis, and such an assessment should follow the agency's 2005 guidance. The mutagenicity database for TCVP suggests that this chemical is not mutagenic in both the gene mutation assay and primary rat hepatocyte unscheduled DNA synthesis assay and, therefore, only adult cancer risk estimates have been estimated.

Summary of Residential Post-application Cancer Exposure and Risk Estimates

Dust/Powder and Pump/Trigger Spray: Residential post-application cancer (adult only) risks estimated for TCVP pump/trigger sprays range from 10^{-7} to 10^{-6} and, for TCVP dust/powder products estimated cancer risks are 10^{-7}.

Pet Collars: Residential post-application cancer risk estimates for the TCVP pet collar formulation have also been assessed with use of the exposure data and 2012 Residential SOP inputs as described for post-application non-cancer risks. The post-application exposure and risk estimates for the various pet collar assumptions are provided below:

> *Liquid formulation/Amitraz study assumption:* With use of the amitraz pet collar residue data and SOP inputs specific for liquid formulations, estimated cancer (adult only) risks range from 10^{-7} to 10^{-6}.
>
> *Liquid formulation/Davis study assumption:* With use of the Davis study and SOP inputs specific for liquid formulations, estimated cancer risks range from 10^{-6} to 10^{-5}.
>
> *Solid formulation/Amitraz study assumption:* With use of the amitraz pet collar residue transfer data and SOP inputs specific for dust formulations, all cancer risks are estimated to be 10^{-5}.
>
> *Solid formulation/Davis study assumption:* A quantitative post-application cancer assessment was not performed using the Davis study and assuming the collars are dust formulations since the mean residue transfer measured in the Davis study was greater

than that in the amitraz study. Cancer risk estimates would be lower using the Davis study than when using the amitraz study.

Adult residential post-application dermal cancer risk estimates are presented in Appendix I.

6.3 Non-Occupational Spray Drift Exposure and Risk Estimates

A quantitative spray drift assessment was not conducted because the use of TCVP for direct animal treatment to livestock and their premises, in kennels, outdoors as a perimeter treatment, and as a flea treatment on cats and dogs are either 1) not applied via aircraft, groundboom, or airblast equipment or 2) for applications to poultry buildings with groundboom equipment, the use is indoors and not anticipated to be a significant source of significant source of spray drift.

6.4 Residential Bystander Post-Application Inhalation Exposure

A quantitative residential post-application inhalation exposure assessment was not performed as inhalation exposure is expected to be negligible from applications to pets. However, an inhalation exposure assessment was performed for handlers (i.e., veterinarians, veterinary assistants, and groomers) and this exposure scenario should be considered protective of any potential low-level post-application inhalation exposure that could result from these types of applications. There are no post-application inhalation risks of concern.

7.0 Aggregate Exposure/Risk Characterization

In accordance with the FQPA, when there are potential residential exposures to a pesticide, aggregate risk assessment must consider exposures from three major routes: oral, dermal, and inhalation. There are three sources for these types of exposures: food, drinking water, and residential uses. In an aggregate assessment, exposures from relevant sources are added together and compared to quantitative estimates of hazard (e.g., a NOAEL or PAD), or the risks themselves can be aggregated. When aggregating exposures and risks from various sources, HED considers both the route and duration of exposure.

7.1 Acute Aggregate Risk

The acute aggregate risk assessment combines exposures to TCVP from food and drinking water. There are no acute aggregate risk estimates of concern for (see Section 5.4.3 Acute Dietary Assessment).

7.2 Steady State Aggregate Risk

There is a potential for steady state exposure to TCVP via dietary and residential exposure pathways. The steady state aggregate risk assessment combines steady state exposures from food, drinking water, and residential (pet product) uses. Steady state aggregate risk assessments were performed for adult handlers (females, age 13-49 years) applying registered pet collars, dust/powders, and pump/trigger spray products to cats and dogs. Residential post-application

steady state aggregate risk assessments were also performed for children (age 1-2) contacting pets that have been treated with the collar, dust/powder, and pump/trigger spray products.

Residential Handler Noncancer Steady State Aggregate

Table 7.2.1 below shows the steady state aggregate risk estimates for the residential handler scenarios. Since there is no dermal hazard for TCVP, the residential exposure consists of only inhalation for the adult handler. An Aggregate Risk Index (ARI) approach was used to aggregate the steady state dietary and residential exposures since the levels of concern are not the same for those exposures (1000 and 300, respectively).

Residential handler steady state aggregate (food, water, residential) risk estimates for all registered TCVP pet product scenarios (collars, dust/powders, pump/trigger sprays) are not of concern (ARIs ≥ 1).

Table 7.2.1 TCVP Noncancer (Steady State) Residential Handler AGGREGATE Risk Calculations for ADULTS [1]

EPA Reg. No/Animal	Animal Size (or collar size in grams)	Residential Handler Aggregate				
		Dietary Exposure [2]		Inhalation Residential Exposure[3]		Aggregate ARI (food, water, and residential; LOC = 1)[4]
		MOE (LOC = 1000)	ARI (LOC = 1)	MOE (LOC = 300)	ARI (LOC = 1)	
Pet Collars (Liquid Assumption): 2012 Residential SOPs (Spot-on Surrogate Data)						
2596-49; Cat	11g	5,100	5.1	N/A[5]	N/A	5.1
2596-50, 62: Dog	19g	5,100	5.1	N/A	N/A	5.1
	32g	5,100	5.1	N/A	N/A	5.1
2596-83: Cat	12g	5,100	5.1	N/A	N/A	5.1
	25g	5,100	5.1	N/A	N/A	5.1
2596-139: Cat	10g	5,100	5.1	N/A	N/A	5.1
11556-164: Dog	24g	5,100	5.1	N/A	N/A	5.1
11556-165: Cat	15g	5,100	5.1	N/A	N/A	5.1
2596-84: Dog	19g	5,100	5.1	N/A	N/A	5.1
	32g	5,100	5.1	N/A	N/A	5.1
2596-139: Dog	50g	5,100	5.1	N/A	N/A	5.1
2596-63: Cat	15g	5,100	5.1	N/A	N/A	5.1
	17g	5,100	5.1	N/A	N/A	5.1
Pet Collars (Solid Assumption): TCVP Dust/Powder Applicator Study (MRID 45519601)						
2596-49; Cat	11g	5,100	5.1	4900	16	3.9
2596-50, 62: Dog	19g	5,100	5.1	2900	9.7	3.3
	32g	5,100	5.1	1700	5.7	2.7
2596-83: Cat	12g	5,100	5.1	4600	15	3.8
	25g	5,100	5.1	2200	7.3	3.0
2596-139: Cat	10g	5,100	5.1	4600	15	3.8

Table 7.2.1 TCVP Noncancer (Steady State) Residential Handler AGGREGATE Risk Calculations for ADULTS [1]						
EPA Reg. No/Animal	**Animal Size (or collar size in grams)**	**Residential Handler Aggregate**				
		Dietary Exposure [2]		**Inhalation Residential Exposure[3]**		**Aggregate ARI (food, water, and residential; LOC = 1)[4]**
		MOE (LOC = 1000)	**ARI (LOC = 1)**	**MOE (LOC = 300)**	**ARI (LOC = 1)**	
11556-164: Dog	24g	5,100	5.1	2500	8.3	3.2
11556-165: Cat	15g	5,100	5.1	3900	13	3.7
2596-84: Dog	19g	5,100	5.1	2900	9.7	3.3
	32g	5,100	5.1	1700	5.7	2.7
2596-139: Dog	50g	5,100	5.1	1100	3.7	2.1
2596-63: Cat	15g	5,100	5.1	3700	12	3.6
	17g	5,100	5.1	3300	11	3.5
Dust/Powder : TCVP Dust/Powder Applicator Study (MRID 45519601)						
4700-123: Dog	small	5,100	5.1	47,000	160	4.9
	medium	5,100	5.1	19,000	63	4.7
	large	5,100	5.1	12,000	40	4.5
47000-123: Cat	small	5,100	5.1	190,000	630	5.1
	medium	5,100	5.1	79,000	260	5.0
	large	5,100	5.1	53,000	180	5.0
2596-78: Cat	small	5,100	5.1	29,000	97	4.8
	large	5,100	5.1	17,000	57	4.7
2596-79: Dog	small	5,100	5.1	17,000	57	4.7
	medium	5,100	5.1	8,600	29	4.3
	large	5,100	5.1	6,900	23	4.2
67517-82: Dog	small	5,100	5.1	16,000	53	4.7
	medium	5,100	5.1	6,300	21	4.1
	large	5,100	5.1	3,900	13	3.7
67517-82: Cat	small	5,100	5.1	63,000	210	5.0
	medium	5,100	5.1	26,000	87	4.8
	large	5,100	5.1	18,000	60	4.7
Pump/Trigger Spray: 2012 Residential SOPs (Surrogate Data)						
2596-126,140: Cat (trigger)	small	5,100	5.1	30,000	100	4.9
	large	5,100	5.1	22,000	73	4.8
2596-140: Cat (pump)	small	5,100	5.1	150,000	500	5.0
	large	5,100	5.1	110,000	370	5.0
2596-125, -140: Dog (trigger)	small	5,100	5.1	22,000	73	4.8
	medium	5,100	5.1	19,000	63	4.7
	large	5,100	5.1	11000	37	4.5

[1] HED is concerned if the ARI is less than 1. (ARI = Aggregate Risk Index.) ARIs<1 are **Bolded**.

[2] MOE dietary = [(Steady State BMDL10)/(chronic dietary exposure)]. ARI dietary = [(MOE dietary)/(MOE target)]. BMDL10=8.0 mg/kg day; Target MOE=LOC=1000.

[3] MOE inhalation = [(Steady State HED)/(inhalation residential exposure)]. ARI inhalation = [(MOE inhalation)/(MOE target)]. HED=1.59 mg/kg/day; target MOE=LOC=300.
[4] ARI Aggregate = 1/[(1/ARI dietary) + (1/ARI oral) + (1/ARI dermal) + (1/ARI inhalation)]
[5] N/A= not applicable, negligible inhalation exposure from liquid collars.

Residential Post-Application Steady State Aggregate

Table 7.2.2 below shows the steady state aggregate risk estimates for the residential post-application scenarios for children contacting treated pets. Since there is no dermal hazard for TCVP, and post-application inhalation exposures are negligible, the residential post-application exposure consists of only incidental oral exposure for children.

Assuming liquid formulation and using the amitraz study, steady state post-application aggregate MOEs for children were not of concern (MOEs > 1000) for all 23 pet collar scenarios. Assuming liquid formulation and using the Davis study, 8 of the 23 scenarios resulted in aggregate MOEs of concern. Assuming solid formulation and using the amitraz study, all 23 scenarios resulted in aggregate MOEs of concern. Quantitative assessments were not presented assuming solid formulation and the Davis study; those MOEs would be even lower than for the solid/amitraz assessments.

For the TCVP dust/powder pet products, the steady state post-application aggregate assessments resulted in 16 of the 17 scenarios with risk estimates of concern (MOEs < 1000).

For all TCVP and pump/trigger spray product scenarios, steady state post-application aggregate risk estimates are not of concern.

Table 7.2.2 TCVP Noncancer (Steady State) Residential Post-Application AGGREGATE Risk Calculations for CHILDREN

EPA Reg. No/Animal	Animal Size	Residential Post-Application Aggregate						
		$BMDL_{10}$ mg/kg/day	LOC[1]	Max Allowable Exposure[2] mg/kg/day	Average Food and Water Exposure mg/kg/day	Residential Exposure (Incidental Oral) mg/kg/day[3]	Total Exposure mg/kg/day[4]	Aggregate MOE (food, water, and residential)[5]
Pet Collars (Liquid Assumption): Amitraz Exposure Data (MRID 49468801)								
2596-49: Cat	small	8.0	1000	0.008	0.003273	0.002	0.005273	1500
	medium	8.0	1000	0.008	0.003273	0.0012	0.004473	1800
	large	8.0	1000	0.008	0.003273	0.00074	0.004013	2000
2596-50, 62: Dog	small	8.0	1000	0.008	0.003273	0.0016	0.004873	1600
	large	8.0	1000	0.008	0.003273	0.00076	0.004033	2000
2596-83: Cat	small	8.0	1000	0.008	0.003273	0.0021	0.005373	1500
	large	8.0	1000	0.008	0.003273	0.0016	0.004873	1600
2596-139: Cat	small	8.0	1000	0.008	0.003273	0.0017	0.004973	1600
	medium	8.0	1000	0.008	0.003273	0.001	0.004273	1900
	large	8.0	1000	0.008	0.003273	0.00065	0.003923	2000
	small	8.0	1000	0.008	0.003273	0.0019	0.005173	1500

Table 7.2.2 TCVP Noncancer (Steady State) Residential Post-Application AGGREGATE Risk Calculations for CHILDREN								
EPA Reg. No/Animal	**Animal Size**	**Residential Post-Application Aggregate**						
		$BMDL_{10}$ mg/kg/day	**LOC[1]**	**Max Allowable Exposure[2] mg/kg/day**	**Average Food and Water Exposure mg/kg/day**	**Residential Exposure (Incidental Oral) mg/kg/day[3]**	**Total Exposure mg/kg/day[4]**	**Aggregate MOE (food, water, and residential)[5]**
11556-164: Dog	medium	8.0	1000	0.008	0.003273	0.00084	0.004113	1900
	large	8.0	1000	0.008	0.003273	0.00053	0.003803	2100
11556-165: Cat	small	8.0	1000	0.008	0.003273	0.0024	0.005673	1400
	medium	8.0	1000	0.008	0.003273	0.0015	0.004773	1700
	large	8.0	1000	0.008	0.003273	0.00092	0.004193	1900
2596-84: Dog	small	8.0	1000	0.008	0.003273	0.0016	0.004873	1600
	large	8.0	1000	0.008	0.003273	0.00076	0.004033	2000
2596-139: Dog	small	8.0	1000	0.008	0.003273	0.0043	0.007573	1000
	medium	8.0	1000	0.008	0.003273	0.0019	0.005173	1500
	large	8.0	1000	0.008	0.003273	0.0012	0.004473	1800
2596-63: Cat	small	8.0	1000	0.008	0.003273	0.0026	0.005873	1400
	large	8.0	1000	0.008	0.003273	0.0011	0.004373	1800
Pet Collars (Liquid Assumption): TCVP/Davis Study								
2596-49: Cat	small	8.0	1000	0.008	0.003273	0.0056	0.008873	**900**
	medium	8.0	1000	0.008	0.003273	0.0033	0.006573	1200
	large	8.0	1000	0.008	0.003273	0.0021	0.005373	1500
2596-50, 62: Dog	small	8.0	1000	0.008	0.003273	0.0047	0.007973	1000
	large	8.0	1000	0.008	0.003273	0.0021	0.005373	1500
2596-83: Cat	small	8.0	1000	0.008	0.003273	0.0059	0.009173	**870**
	large	8.0	1000	0.008	0.003273	0.0046	0.007873	1000
2596-139: Cat	small	8.0	1000	0.008	0.003273	0.0049	0.008173	**980**
	medium	8.0	1000	0.008	0.003273	0.003	0.006273	1300
	large	8.0	1000	0.008	0.003273	0.0018	0.005073	1600
11556-164: Dog	small	8.0	1000	0.008	0.003273	0.0055	0.008773	**910**
	medium	8.0	1000	0.008	0.003273	0.0024	0.005673	1400
	large	8.0	1000	0.008	0.003273	0.0015	0.004773	1700
11556-165: Cat	small	8.0	1000	0.008	0.003273	0.0069	0.010173	**790**
	medium	8.0	1000	0.008	0.003273	0.0042	0.007473	1100
	large	8.0	1000	0.008	0.003273	0.0026	0.005873	1400
2596-84: Dog	small	8.0	1000	0.008	0.003273	0.0047	0.007973	1000
	large	8.0	1000	0.008	0.003273	0.0021	0.005373	1500
2596-139: Dog	small	8.0	1000	0.008	0.003273	0.012	0.015273	**520**
	medium	8.0	1000	0.008	0.003273	0.0053	0.008573	**930**
	large	8.0	1000	0.008	0.003273	0.0034	0.006673	1200
2596-63: Cat	small	8.0	1000	0.008	0.003273	0.0074	0.010673	**750**
	large	8.0	1000	0.008	0.003273	0.0031	0.006373	1300

Table 7.2.2 TCVP Noncancer (Steady State) Residential Post-Application AGGREGATE Risk Calculations for CHILDREN								
EPA Reg. No/Animal	**Animal Size**	**Residential Post-Application Aggregate**						
		$BMDL_{10}$ mg/kg/day	**LOC[1]**	**Max Allowable Exposure[2] mg/kg/day**	**Average Food and Water Exposure mg/kg/day**	**Residential Exposure (Incidental Oral) mg/kg/day[3]**	**Total Exposure mg/kg/day[4]**	**Aggregate MOE (food, water, and residential)[5]**
Pet Collars (Solid Assumption): Amitraz Exposure Data (MRID 49468801)								
2596-49: Cat	small	8.0	1000	0.008	0.003273	0.49	0.493273	**16**
	medium	8.0	1000	0.008	0.003273	0.3	0.303273	**26**
	large	8.0	1000	0.008	0.003273	0.18	0.183273	**44**
2596-50, 62: Dog	small	8.0	1000	0.008	0.003273	0.41	0.413273	**19**
	large	8.0	1000	0.008	0.003273	0.19	0.193273	**41**
2596-83: Cat	small	8.0	1000	0.008	0.003273	0.52	0.523273	**15**
	large	8.0	1000	0.008	0.003273	0.41	0.413273	**19**
2596-139: Cat	small	8.0	1000	0.008	0.003273	0.44	0.443273	**18**
	medium	8.0	1000	0.008	0.003273	0.26	0.263273	**30**
	large	8.0	1000	0.008	0.003273	0.16	0.163273	**49**
11556-164: Dog	small	8.0	1000	0.008	0.003273	0.49	0.493273	**16**
	medium	8.0	1000	0.008	0.003273	0.21	0.213273	**38**
	large	8.0	1000	0.008	0.003273	0.13	0.133273	**60**
11556-165: Cat	small	8.0	1000	0.008	0.003273	0.61	0.613273	**13**
	medium	8.0	1000	0.008	0.003273	0.37	0.373273	**21**
	large	8.0	1000	0.008	0.003273	0.23	0.233273	**34**
2596-84: Dog	small	8.0	1000	0.008	0.003273	0.41	0.413273	**19**
	large	8.0	1000	0.008	0.003273	0.19	0.193273	**41**
2596-139: Dog	small	8.0	1000	0.008	0.003273	1.1	1.103273	**7**
	medium	8.0	1000	0.008	0.003273	0.47	0.473273	**17**
	large	8.0	1000	0.008	0.003273	0.3	0.303273	**26**
2596-63: Cat	small	8.0	1000	0.008	0.003273	0.65	0.653273	**12**
	large	8.0	1000	0.008	0.003273	0.28	0.283273	**28**
Dust/Powder: TCVP Dust and Pump Spray Study (MRID 45485501)								
4700-123: Dog	small	8.0	1000	0.008	0.003273	0.0087	0.011973	**670**
	medium	8.0	1000	0.008	0.003273	0.0093	0.012573	**640**
	large	8.0	1000	0.008	0.003273	0.0095	0.012773	**630**
47000-123: Cat	small	8.0	1000	0.008	0.003273	0.0043	0.007573	1000
	medium	8.0	1000	0.008	0.003273	0.0063	0.009573	**840**
	large	8.0	1000	0.008	0.003273	0.0059	0.009173	**870**
2596-78: Cat	small	8.0	1000	0.008	0.003273	0.029	0.032273	**250**
	large	8.0	1000	0.008	0.003273	0.018	0.021273	**380**
2596-79: Dog	small	8.0	1000	0.008	0.003273	0.024	0.027273	**290**
	medium	8.0	1000	0.008	0.003273	0.021	0.024273	**330**
	large	8.0	1000	0.008	0.003273	0.016	0.019273	**420**

Table 7.2.2 TCVP Noncancer (Steady State) Residential Post-Application AGGREGATE Risk Calculations for CHILDREN								
EPA Reg. No/Animal	**Animal Size**	**Residential Post-Application Aggregate**						
		$BMDL_{10}$ mg/kg/day	**LOC[1]**	**Max Allowable Exposure[2] mg/kg/day**	**Average Food and Water Exposure mg/kg/day**	**Residential Exposure (Incidental Oral) mg/kg/day[3]**	**Total Exposure mg/kg/day[4]**	**Aggregate MOE (food, water, and residential)[5]**
67517-82: Dog	small	8.0	1000	0.008	0.003273	0.026	0.029273	**270**
	medium	8.0	1000	0.008	0.003273	0.028	0.031273	**260**
	large	8.0	1000	0.008	0.003273	0.028	0.031273	**260**
67517-82: Cat	small	8.0	1000	0.008	0.003273	0.013	0.016273	**490**
	medium	8.0	1000	0.008	0.003273	0.019	0.022273	**360**
	large	8.0	1000	0.008	0.003273	0.018	0.021273	**380**
Pump/Trigger Spray: TCVP Dust and Pump Spray Study (MRID 45485501)								
2596-126,140: Cat (trigger)	small	8.0	1000	0.008	0.003273	0.0017	0.004973	1600
	large	8.0	1000	0.008	0.003273	0.0009	0.004173	1900
2596-140: Cat (pump)	small	8.0	1000	0.008	0.003273	0.00035	0.003623	2200
	large	8.0	1000	0.008	0.003273	0.00018	0.003453	2300
2596-125, -140: Dog (trigger)	small	8.0	1000	0.008	0.003273	0.0012	0.004473	1800
	medium	8.0	1000	0.008	0.003273	0.00059	0.003863	2100
	large	8.0	1000	0.008	0.003273	0.00066	0.003933	2000

[1] LOC = 1000 (10X inter- and 10X intra- species uncertainty factors plus 10X FQPA SF)
[2] Maximum Allowable Exposure (mg/kg/day) = $BMDL_{10}$/LOC
[3] Residential Exposure = Oral exposure only (Appendix H).
[4] Total Exposure = Avg Food & Water Exposure + Residential Exposure
[5] Aggregate MOE = [$BMDL_{10}$ / Total Exposure]; Aggregate MOEs < 1000 (LOC) are **BOLDED**

7.3 Cancer Aggregate Risk

The cancer aggregate risk assessment combines residential and dietary (food and drinking water) expected lifetime exposures for adults. For TCVP, a cancer aggregate assessment was performed for adult handlers and adult post-application activities related to pet product use.

The residential exposure for use in the cancer handler assessment is the combined dermal and inhalation exposures from applying TCVP products to pets (collars, dust/powders, and pump/trigger sprays).

All pet product scenarios (collars, dust/powders, and pump/trigger sprays) result in residential handler cancer aggregate (residential and dietary) risk estimates in the 10^{-6} range.

All dust/powder and pump/trigger spray product scenarios result in residential post-application cancer aggregate (residential and dietary) risk estimates in the 10^{-6} range. When collars are assumed to be liquid formulations, post-application cancer aggregate risk estimates aren the 10^{-6} range using the amitraz data and are 10^{-5} to 10^{-6} when using the Davis data. For the solid formulation assumption, only the amitraz data were presented and those cancer aggregate risk estimates are in the 10^{-5} range (cancer aggregate risk estimate values would be lower if using the

Davis).

Table 7.3.1. Range of Adult Handler Aggregate Cancer Risk Estimates for TCVP Pet Products *(Risk is estimated using a Q* of 0.00183)*				
Relative Exposure- All Products	**Reg No.; Animal type; Animal size**	**Food and Water Exposure (mg/kg/day)[1]**	**Residential Exposure (LADD, mg/kg/day)[2]**	**Aggregate Cancer Risk (food, water, residential)**
Pet Collars (Liquid Assumption): 2012 Residential SOPs (Spot-on Surrogate Data)				
Lowest	2596-139; Cat; Any	5.66×10^{-4}	7.5×10^{-6}	1×10^{-6}
Highest	2596-139; Dog; Any	5.66×10^{-4}	3.8×10^{-5}	1×10^{-6}
Pet Collars (Solid Assumption): TCVP Dust/Powder Applicator Study (MRID 45519601)				
Lowest	2596-139; Cat; Any	5.66×10^{-4}	1.1×10^{-4}	1×10^{-6}
Highest	2596-139; Dog; Any	5.66×10^{-4}	5.4×10^{-4}	2×10^{-6}
Dust/Powder: TCVP Dust/Powder Applicator Study (MRID 45519601)				
Lowest	47000-123; Cat; Small	5.66×10^{-4}	4.7×10^{-6}	1×10^{-6}
Highest	67517-82; Dog; Large	5.66×10^{-4}	2.3×10^{-4}	$1. \times 10^{-6}$
Pump/Trigger Spray: 2012 Residential SOPs (Surrogate Data)				
Lowest	2596-140; Cat; Small (Pump)	5.66×10^{-4}	2.8×10^{-6}	1×10^{-6}
Highest	2596-125, -140; Dog; Large (Trigger)	5.66×10^{-4}	3.9×10^{-5}	1×10^{-6}

[1] Table 5.4.5.1
[2] Appendix G.
[3]Aggregate Cancer Risk = (Q_1*) (Food & Water Exposure + LADD)

Table 7.3.2. Range of Adult Post-Application Aggregate Cancer Risk Estimates for TCVP Pet Products *(Risk is estimated using a Q* of 0.00183)*				
Relative Exposure- Pet Products	**Reg No., Animal type, Animal size**	**Food and Water Exposure (mg/kg/day)[1]**	**Residential Exposure (LADD, mg/kg/day)[2]**	**Aggregate Cancer Risk (food, water, residential)**
Pet Collars (Liquid Assumption): Amitraz Exposure Data (MRID 49468801)				
Lowest	11556-164, Dog, Large	5.66×10^{-4}	2.5×10^{-4}	1×10^{-6}
Highest	2596-139, Dog, Small	5.66×10^{-4}	2.0×10^{-3}	5×10^{-6}
Pet Collars (Liquid Assumption): TCVP/Davis Study				
Lowest	2596-49, Cat, Large; 2596-50, -62, Dog, Large; 2596-84, Dog, Large	5.66×10^{-4}	$2.2 \times 10\text{-}^{3}$	5×10^{-6}
Highest	2596-139, Dog, Small	5.66×10^{-4}	1.3×10^{-2}	2×10^{-5}
Pet Collars (Solid Assumption): Amitraz Exposure Data (MRID 49468801)				
Lowest	11556-164, Dog, Large	5.66×10^{-4}	6.6×10^{-3}	1×10^{-5}
Highest	2596-139, Dog, Small	5.66×10^{-4}	5.4×10^{-2}	1×10^{-5}
Dust/Powder: TCVP Dust and Pump Spray Study (MRID 45485501)				
Lowest	4700-123, Cat, Small	5.66×10^{-4}	2.9×10^{-4}	2×10^{-6}
Highest	67517-82, Dog, Medium/Large	5.66×10^{-4}	1.9×10^{-3}	4×10^{-6}
Pump/Trigger Spray: TCVP Dust and Pump Spray Study (MRID 45485501)				
Lowest	2596-140, Cat, Large (Pump)	5.66×10^{-4}	5.6×10^{-5}	1×10^{-6}
Highest	2596-140, Cat, Small (Pump)	5.66×10^{-4}	1.1×10^{-4}	1×10^{-6}

[1] Table 5.4.5.1
[2] Appendix I
[3]Aggregate Cancer Risk = (Q_1*) (Food & Water Exposure + LADD)

8.0 Occupational Exposure/Risk Characterization

Occupational and Residential Exposure Memo: DP#426984, 12/21/15, W. Britton.

8.1 Occupational Handler Exposure/Risk Estimates (Non-Cancer and Cancer)

HED uses the term handlers to describe those individuals who are involved in the pesticide application process. HED believes that there are distinct job functions or tasks related to applications and exposures can vary depending on the specifics of each task. Job requirements (amount of chemical used in each application), the kinds of equipment used, the target being treated, and the level of protection used by a handler can cause exposure levels to differ in a manner specific to each application event.

Occupational handler exposures are expected from use of TCVP on pets by veterinarians, veterinary assistants, and groomers. The pet use formulations include collars, dusts/powders, and pump and trigger sprays. Based on the anticipated use patterns and current labeling, types of equipment and techniques that can potentially be used, occupational handler exposure (dermal and inhalation) is expected.

Occupational handler exposures for the TCVP uses are anticipated to be short-term (1 to 30 days) to intermediate-term (1 to 6 months) in duration. However, because of the steady state AChE inhibition exhibited by the OPs, non-cancer steady state exposures (21 days) were assessed for occupational exposures to TCVP. Only inhalation exposures were assessed for the steady state duration for TCVP. A quantitative dermal assessment was not performed for the steady state as there were no treatment related effects, including a lack of effect on RBC and brain cholinesterase activity, in the dermal toxicity study. A cancer assessment was also performed for handlers that included both inhalation and dermal exposures to TCVP.

For adults, when an endpoint is not sex-specific (i.e., the endpoints are based on developmental or fetal effects) a body weight of 80 kg is typically used in risk assessment. However, for the OP chemical class, a female-specific body weight of 69 kg is now assumed for adults. While the endpoint of concern, RBC AChE inhibition, is not sex-specific, the female body weight is used in the TCVP occupational assessments for adult workers due to concerns for potentially pregnant women and the uncertainties regarding neurodevelopmental effects.

The quantitative exposure/risk assessment developed for occupational handlers is based on the following scenarios:

Mixer/Loaders:

(1a) Liquid: Groundboom Applications
(1c) Liquid: Paint Applications
(2a) Wettable Powder: Groundboom Applications
(2b) Wettable Powder: Handheld Fogger Applications
(2c) Wettable Powder: Stationary Fogger Applications
(2d) Wettable Powder: Paint Applications
(3a) Dust: Paint Applications

Applicators:

(4) Groundboom Applications
(5) Open Pour Liquid Additive for Feed Through
(6a) RTU Pet Collar - Liquid Formulation
(6b) RTU Pet Collar - Dust Formulation
(7) RTU Dust/Powder – Pets
(8) RTU Pump/Trigger Sprays - Pets

Mixer/Loader/Applicators:

(9a) Liquid: Backpack Sprayer
(9b) Liquid: Manually-Pressurized Handwand
(9c) Liquid: Mechanically-Pressurized Handgun
(9d) Liquid: Backrubber or Facerubber
(10a) Wettable Powder: Backpack Sprayer
(10b) Wettable Powder: Manually-Pressurized Handwand
(10c) Wettable Powder: Mechanically-Pressurized Handgun
(10d) Wettable Powder: Handheld Fogger
(10e) Wettable Powder: Stationary Fogger
(10f) Wettable Powder: Rotary Duster
(10g) Wettable Powder: Plunger Duster
(11a) Dust: Self-Treating Dust Bag
(11b) Dust: Shaker Can
(11c) Dust: Rotary Duster
(11d) Dust: Plunger Duster
(12a) Paint: Brush or Roller
(12b) Paint: Airless Sprayer
(13) Solid Feed Additive for Feed Through: Cup

Occupational Handler Exposure Data and Assumptions

Sources of generic handler data, used as surrogate data in the absence of chemical-specific data, include PHED 1.1, the AHETF database, and the Outdoor Residential Exposure Task Force (ORETF) database.

A single chemical-specific exposure study, Monitoring Exposure of Mixer/Loaders and Applicators Treating Agricultural Premises with Tetrachlorvinphos (Rabon® 50 WP Insecticide) in Handheld Wand-Type Sprayers (MRID 42622301) was used as appropriate (i.e., exposure scenario 10c for mixing/loading and applying WP with mechanically-pressurized handwand) for the occupational risk assessment for TCVP. Risks for this exposure scenario were estimated with use of the chemical-specific exposure data as well as surrogate PHED data.

The detailed exposure data and assumptions (e.g., unit exposure, area treated or amount handled, duration) used in the occupational handler assessment can be found in D426984 (W. Britton).

Estimates of inhalation exposure were calculated for various levels of personal protective equipment (PPE). Results are presented for "baseline," defined as a single layer of clothing consisting of a long sleeved shirt, long pants, shoes plus socks, no protective gloves, and no respirator, as well as baseline with various levels of PPE as necessary (e.g., gloves, respirator, etc).

The PPE required for occupational use of TCVP varies by formulation type. The respiratory protection required for the occupational handling of TCVP can, at times, differ from label to label with consideration of the same formulation and exposure scenario. All but one of the TCVP pet product labels do not require PPE, as these are intended for residential sale as well as for occupational use. A summary of PPE required for all TCVP products is presented in Appendix L of this document.

Although occupational dermal and inhalation exposures are anticipated for TCVP, risks have been estimated for inhalation exposures only due to the lack of dermal hazard. Therefore, no combined occupational exposures/risk estimates have been quantified.

Occupational Handler (Non-Cancer) Exposure and Risk Estimate Equations

The algorithms used to estimate non-cancer exposure and dose for occupational handlers can be found in Appendix D of D426984.

Summary of Occupational Handler Steady State (Non-Cancer) Exposure and Risk Estimates

Of the 172 total occupational handler exposure scenarios assessed, the majority (152) are not of concern (i.e., steady state inhalation MOEs are ≥ 300) with currently required personal protective equipment (PPE) (i.e., respiratory protection). Of the remaining 20 handler exposure scenarios, an additional 16 are not of concern with consideration of increasing levels of respiratory protection (i.e., four occupational handler exposure scenarios result in estimated risks of concern despite the addition of respiratory protection or engineering controls). These four handler scenarios are all dust formulations (mixing/loading/applying TCVP by rotary duster, self-treating dust bag, or shaker can).

A summary of all non-cancer occupational handler exposure scenarios is presented in Appendix J. For risk management purposes, the currently labeled level of respiratory protection and engineering controls has been identified (bolded) for each individual exposure scenario.

Occupational Handler Cancer Exposure and Risk Equations

Cancer risk estimates were calculated using a linear low-dose extrapolation approach in which an LADD is first calculated and then compared with a Q1* that has been calculated for TCVP based on dose response data in the appropriate toxicology study ($Q1^* = 1.83 \times 10^{-3}$ (mg/kg/day)-1). ADD levels were used as the basis for calculating the LADD values. Dermal and inhalation ADD values were first added together to obtain combined ADD values. LADD values were then calculated and compared to the Q1* to obtain cancer risk estimates. The algorithms used to

estimate the LADD and cancer risk for occupational handlers can be found in Appendix D of D426984.

Summary of Occupational Handler Cancer Exposure and Risk Estimates

Occupational cancer risks were estimated for both private/farmer and contract/commercial handlers. Cancer risks range from 10^{-10} to 10^{-5} for private/farmer handlers and from 10^{-10} to 10^{-4} for contract/commercial handlers with currently required PPE.

Unlike the occupational handler non-cancer risk estimates which were based only on inhalation exposures, the occupational handler cancer risk estimates are quantified based on both dermal and inhalation exposures. This is because, despite the determination of the lack of dermal hazard for TCVP, dermal exposures from TCVP must be quantified for purpose of cancer risk assessment. As previously described, the PPE required for the occupational use of TCVP varies by formulation type. For example, for feed through (solid and liquid food additives) and feed blocks, occupational handlers are required to wear baseline clothing (i.e., long sleeved shirt, long pants, shoes and socks) and gloves. For all other end-use labels with livestock and outdoor perimeter uses, required PPE can vary dependent on the application type or equipment and can range from baseline clothing and gloves, to the addition of coveralls, or respiratory protection.

A summary of occupational cancer risks as estimated at all levels of personal protection and with use of engineering controls is presented in Appendix K of D426984. Table K.1 presents cancer risks for private/farmer handlers and Table K.2 risks for contract/commercial handlers. For risk management purposes, the currently labeled level of respiratory protection and engineering controls has been identified (bolded) for each individual exposure scenario.

8.2 Occupational Post-application Exposure/Risk Estimates

Occupational post-application exposures are not expected as reentry activities are not anticipated for this use pattern. Restricted entry intervals (REIs) are not included on TCVP product labeling as the registered uses (i.e., livestock or other animals, or in or around animal premises) are not covered by the Worker Protection Standard (WPS).

9.0 Public Health and Pesticide Epidemiology Data

Incident Report Memo: DP#426986, 5/21/15, S. Recore.

HED has prepared a Tier I review of human incidents report. For this evaluation, both OPP Incident Data System (IDS) and the Centers for Disease Control and Prevention/National Institute for Occupational Safety and Health (CDC/NIOSH) Sentinel Event Notification System for Occupational Risk-Pesticides (SENSOR) databases were consulted for pesticide incident data on the active ingredient TCVP. The purpose of the database search is to identify potential patterns in the frequency and severity of the health effects attributed to TCVP exposure.

The Agricultural Health Study (AHS) is a high quality, prospective epidemiology study evaluating the link between pesticide use and various health outcomes including cancer. TCVP is not included in the AHS, and therefore this study does not provide information for this report.

Although there were a moderate number of TCVP incidents reported to Main and Aggregate IDS (n=374) and SENSOR-Pesticides (n=61), most of these incidents were classified as low severity. The effects experienced were generally minimally traumatic and resolving rapidly and usually involve skin, eye or respiratory irritation. Most of the reported incidents were due to handling and applying TCVP products to pets. Based on the low severity of incident cases reported for TCVP in both IDS and NIOSH SENSOR-Pesticides, there does not appear to be a concern at this time that would warrant further investigation. The agency will continue to monitor the incident information and if a concern is triggered, additional analysis will be conducted.

10.0 Cumulative Exposure/Risk Characterization

OPs, like TCVP, share the ability to inhibit AChE through phosphorylation of the serine residue on the enzyme leading to accumulation of acetylcholine and ultimately cholinergic neurotoxicity. This shared MOA/AOP is the basis for the OP common mechanism grouping per OPP's *Guidance For Identifying Pesticide Chemicals and Other Substances that have a Common Mechanism of Toxicity* (USEPA, 1999). The 2002 and 2006 cumulative risk assessments (CRAs) used brain AChE inhibition in female rats as the source of dose response data for the relative potency factors and PODs for each OP, including TCVP. Prior to the completion of registration review, OPP will update the OP CRA on AChE inhibition to incorporate new toxicity and exposure information available since 2006.

As described in Section 4.4, OPP has retained the FQPA Safety Factor for OPs, including TCVP, due to uncertainties associated with neurodevelopmental effects in children and exposure to OPs. There is a lack of an established MOA/AOP for the neurodevelopment outcomes which precludes the agency from formally establishing a common mechanism group per the *Guidance For Identifying Pesticide Chemicals and Other Substances that have a Common Mechanism of Toxicity* (USEPA, 1999) based on that outcome. Moreover, the lack of a recognized MOA/AOP and other uncertainties with exposure assessment in the epidemiology studies prevent the agency from establishing a causal relationship between OP exposure and neurodevelopmental outcomes. The agency will continue to evaluate the epidemiology studies associated with neurodevelopmental outcomes and OP exposure prior to the release of the revised PRA. During this period, the agency will determine whether or not it is appropriate to apply the draft guidance document entitled, *Pesticide Cumulative Risk Assessment: Framework for Screening Analysis* for the neurodevelopment outcomes.

11.0 EPA References

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C. Peck, 11/6/14, D419448, *Tetrachlorvinphos (TCVP) Drinking Water Assessment for Registration Review.*\

S. Recore, 5/21/15, D426986, *Tetrachlorvinphos (TCVP): Tier I Review of Human Incidents for Draft Risk Assessment.*

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W. Britton, 12/21/15, D426984, *Tetrachlorvinphos: Occupational and Residential Exposure Assessment for Registration Review*.

12.0 Appendices

Appendix A. Toxicology Profile
Appendix B. Results for BMD/BMDL modeling for TCVP
Appendix C. Physical/Chemical Properties for Tetrachlorvinphos
Appendix D. TCVP and Metabolites
Appendix E. International MRLs and U.S. Tolerances
Appendix F. Summary of Residential Handler Non-Cancer Exposures and Risk Estimates
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Appendix I. Summary of Residential Post-Application Cancer Exposure and Risk Estimates
Appendix J. Summary of Occupational Handler Non-Cancer Exposures and Risk Estimates
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Appendix L. Summary of TCVP Labels and Use Directions

Appendix M. Calculation of Inhalation Human-Equivalent Concentrations (HECs) and Human-Equivalent Doses

Appendix A. Toxicology Profile

Table A.2.1 Acute Toxicity of Tetrachlorvinphos Technical				
Guideline No.	**Study Type**	**MRID No.**	**Results**	**Toxicity Category**
870.1100	Acute Oral – Rat	41222504	LD_{50} = 1480 mg/kg (M) 465-965 mg/kg (F)	III
870.1200	Acute Dermal – Rabbit	41222505	LD_{50} > 2000 mg/kg	III
870.1300	Acute Inhalation – Rat	00138933	LC50 > 3.61mg/L	IV
870.2400	Acute Eye Irritation - Rabbit	41222506	moderate	III
870.2500	Acute Dermal Irritation - Rabbit	41222507	slight	IV
870.2600	Skin Sensitization - Guinea Pig	41377902 42981001	sensitizer	N/A
870.6100	Acute Delayed Neurotoxicity	41905901	No clinical signs of neurotoxicity observed (NTE not measured)	N/A

Table A.2.2 Subchronic, Chronic and Other Toxicity Profile of Tetrachlorvinphos (TCVP)		
Guideline No./ Study Type	**MRID No. (year)/ Classification /Doses**	**Results**
870.3100 21-Day Oral Toxicity in (Crl:CD®(SD)IGS BR rats)	45570601 (2001) Acceptable/non-guideline (21-day study; gavage) 0, 8, 12, 20, or 50 mg/kg/day	**Repeat exposure**: Brain ChEI NOAEL = 12 mg/kg/day Brain ChEI LOAEL = 20 mg/kg/day, based on brain cholinesterase activity inhibition in females (day 21). RBC ChEI NOAEL = 8 mg/kg/day RBC ChEI LOAEL = 12 mg/kg/day, based on RBC cholinesterase activity inhibition in males and females **Single dose exposure**: RBC ChEI NOAEL = 20 mg/kg. RBC ChEI LOAEL = 50 mg/kg, based on RBC cholinesterase activity in both sexes. Brain ChEI NOAEL =12 mg/kg. Brain ChEI LOAEL = 20 mg/kg, based on brain cholinesterase activity inhibition (ChEI) in males (22%). At 50 mg/kg, males had 54% and females had 23% brain cholinesterase inhibition. $BMDL_{10}$ = 6.7 mg/kg/day BMD_{10} = 9.9 mg/kg/day, based on female RBC ChE inhibition $BMDL_{10}$ = 12.2 mg/kg/day BMD_{10} = 14.7 mg/kg/day, based on female brain ChE inhibition

Table A.2.2 Subchronic, Chronic and Other Toxicity Profile of Tetrachlorvinphos (TCVP)

Guideline No./ Study Type	MRID No. (year)/ Classification /Doses	Results
870.3150 90-Day Oral Toxicity (Sprague Dawley rats)	43371201 (1990) Acceptable/guideline 0, 100, 2000, or 5000 ppm (diet) Males: 0, 6.7, 142, and 375 mg/kg/day; Females: 0, 10.0, 197, and 467 mg/kg/day. $BMDL_{10}$ = 8.0 mg/kg/day BMD_{10} = 10.49 mg/kg/day, based on female RBC ChE inhibition	RBC ChEI NOAEL = 6.7 mg/kg/day RBC ChEI LOAEL = 142 mg/kg/day, based on RBC ChEI in both sexes, reduced body weights (both sexes), bilateral basophilic tubules of the kidneys in males, increased fat deposition in the adrenal cortex of females, centrilobular hepatocellular hypertrophy in females and mid-dose males, higher adjusted liver weights (both sexes), higher adjusted adrenal weights in females, and thyroid follicular cell hypertrophy in both sexes. At 467 mg/kg/day, females had a 24% brain cholinesterase activity inhibition, although statistical significance was not attained. $BMDL_{10}$ = 8.0 mg/kg/day BMD_{10} = 10.49 mg/kg/day, based on female RBC ChE inhibition $BMDL_{10}$ = 26.3 mg/kg/day BMD_{10} = 61.6 mg/kg/day, based on male RBC ChE inhibition No dose-response for brain ChE inhibition (BMD not run)
870.3200 21/Day Dermal Toxicity (Crl:CD BR rat)	41342001 (1989) Acceptable/guideline 0, 10, 100, or 1000 mg/kg/day 6 hours/day, 5 days/week for 15 treatments over a 21-day period	NOAEL = 100 mg/kg/day LOAEL = 1000/kg/day, based on plasma cholinesterase inhibition in both sexes. Brain and RBC cholinesterase inhibition were not observed in either sex.
870.3465 28-Day Inhalation Toxicity (Sprague-Dawley rat)	48803501 (2012) Acceptable/guideline nose-only aerosol 6 hours/day, 5 days/week for 3 weeks at exposure concentrations of 0, 0.05, 0.5, or 1.0 mg/L; during the final week of exposure (week 4), the animals were exposed for 7 days	NOAEL= 0.05 mg/L/day LOAEL = 0.5 mg/L/day, based on an increase in RBC cholinesterase inhibition in both sexes. *Brain cholinesterase activity was not monitored.* Systemic NOAEL not identified. Systemic LOAEL = 0.05 mg/L, based on diffuse adrenal cortical cell vacuolation in both sexes, enlarged adrenals in females, and increased adrenal weights in females. At 0.5 mg/L and 1.0 mg/L, in addition to the adrenal findings, there was a dose-related increase in vacuolation of the ovaries in females, an increase in squamous metaplasia of the larynx in both sexes, and an increase in follicular cell hyperplasia of the thyroids in both sexes.

Sex/Age	Compartment	BMD_{10}	$BMDL_{10}$
Female	RBC	0.394	0.050
Male	RBC	0.122	0.022

Table A.2.2 Subchronic, Chronic and Other Toxicity Profile of Tetrachlorvinphos (TCVP)		
Guideline No./ Study Type	**MRID No. (year)/ Classification /Doses**	**Results**
870.3700a Prenatal developmental in (Sprague Dawley Crl:COBS®CD® (SD)BR) TXR# 008124, 008616, 018781	40152701 (1987) 41828001(1991) 41967201 (1991) 42520101 (1992) Acceptable/guideline 0 (aqueous 0.5% methyl cellulose), 75, 150, or 300 mg/kg/day GD 6-15; 10 mL/kg (gavage)	**Maternal** NOAEL = 75 mg/kg/day **Maternal** LOAEL = 150 mg/kg/day, based on a reduction in BWG/FC At 300 mg/kg/day, there were clinical signs of toxicity (tremors and chromodacryorrhea) **Developmental** NOAEL =300 mg/kg/day **Developmental** LOAEL = not identified. *NOTE: Cholinesterase activity was not assessed (RBC, brain).*
870.3700b Prenatal developmental in (New Zealand white rabbit)	00127831 (1982) Acceptable/guideline 0, 150, 375, or 750 mg/kg/day (1% CMC) GD 6-19; 5 mL/kg (gavage)	**Maternal** NOEL = 375 mg/kg/day **Maternal** LOEL = 750 mg/kg/day, based on mortality, abortions, and red vaginal fluid. **Developmental** NOAEL = 375 mg/kg/day **Developmental** LOAEL = 750 mg/kg/day, based on an increase in early resorptions and corresponding increase in post implantation loss, and a decrease in live fetuses/doe. *NOTE: Cholinesterase activity was not assessed (RBC, brain).*
870.3800 Reproduction and Fertility Effects (Charles River CD Crl®SD) BR rats)	42054301 (1991) acceptable/guideline 0, 100, 500, or 2000 ppm (diet) F0 Males 0, 5.2, 26, 102 mg/kg/day F1 Males 0, 6.7, 34, 130 mg/kg/day F0 Females 0, 7.3, 40, or 155 mg/kg/day F1 Females 0, 8.3, 43, or 168 mg/kg/day	**Parental** NOAEL = 500 ppm (males 26/females 40 mg/kg/day) **Parental** LOAEL = 2000 ppm (males 102/females 155 mg/kg/day), based on decreased body weight gain in F1 generation, increased adrenal weights of F0 females, and decreased body weight gains in F0 males. **Offspring** NOAEL = 2000 ppm (males 102/females 155 mg/kg/day) **Offspring** LOAEL was not identified. **Reproductive** NOAEL = 2000 ppm (males 102/females 155 mg/kg/day) **Reproductive** LOAEL was not identified. *NOTE: Cholinesterase activity was not assessed (RBC, brain).*

Table A.2.2 Subchronic, Chronic and Other Toxicity Profile of Tetrachlorvinphos (TCVP)		
Guideline No./ Study Type	**MRID No. (year)/ Classification /Doses**	**Results**
870.4100a Chronic Toxicity (Sprague-Dawley rat)	42980901 (1993) 43335101 (1994) Acceptable/guideline 0, 100, 1000, or 2000 ppm (diet) Males 0, 4.23, 43.2, or 88.5 mg/kg/day Females 0, 5.93, 62.7, or 125.3 mg/kg/day (2-year study)	NOAEL = 100 ppm (4.23/5.93 mg/kg/day) LOAEL = 1000 ppm (43.2/62.7 mg/kg/day), based on histological liver (hypertrophy of periacinar hepatocytes in both sexes and centriacinar degenerative change in males) and adrenal changes (increased incidence of diffuse lipidosis of adrenal zona fasciculata in both sexes); reduced body weight; -RBC cholinesterase inhibition in females. RBC cholinesterase inhibition was observed in females at 1000 ppm (29%*) and 2000 ppm (36%**) at week 77/78; 18% and 22% at week 103/104 (not **); brain ChEI in females at 52 and 104 weeks was 17% and 16% (not **). NOAEL = 100 ppm (4.23/5.93 mg/kg/day) LOAEL = 1000 ppm (43.2/62.7 mg/kg/day), based on RBC cholinesterase inhibition in females BMD not run due to lack of dose-response
870.4100b Chronic toxicity (Beagle dog)	42679401 (1993) Acceptable/guideline 0, 0, 6.25, 500, 1000 mg/kg/day; (capsule) 4/sex/group Cholinesterase pre-test, 12, 26, 52 weeks (plasma, RBC) Brain at termination (1 year)	NOAEL = 6.25 mg/kg/day LOAEL = 500 mg/kg/day, based on plasma cholinesterase inhibition (both sexes), decreased red blood cell counts, hemoglobin, hematocrit, MCHC, MCV, alkaline phosphatase, urine specific gravity, and decreased liver and kidney weights. At 1000 mg/kg/day, increased white blood cell counts (females), increased prostate weight, decreased cholesterol (males). RBC and brain cholinesterase inhibition were not observed at any dose level in either sexes.
870.4200a Combined Chronic Toxicity/Carcinogenicity (Sprague Dawley rat)	42980901 (1993) 43335101 (1994) acceptable/guideline 0, 100, 1000, or 2000 ppm (diet) Males 0, 4.23, 43.2, or 88.5 mg/kg/day Females 0, 5.93, 62.7, or 125.3 mg/kg/day	NOAEL = 100 ppm (4.23/5.93 mg/kg/day) LOAEL = 1000 ppm (43.2/62.7 mg/kg/day), based on histological liver (hypertrophy of periacinar hepatocytes in both sexes and centriacinar degenerative change in males) and adrenal changes (increased incidence of diffuse lipidosis of adrenal zona fasciculata in both sexes); reduced body weight; RBC cholinesterase inhibition in females. RBC cholinesterase inhibition was observed in females at 1000 ppm (29%*) and 2000 ppm (36%**) at week 77/78; 18% and 22% at week 103/104 (not **); brain ChEI in females at 52 and 104 weeks was 17% and 16% (not **). NOAEL = 100 ppm (4.23/5.93 mg/kg/day) LOAEL = 1000 ppm (43.2/62.7 mg/kg/day), based on RBC cholinesterase inhibition in females Increased incidence of thyroid C-cell adenomas in male rats at HDT and adrenal pheochromocytomas in males

Table A.2.2 Subchronic, Chronic and Other Toxicity Profile of Tetrachlorvinphos (TCVP)		
Guideline No./ Study Type	**MRID No. (year)/ Classification /Doses**	**Results**
870.4200b Carcinogenicity (B6C3F1 mouse)	00117443 (1978) Acceptable/guideline 0, 17.5, 64, 320, 1600, 8000, 16000 ppm 0, 2.6, 9.6, 48, 240, 1200, or 2400 mg/kg/day	NOAEL = 1600 ppm (240 mg/kg/day) LOAEL = 8000 ppm (1200 mg/kg/day), based on decreased body weight gain Statistically significant increases in combined hepatocellular adenoma/carcinoma (primarily carcinomas) in female B6C3F1 mice at 1600 ppm. Other doses considered excessive; combined adenomas/carcinomas in males, renal adenomas/carcinomas and combined in males at 16000 ppm
870.4300 Combined Chronic Toxicity/Carcinogenicity (Sprague Dawley rat)	42980901 (1993) 43335101 (1994) acceptable/guideline 0, 100, 1000, or 2000 ppm Males 0, 4.23, 43.2, or 88.5 mg/kg/day Females 0, 5.93, 62.7, or 125.3 mg/kg/day	See above
Gene Mutation 870.5100 *Salmonella/Escherichia* bacterial reverse mutation assay	41222508 (1989) 66.7, 100, 333, 667, 1000, or 3300 µg/plate in the presence of or 10, 33.3, 66.7, 100, 333, or 667 µg/plate absence of mammalian metabolic activation (S9-mix)	Strains TA98, TA100, TA1535, TA1537, and TA 1538 of *S. typhimurium* were exposed to TCVP from concentrations of 66.7 to 3300 µg/plate in the presence and 10-667 µg/plate absence of mammalian metabolic activation (S9-mix). There was no evidence of induced mutant colonies over background. Acceptable/Guideline
In vitro mammalian cytogenetics 870.5375 Chinese hamster ovary cells	41312901 (1989) Concentrations of 22.9, 44.9, 59.9, 79.8, or 99.8 µg/mL without S9; 12.5, 25, 37,6, or 75.1 µg/mL in the presence of S9-mix.	Positive for inducing chromosomal aberrations at 59.9, 79.8 and 99.8 µg/mL in absence of metabolic activation, but negative at 29.9 or 44.9 µg/mL in absence of metabolic activation. Negative for inducing chromosomal aberrations at 12.5, 25, 37.6, or 75.1 µg/mL in the presence of rat S9 metabolic activation. Acceptable/Guideline
Unscheduled DNA Synthesis 870.5550 in mammalian cells in culture	42156401 (1992) Doses of 5, 7.5, 10, 15, 20, 23, 25, 27, 30, 35, or 40 µg/mL of TCVP.	Concentrations of 35 and 40 µg/mL were lethal. Results were negative. Acceptable/Guideline
870.6100 Acute and 28-Day Delayed Neurotoxicity (Domestic hen)	41905901 (1990) Acceptable/guideline 2500 mg/kg x 2 (21 days apart)	Negative

Table A.2.2 Subchronic, Chronic and Other Toxicity Profile of Tetrachlorvinphos (TCVP)		
Guideline No./ Study Type	**MRID No. (year)/ Classification /Doses**	**Results**
870.6200a Acute Neurotoxicity Screening Battery (Sprague-Dawley Crl:CD®BR rats)	42912501 (1993) Acceptable/guideline 0, 65, 325, or 650 mg/kg (gavage)	NOAEL = 65 mg/kg LOAEL = 325 mg/kg, based on transient neurotoxic effects in both sexes consistent with cholinesterase inhibition. No neuropathological effects. *Cholinesterase activity was not monitored in the study.*
870.6200b Subchronic Neurotoxicity Screening Battery (Crl:CD® BR rats)	43294101 (1994) Acceptable/guideline 0, 200, 1000, or 5000 ppm (diet) (0, 100, 500, or 250 mg/kg/day; standard conversion)	NOAEL = 5000 ppm (250 mg/kg/day); HDT LOAEL = not identified. *Cholinesterase activity was not monitored in the study.*
870.6300 Developmental Neurotoxicity (Crl: CD® (SD)IGS BR VAF/Plus® rats)	46660601 (2005) acceptable/guideline 0, 10, 50, or 200 mg/kg/day GD 6 –LD 6 (gavage)	**Maternal** NOAEL = 200 mg/kg/day LOAEL = not identified. **Offspring** NOAEL = 50 mg/kg/day LOAEL = 200 mg/kg/day, based on deceased body weight, body weight gain, several morphometric linear brain measurements in both sexes, and decreased absolute brain weight in males on PND 70 *Cholinesterase activity was not monitored in the study.*
870.7485 Metabolism and Pharmacokinetics (Sprague-Dawley CD rat)	MRID 41988401 (1991) Acceptable/guideline 5 mg/kg [single and repeat (14 days)] and 250 mg/kg (single)	Most of radioactivity recovered in urine (46%-60%) and feces (38%-56%) within 48 hours post dose; major metabolite in urine was trichloromandelic acid (18%-26%); major metabolite in feces was trichlorophenylethanol (>13%) . Since the oral LD50 for female rats is lower the male LD50, it is noteworthy that males of all groups excreted more total label as trichloromandelic acid, a more completely metabolized form of TCVP; high-dose females tended to excrete more of the label as desmethyl TCVP (with the phosphate group still attached to the remainder of the molecule), a compound that could be derived from TCVP with only a single metabolic step.
870.7600 Dermal Penetration (Sprague Dawley CD rats)	MRID 42111501 (1991) Acceptable/Guideline 0, 0.01, 0.1, 1, or 5 mg/cm^2 for exposures of 0.5, 1, 2, 4, and 10 hours and 10 hour wash with 72 hour exposure	Absorbed dose following 0.01 mg/cm^2 dose is 9.57% following 10-hour exposure.
870.7800 Immunotoxicity (Crl:CD-1(ICR) female mouse)	48794701 (2012) acceptable/guideline 0, 75, 300, 1200 mg/kg/day	Systemic NOAEL = 1200 mg/kg/day, Systemic LOAEL = not identified. Immunotoxicity NOAEL = 1200 mg/kg/day. Immunotoxicity LOAEL = not identified.

Table A.2.2 Subchronic, Chronic and Other Toxicity Profile of Tetrachlorvinphos (TCVP)		
Guideline No./ Study Type	**MRID No. (year)/ Classification /Doses**	**Results**
Special study Comparative cholinesterase gestational CCA (Crl:CD(SD)IGS BR VAF/Plus rats)	MRID 48291101 (2010) Acceptable/non-guideline 1% aqueous (w/v) methylcellulose 0, 75, 150, 300 mg/kg/day GD 6-21 (gavage)	The main purpose of this study was to determine whether there is differential sensitivity between dams and fetuses with respect to cholinesterase inhibition following oral exposure to TCVP. ***RBC ChE***: Neither the dams nor the fetuses demonstrated RBC ChE inhibition at dose levels where RBC ChE inhibition (ChEI) would be expected. The repeat dosing study (2012, 48773401) conducted in the same laboratory in the same strain of rat clearly demonstrated RBC ChE inhibition at 50 and 200 mg/kg/day in female rats. In the gestational/fetal study, RBC results in the dams were ↓5.1%, ↓15%, and ↓3% RBC ChEI, with increasing dose. The fetal RBC data were of little value because only one or two fetal samples were available for the control, low, and high dose groups and no sample was available for the mid dose group. *There was no way to compare adult and fetal RBC ChE.*activity ***Brain ChE.*** Brain ChE inhibition was dose dependent in dams (↓31%, ↓44% and ↓67% with increasing dose). Fetal brain ChE values (↓20%, ↓20.9% and ↓20.8%, with increasing dose) showed no dose-response and are questionable. However, the data suggest that the fetal brain ChE is not more sensitive to inhibition by TCVP than the dams. ***Plasma ChE***. Plasma ChE inhibition in dams was dose dependent ↓62%, ↓71% and ↓77%, with increasing dose). Fetal plasma ChE values were ↓22%, ↓18.5% and ↓20.8%, with increasing dose. The lack of a dose response raises questions as to whether these lower values are actually inhibition. However, the data do not indicate that the fetuses are more sensitive than the dams. ***Classification:*** This *in vivo* comparative ChE study is classified as A**cceptable/non-guideline**. The inability of the laboratory to detect RBC ChE in the dams and the flat dose response curves for the brain ChE in both pups and adults confounds the interpretation of the study. However, no additional gestational CCA study is being requested at this time because there is no indication that the fetuses were more sensitive than the dams.

Table A.2.2 Subchronic, Chronic and Other Toxicity Profile of Tetrachlorvinphos (TCVP)		
Guideline No./ Study Type	**MRID No. (year)/ Classification /Doses**	**Results**
Special studies Comparative cholinesterase Acute CCA (Crl:CD(SD)IGS BR VAF/Plus strain rat)	MRID 48294601 (2010) Acceptable/non-guideline Single gavage dose (1% aqueous methylcellulose) young adult, PND 11, PND 21 0, 75, 150 or 300 mg/kg	The main purpose of this study was to determine whether there is differential sensitivity among the PND11, PND21 and adults with respect to cholinesterase inhibition following exposure to TCVP. Overall, there is little confidence in the ChE data mainly because of the lack of clear dose and temporal responses. The number of samples in many cases was inadequate due to sample loss (no sample available, 1, 2, or 3 samples). Also, duplicate samples that did not replicate contributed to the low number of samples available for a meaningful assessment. Brain ChE assessment also appeared to be affected by the low number of samples. The results for all three enzyme sources indicated that there was inhibition at all doses but there was poor dose response with the degree of apparent inhibition at the higher doses often less that at the low dose of 75 mg/kg/day. There was also a lack of temporal concordance with high apparent inhibition at one time, a much lower degree at the following time point, and back to the higher level at the next time point. Further, there was more or similar apparent inhibition at the low dose of 75mg/kg in this acute study than there was in the repeat dosing study (2012, MRID 48773401, eleven daily doses) at 200 mg/kg/day and in the gestational study (2010, MRID 48291101, fifteen daily doses). It is noted that the repeat dosing study clearly indicated that there was no increase in sensitivity of the pups relative to the adults with regard to ChEI by TCVP. However, in this acute study, there were several comparisons among the PND11, PND21 and adults that suggested the pups were more sensitive. Although there is little confidence in the ChEI data in this study, no additional acute CCA study is being requested at this time. ***Benchmark Dose (BMD) modeling.*** BMD modeling was performed but could not be done with the RBC data or for the PND11 brain data because of too few samples and/or the data would not otherwise fit the models. BMD modeling for the brain ChE data (3- hour time point) indicated that for males, the adults were slightly more sensitive than the PND 21 pups but the females were considered similar with respect to the BMD_{10} and $BMDL_{10.}$ This study is classified as A**cceptable/Non-Guideline.** There is too much variability in the ChE data to make meaningful comparisons for sensitivity for RBC and brain ChE inhibition. Although there is little confidence in the ChEI data in this study, no additional acute CCA study is being requested at this time.

<table>
<tr>
<td>Special studies
Comparative cholinesterase repeat CCA

(Crl:CD(SD)IGS BR VAF/Plus strain rat)</td>
<td>48773401 (2012)
Acceptable/Non-guideline.
0, 5, 10, 50 or 200 mg/kg/day for both ages.</td>
<td>The main purpose of this study was to determine whether there is differential sensitivity between young adults and PND 11 pups with respect to cholinesterase inhibition following repeat oral exposure (11 doses) to TCVP.

Table 1 shows the adult ChEI data (3 hours after last dose) and Table 2 shows the pup ChEI data. There was a dose-related reduction in RBC and brain cholinesterase activity in both sexes and both age groups
<table>
<tr><td colspan="3">Table 1. Inhibition (%) of RBC and Brain ChE Activity in Adult Rats (repeat)</td></tr>
<tr><th>Dose (mg/kg/day)</th><th>Males</th><th>Females</th></tr>
<tr><td colspan="3">RBC</td></tr>
<tr><td>5</td><td>12%</td><td>8%</td></tr>
<tr><td>10</td><td>13%*</td><td>8.7%</td></tr>
<tr><td>50</td><td>30%**</td><td>40%**</td></tr>
<tr><td>200</td><td>36%**</td><td>62%**</td></tr>
<tr><td colspan="3">Brain</td></tr>
<tr><td>5</td><td>2%</td><td>-</td></tr>
<tr><td>10</td><td>7%</td><td>12%*</td></tr>
<tr><td>50</td><td>14.9%**</td><td>42%**</td></tr>
<tr><td>200</td><td>17.8%**</td><td>57%**</td></tr>
</table>
<table>
<tr><td colspan="3">Table 2. Inhibition (%) of RBC and Brain ChE Activity in Pups (repeat)</td></tr>
<tr><th>Dose (mg/kg/day)</th><th>Males</th><th>Females</th></tr>
<tr><td colspan="3">RBC</td></tr>
<tr><td>5</td><td>2%</td><td>-</td></tr>
<tr><td>10</td><td>2%</td><td>-</td></tr>
<tr><td>50</td><td>33%**</td><td>19%**</td></tr>
<tr><td>200</td><td>60%**</td><td>62%</td></tr>
<tr><td colspan="3">Brain</td></tr>
<tr><td>5</td><td>4%</td><td>4%</td></tr>
<tr><td>10</td><td>6%</td><td>6%</td></tr>
<tr><td>50</td><td>16%**</td><td>18.7%**</td></tr>
<tr><td>200</td><td>46%**</td><td>45%**</td></tr>
</table>
RBC ChE inhibition. At 50 mg/kg/day, both male pups and male adults had similar levels of inhibition (30% to 33%), whereas at 200 mg/kg/day, the male pups were inhibited to ≈60% compared to 36% in the male adult rats. At 50 mg/kg/day, adult females demonstrated more inhibition (≈40%) than the female pups (19%) but at 200 mg/kg/day, both female pups and female adults had ~62% inhibition.
Brain ChE inhibition. Adult females displayed greater brain ChE inhibition at all dose levels than the adult males, whereas a similar magnitude of brain ChE inhibition was observed in male and female pups. Adult females displayed brain ChE inhibition at all dose levels.</td>
</tr>
</table>

Table A.2.2 Subchronic, Chronic and Other Toxicity Profile of Tetrachlorvinphos (TCVP)

Guideline No./ Study Type	MRID No. (year)/ Classification /Doses	Results
		A benchmark dose analysis of the cholinesterase data (RBC and brain) was performed that provides both the BMD_{10} and $BMDL_{10}$ of adults and PND11 pups.

BMD_{10}s and $BMDL_{10}$s for Adult Rat and PND 11 Pup Cholinesterase

	RBC BMD_{10}	RBC $BMDL_{10}$	Brain BMD_{10}	Brain $BMDL_{10}$
Adult ♂	7.7178	3.5942	33.803	24.4489
Adult ♀	8.6762	6.1335	7.1764	5.4980
PND 11 ♂	20.4688	15.9719	33.4825	26.5707
PND 11 ♂	20.5608	13.1692	24.2224	18.9412

Overall conclusion. The main objective of this study was to attempt to determine if the pups are more sensitive than the adults to the inhibitory potential of TCVP. Based on assignment of the NOAEL and LOAEL and the BMD modeling, there was no demonstration for increased sensitivity of the pups relative to the adults for either RBC or brain ChE. It is noted, however, that the magnitude of the high dose male pup brain and RBC ChE inhibition is greater than that in the adult males, but the significance is not established.

Classification: The classification of this repeat dosing *in vivo* comparative cholinesterase inhibition study is Acceptable/Non-Guideline. The study does not satisfy a guideline requirement. It satisfies a data call-in-requirement for TCVP for an 11-day repeat dosing comparative ChE study in adult rats versus postnatal day 11-21 pups.

Table A.3.1 TCVP - RBC and Brain Cholinesterase Inhibition NOAELs and LOAELs- % AChEI at LOAEL

Study	Compartment	NOAEL (mkd)	LOAEL (mkd)	% ChEI
ORAL				
MRID 48294601 Acute CCA (PND 11)	RBC Brain	- -	75[A]	♀24-28%[B]; ♂42-64%[C] ♀22-38%; ♂19-40%
MRID 48294601 Acute CCA (PND 21)	RBC Brain	- -	75[A]	♀27-36%; ♂19-49% ♀25-54%; ♂24-45%
MRID 48294601 Acute CCA (young adult)	RBC Brain	- -	75[A]	♀22%; ♂26-35% ♀40%; ♂28-56%
MRID Single dose	RBC Brain	20 12	50 20	♀37%; ♂46% ♀10%; ♂22%
MRID 48773401 Repeat CCA (adult male 11 doses)	RBC Brain	5 10	10 50	13%[D] 15%
MRID 48773401 Repeat CCA	RBC Brain	10 5	50 10	40% 12%

Table A.3.1 TCVP - RBC and Brain Cholinesterase Inhibition NOAELs and LOAELs- % AChEI at LOAEL				
Study	**Compartment**	**NOAEL (mkd)**	**LOAEL (mkd)**	**% ChEI**
(adult female 11 doses)				
MRID 48773401 Repeat CCA (male pup)	RBC Brain	10 10	50 50	33% 16%
MRID 48773401 Repeat CCA (female pup)	RBC Brain	10 10	50 50	19% 19%
MRID 48291101 Gestational CCA (dams 16 doses)	RBC Brain	-	75[A]	- 31%
MRID 48291101 Gestational CCA (fetuses)	RBC Brain	-	75[A]	- 10%
MRID 45570601 21-day	RBC Brain	12 8	20 12	♀14-35%; ♂19-30% ♀16%
MRID 43371201 90-day	RBC Brain	6 142	142 467	♀80%; ♂30% ♀24%
MRID 42980901 MRID 43335101 Chronic 365 days	RBC Brain	5.9	63	♀29% ♀17%
INHALATION – DERMAL				
MRID 48803501 28-day inhalation	RBC	0.05 mg/L	0.5 mg/L	♀35%♂24%
MRID 41342001 21-day dermal	RBC Brain	- -	- -	No inhibition at 1000 mg/kg/day

[A]Lowest dose tested; [B]pre-test was 27%; [C]pre-test was 34%; [D]30% at 50 mkd; 36% at 200 mkd;

Appendix B. Results for BMD/BMDL modeling for TCVP

Benchmark dose (BMD) analyses were performed with EPA's Benchmark Dose Software (Version 2.4) using an exponential model for continuous data[14]. The Hill model was also performed for some data sets, but did not result in the best fit for the data. The data selected for evaluation consisted of decreased brain and red blood cell (RBC) cholinesterase (ChE) activities. Data were analyzed from a 21-day oral toxicity study (MRID 45570601), a 13-week subchronic oral toxicity study (MRID 43371201), and a 2 year chronic oral toxicity study (MRID 42980901); a gestational comparative cholinesterase assay (CCA; MRID 48291101); and a 28-day inhalation toxicity study (MRID 48803501). All data from these studies were considered; however, some data were not amenable to BMD analysis.

OPP has used the exponential model for modeling AChE activity for the OP and *N*-methyl carbamate cumulative risk assessments and with multiple single chemical risk assessments of AChE-inhibiting pesticides. Model runs for AChE activity were conducted with an appropriate benchmark response level (10%). As such the BMD_{10} (estimated dose to result in 10% change from background levels) and $BMDL_{10}$ (the lower 95% confidence level on the BMD_{10}) are provided in the output. Statistical (e.g., goodness of fit values) and graphical results were used in model evaluation.

The results of the repeated oral and inhalation dosing BMD analyses are summarized below in Table B. Good model fit ($p>0.1$) was obtained for the majority of the analyses, with any exceptions being noted.

For exposure to repeated doses the $BMDL_{10}$ for AChE inhibition in the adult female RBCs were similar in the 13-week subchronic study and the 21-day oral toxicity study (8.0 mg/kg/day vs 6.7 mg/kg/day, respectively). Although data from the shorter duration study resulted in a slightly lower BMDL, visual examination of the modeled data provided greater confidence in the 13-week study. For inhalation exposure, the adult male was about twice as sensitive as the adult female (0.023 mg/L in males vs 0.050 mg/L in females).

Table B.1. Results of BMD Exponential Modeling for Brain and RBC AChE Data on TCVP, Repeated Oral Dosing Studies in Rats, Ranging in Duration from 21 days to 2 years.

TCVP Study	Age/Sex	Compartment	BMD Results	
			BMD_{10}	**$BMDL_{10}$**
MRID 43371201 13W Oral – 13 Weeks	Adult Male	Brain	No dose response (analysis not performed)	
	Adult Female	Brain	No dose response	
	Adult Male	RBC	61.6 mg/kg/day	26.3 mg/kg/day
	Adult Female	RBC	10.5 mg/kg/day	8.0 mg/kg/day
MRID 42980901 Chronic Oral Tox – 364, 539, and 721 Days	Adult Female	RBC	No dose-response effect was observed at 364, 539, or 721 days	

[14] J. Bever. Tetrachlorvinphos: Benchmark Dose Analysis of Subchronic and Chronic Studies to Support Derivation of Points of Departure. 5/20/2014. TXR # 0056970. D420286.

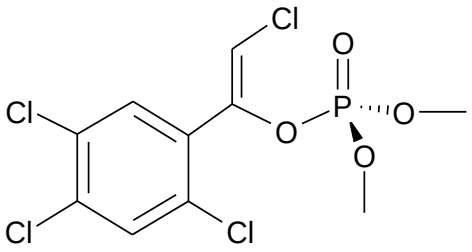
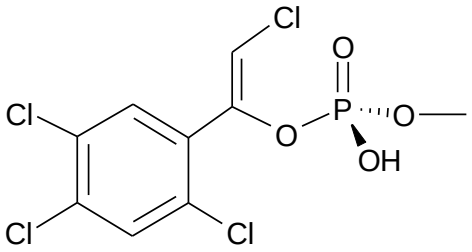
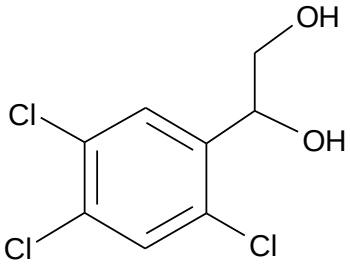
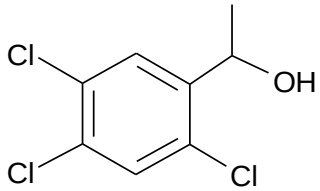
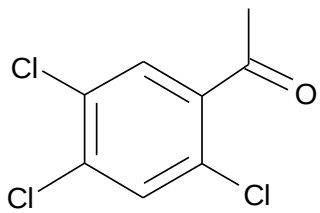
Table B.1. Results of BMD Exponential Modeling for Brain and RBC AChE Data on TCVP, Repeated Oral Dosing Studies in Rats, Ranging in Duration from 21 days to 2 years.				
			BMD Results	
TCVP Study	**Age/Sex**	**Compartment**	**BMD_{10}**	**$BMDL_{10}$**
MRID 45570601 21D Oral Tox – 21 Days	Adult Female	Brain	14.7 mg/kg/day	12.2 mg/kg/day
		RBC	9.9 mg/kg/day	6.7 mg/kg/day
MRID 48803501 28D Inhalation – 28 Days	Adult Male	RBC	0.122 mg/L	0.022 mg/L
	Adult Female	RBC	0.394 mg/L	0.050 mg/L

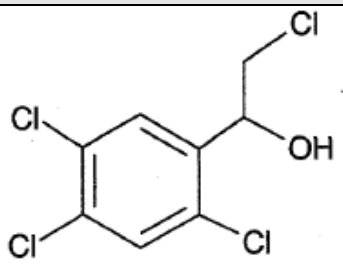
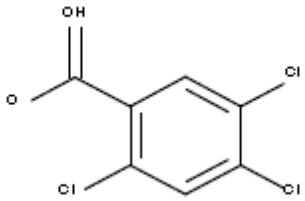
Appendix C. Physical/Chemical Properties for Tetrachlorvinphos

Table C.1 Physicochemical Properties of the Technical Grade Test Compound: Tetrachlorvinphos		
Parameter	Value	Reference [1]
Melting point/range	94.5 ºC	(MRID 41222503)
pH	5.5; 1% solution	(MRID 41222503)
Density	0.83 g/mL	(MRID 41222503)
Water solubility	(25°C) 0.00116 g/100g	(MRID 41222503)
Solvent solubility	(mg/100mg at 25°C) chloroform 80 methanol 21 acetone 44 hexane 0.8 toluene 28	(MRID 41222503)
Vapor pressure	(25°C) 2.6 x 10^{-7} mm Hg	(MRID 41222503)
Dissociation constant, pK_a	non-ionizable	(MRID 41222503)
Octanol/water partition coefficient, Log(K_{OW})	3350 average K_{OW} at 25 ºC	(MRID 41222503)
UV/visible absorption spectrum	Not available	

[1] Cited reference was reviewed under CB No. 7468, 4/3/91, R. Perfetti.

Appendix D. TCVP and Metabolites

Chemical Name	Structure	Physical/Chemical Properties[1]
Tetrachlorvinphos IUPAC: (*Z*)-2-chloro-1-(2,4,5-trichlorophenyl)vinyl dimethyl phosphate CAS: (*1Z*)-2-chloro-1-(2,4,5-trichlorophenyl)ethenyl dimethyl phosphate CAS Reg. No. 22248-79-9 COP(=O)(OC)OC(=CCl)c1cc(Cl)c(Cl)cc1Cl		Molecular weight: 365.96 g/mol VP: 2.6E-07 torr Solubility: 11.6 mg/L Log Kow: 3.53 Koc: 520-1100 L/kg$_{oc}$
Des-O-methyl tetrachlorvinphos IUPAC: (*Z*)-2-chloro-1-(2,4,5-trichlorophenyl)vinyl methyl phosphate CAS: (*1Z*)-2-chloro-1-(2,4,5-trichlorophenyl)ethenyl methyl phosphate COP(=O)(O)OC(=CCl)c1cc(Cl)c(Cl)cc1Cl		Molecular weight: 351.94 g/mol VP: 4.27E-08 torr Solubility: 3.768 mg/L Log Kow: 3.75 Koc: 702-827 L/kg$_{oc}$
1-(2,4,5-trichlorophenyl)ethanediol C(O)(CO)c1cc(Cl)c(Cl)cc1Cl		Molecular weight: 241.5 g/mol VP: 4.37E-06 torr Solubility: 250 mg/L Log Kow: 2.37 Koc: 29-36 L/kg$_{oc}$
TCPEol (SD 15509, AA849) 1-(2,4,5-trichlorophenyl)ethanol 1-(2,4,5-trichlorophenyl)ethan-1-ol CC(O)c1cc(Cl)c(Cl)cc1Cl		Molecular weight: 225.5 g/mol VP: 2.37E-04 torr Solubility: 123 mg/L Log Kow: 3.43 Koc: 319-359 L/kg$_{oc}$
TCPEone (CO300) 2,4,5-trichloroacetophenone CC(=O)c1cc(Cl)c(Cl)cc1Cl		Molecular weight: 223.5 g/mol VP: 6.32E-03 torr Solubility: 27.4 mg/L Log Kow: 3.61 Koc: 492-1,828 L/kg$_{oc}$

Chemical Name	Structure	Physical/Chemical Properties[1]
TCCEol (SD15125, AA576) l-(2,4,5-trichlorophenyl)-2-chloroethanol C(Cl)C(O)c1cc(Cl)c(Cl)cc1Cl		Molecular weight: 260 g/mol VP: 2.11E-05 torr Solubility: 250 mg/L Log Kow: 3.68 Koc: 494-608 L/kg$_{oc}$
TCBA (SD 15917) 2,4,5-Trichlorobenzoic acid C(=O)(O)c1cc(Cl)c(Cl)cc1Cl		Molecular weight: 225.5 g/mol VP: 5.52E-04 torr Solubility: 35.3 mg/L Log Kow: 3.47 Koc: 157-166 L/kg$_{oc}$

1. Physical and chemical properties for degradates obtained through EPISuite 4.11.

Appendix E. International MRLs and U.S. Tolerances

Table E.1. Tetrachlorvinphos: Summary of U.S. and International Tolerances and Maximum Residue Limits.

Commodity	U.S. Tolerances, 40 CFR §180.252 [1]		Codex MRL	Canada's MRL [2]
	Established U.S. Tolerance, ppm	Reassessed U.S. Tolerance, ppm		
Milk, fat (reflecting negligible residues in whole milk)	0.5 (of which not more than 0.05 ppm is tetrachlorvinphos *per se*)	milk: 0.1 (of which not more than 0.04 ppm is tetrachlorvinphos *per se*)	None	None
Cattle and Hog, Fat	Fat of cattle and hog: 0.2 (of which not more than 0.1 ppm is tetrachlorvinphos *per se*)	Fat of cattle and hog: 1.0 (of which not more than 0.8 ppm is tetrachlorvinphos *per se*)	None	1.5 [3]
Cattle and Hog, Muscle	meat of cattle and hog: 2.0 (of which not more than 2.0 ppm is tetrachlorvinphos *per se*)	meat of cattle and hog: 0.3 (of which not more than 0.2 ppm is tetrachlorvinphos *per se*)	None	1.5 [3]
Cattle and Hog, Kidney	kidney of cattle and hog: 1.0 (of which no more than 0.05 ppm is tetrachlorvinphos *per se*)	meat byproducts of cattle and hog : 1.0 (of which no more than 0.6 ppm is tetrachlorvinphos *per se*)	None	1.5 [3]
Cattle and Hog, Liver	liver of cattle and hog: 0.5 (of which no more than 0.05 ppm is tetrachlorvinphos *per se*)		None	1.5 [3]

Table E.1. Tetrachlorvinphos: Summary of U.S. and International Tolerances and Maximum Residue Limits.				
Commodity	U.S. Tolerances, 40 CFR §180.252 [1]		Codex MRL	Canada's MRL [2]
	Established U.S. Tolerance, ppm	Reassessed U.S. Tolerance, ppm		
Cattle and Hog, Meat byproducts	meat byproducts, except kidney and liver of cattle and hog: 1.0		None	1.5 [3]
Eggs	0.2 (of which not more than 0.05 ppm is tetrachlorvinphos *per se*)	0.3 (of which not more than 0.03 ppm is tetrachlorvinphos *per se*)	None	None
Poultry, muscle	meat of poultry: 3.0 (of which not more than 3.0 ppm is tetrachlorvinphos *per se*)	meat of poultry: 0.4 (of which not more than 0.1 ppm is tetrachlorvinphos *per se*)	None	0.75 [4]
Poultry, liver	2.0 (of which not more than 0.05 ppm is tetrachlorvinphos *per se*)	meat byproducts of poultry: 20 (of which not more than 6.0 ppm is tetrachlorvinphos *per se*)	None	0.75 [4]
Poultry, meat byproducts	meat byproducts, except liver, of poultry: 2.0	meat byproducts of poultry: 20 (of which not more than 6.0 ppm is tetrachlorvinphos *per se*)	None	0.75 [4]
Poultry, fat	7.0 (of which not more than 7.0 ppm is tetrachlorvinphos *per se*)	1.4 (of which not more than 0.1 ppm is tetrachlorvinphos *per se*)	None	0.75 [4]
Apples	None	None	None	10
Grapes	None	None	None	10

[1] Current US residue definition is tetrachlorvinphos, des-O-methyl tetrachlorvinphos, 1-(2,4,5-trichlorophenyl)ethanol (free and conjugated forms), 2,4,5-trichloroacetophenone, and 1-(2,4,5-trichlorophenyl)ethanediol. Des-O-methyl tetrachlorvinphos should be added to the definition.

[2] Canada residue definition is 2-chloro-1-(2,4,5-trichlorophenyl) vinyl dimethyl phosphate (TCVP) and its low melting isomer.

[3] Meat, meat byproducts and fat of cattle and hogs, calculated on the fat content.
[4] Meat, meat byproducts and fat of poultry, calculated on the fat content.

Appendix F. Summary of Residential Handler Non-Cancer Exposures and Risks

Table F.1. Residential Handler Non-cancer (Steady State) Exposure and Risk Estimates from Use of TCVP Pet Collar Products. No dermal hazard.										
Exposure Scenario	**Reg. No.**	**Level of Concern**	**Dermal Unit Exposure (mg/lb ai)**	**Inhalation Unit Exposure (mg/lb ai)**	**Maximum Application Rate[1] (lb ai/pet)**	**Amount Handled Daily[2]**	**Dermal**		**Inhalation**	
							Dose (mg/kg/day)[3]	**MOE[4]**	**Dose (mg/kg/day)[5]**	**MOE[6]**
Use of Spot-On Exposure Data - 2012 Residential SOPs										
Application of TCVP Collars	2596-49: Cat	NA	120	Negligible	0.0036: 11 gram collar	2 animals treated per day	0.0012	NA, No Dermal Hazard	Negligible	
	2596-50, 62: Dog				0.0061: 19 gram collar		0.0020			
					0.010: 32 gram collar		0.0034			
	2596-63: Cat				0.0048: 15 gram collar		0.0016			
					0.0055: 17 gram collar		0.0018			
	2596-83: Cat				0.0039: 12 gram collar		0.0013			
					0.0080: 25 gram collar		0.0027			
	2596-84: Dog				0.0061: 19 gram collar		0.0021			
					0.010: 32 gram collar		0.0034			
	2596-139: Cat				0.0032: 10 gram collar		0.0011			
	2596-139: Dog				0.016: 50 gram collar		0.0054			
	11556-164:				0.0072:		0.0024			

	Dog				24 gram collar					
	11556-165: Cat				0.0045: 15 gram collar		0.0015			
Use of TCVP Dust Applicator Exposure Data										
Application of TCVP Collars	2596-49: Cat	Inhalation; 300	1,700	3.1	0.0036: 11 gram collar	2 animals treated per day	0.043	N/A, No Dermal Hazard	0.00033	4,900
	2596-50, 62: Dog				0.0061: 19 gram collar		0.073		0.00055	2,900
					0.010: 32 gram collar		0.12		0.00092	1,700
	2596-63: Cat				0.0048: 15 gram collar		0.057		0.00043	3,700
					0.0055: 17 gram collar		0.065		0.00049	3,300
	2596-83: Cat				0.0039: 12 gram collar		0.046		0.00035	4,600
					0.0080: 25 gram collar		0.096		0.00072	2,200
	2596-84: Dog				0.0061: 19 gram collar		0.073		0.00055	2,900
					0.010: 32 gram collar		0.12		0.00092	1,700
	2596-139: Cat				0.0032: 10 gram collar		0.038		0.00029	5,500
	2596-139: Dog				0.016: 50 gram collar		0.19		0.00144	1,100
	11556-164: Dog				0.0072: 24 gram collar		0.086		0.00065	2,500
	11556-165: Cat				0.0045: 15 gram collar		0.054		0.00041	3,900

1 Based on registered TCVP pet product labels.
2 Based on HED's 2012 Residential SOPs (http://www2.epa.gov/pesticide-science-and-assessing-pesticide-risks/standard-operating-procedures-residential-pesticide).
3 Dermal Dose = Dermal Unit Exposure (mg/lb ai) × Application Rate (lb ai/pet) × Area Treated or Amount Handled (pets/day) × Dermal Absorption Factor (9.6 %) ÷ Body Weight (69 kg). Dermal dose presented only for purpose of calculation of cancer risks for residential handlers.
4 No dermal MOE estimated due to lack of dermal hazard.
5 Inhalation Dose = Inhalation Unit Exposure (mg/lb ai) × Application Rate (lb ai/pet) × Area Treated or Amount Handled (pets/day) ÷ Body Weight (69 kg).
6 Inhalation MOE = Inhalation NOAEL (1.59 mg/kg/day) ÷ Inhalation Dose (mg/kg/day).

Table F.2. Residential Handler Non-cancer (Steady State) Exposure and Risk Estimates from Use of TCVP Dust/Powder and Pump/Trigger Spray Products. No dermal hazard.

Exposure Scenario	Reg. No.	Level of Concern	Dermal Unit Exposure (mg/lb ai)	Inhalation Unit Exposure (mg/lb ai)	Maximum Application Rate[1] (lb ai/pet)	Amount Handled Daily[2]	Dermal		Inhalation	
							Dose (mg/kg/day)[3]	MOE[4]	Dose (mg/kg/day)[5]	MOE[6]
Application of TCVP Dusts/Powders	47000-123: Dog	Inhalation: 300	1,700	3.1	0.00037: small	2 animals treated per day	0.0018	N/A, No Dermal Hazard	0.000034	47,000
					0.00094: medium		0.0044		0.000084	19,000
					0.0015: large		0.0071		0.00013	12,000
	47000-123: Cat				0.000094: small		0.00044		0.0000084	190,000
					0.00023: medium		0.0011		0.000020	79,000
					0.00034: large		0.0016		0.000030	53,000
	2596-78: Cat				0.00062: small		0.0029		0.000056	29,000
					0.0010: large		0.0049		0.000093	17,000
	2596-79; Dog				0.0010: small		0.0049		0.000093	17,000
					0.0021: medium		0.0097		0.00019	8,600
					0.0026: large		0.0122		0.00023	6,900
	67517-82: Dog				0.0011: small		0.0053		0.00011	16,000

Table F.2. Residential Handler Non-cancer (Steady State) Exposure and Risk Estimates from Use of TCVP Dust/Powder and Pump/Trigger Spray Products. No dermal hazard.

Exposure Scenario	Reg. No.	Level of Concern	Dermal Unit Exposure (mg/lb ai)	Inhalation Unit Exposure (mg/lb ai)	Maximum Application Rate[1] (lb ai/pet)	Amount Handled Daily[2]	Dermal		Inhalation	
							Dose (mg/kg/day)[3]	MOE[4]	Dose (mg/kg/day)[5]	MOE[6]
					0.0028: medium		0.013		0.00025	6,300
					0.0045: large		0.021		0.00040	3,900
	67517-82: Cat				0.00028: small		0.0013		0.000025	63,000
					0.00067: medium		0.0032		0.000061	26,000
					0.0010: large		0.0048		0.000091	18,000
Application of TCVP Pump/Trigger Sprays	2596-126, -140: Cat (Trigger)		820	3.3	0.00055: small		0.0013	N/A, No Dermal Hazard	0.000053	30,000
					0.00077: medium		0.0018		0.000074	22,000
	2596-140 Cat (Pump)				0.00011: small		0.00026		0.000011	150,000
					0.00016: large		0.00036		0.000015	110,000
	2596-125, -140: Dog (Trigger)				0.00077: small		0.0018		0.000074	22,000
					0.00088: medium		0.0020		0.000084	19,000
					0.0015: large		0.0035		0.00015	11,000

1 Based on registered TCVP pet product labels.
2 Based on HED's 2012 Residential SOPs (http://www2.epa.gov/pesticide-science-and-assessing-pesticide-risks/standard-operating-procedures-residential-pesticide)
3 Dermal Dose = Dermal Unit Exposure (mg/lb ai) × Application Rate (lb ai/pet) × Area Treated or Amount Handled (pets/day) × Dermal Absorption Factor (9.6 %) ÷ Body Weight (69 kg). Dermal dose presented only for purpose of calculation of cancer risks for residential handlers.
4 No dermal MOE estimated due to lack of dermal hazard.
5 Inhalation Dose = Inhalation Unit Exposure (mg/lb ai) × Application Rate (lb ai/pet) × Area Treated or Amount Handled (pets/day) ÷ Body Weight (69 kg).
6 Inhalation MOE = Inhalation NOAEL (1.59 mg/kg/day) ÷ Inhalation Dose (mg/kg/day).

Appendix G. Summary of Residential Handler Cancer Exposure and Risk Estimates

Table G.1. Residential Handler Cancer Exposure and Risk Estimates from TCVP Pet Collar Products				
Reg No./ Animal Type	**Animal Size**	**Lifestage**	**LADD[1,2]**	**Cancer Risk Estimate[3]**
Pet Collars - Spot-On Exposure Data (2012 Residential SOPs)				
2596-49: Cat	Any	Adult	8.5E-06	1.6E-08
2596-50, 62: Dog	Small		1.4E-05	2.6E-08
	Medium, Large		2.4E-05	4.4E-08
2596-63: Cat	Small		1.1E-05	2.1E-08
	Medium, Large		1.3E-05	2.3E-08
2596-83: Cat	Small		9.0E-06	1.7E-08
	Medium, Large		1.9E-05	3.4E-08
2596-84: Dog	Small		1.4E-05	2.6E-08
	Medium, Large		2.4E-05	4.4E-08
2596-139: Cat	Any		7.5E-06	1.4E-08
2596-139: Dog	Any		3.8E-05	6.9E-08
11556-164: Dog	Any		1.7E-05	3.1E-08
11556-165: Cat	Any		1.1E-05	1.9E-08
Pet Collars - TCVP Dust Applicator Exposure Data				
2596-49: Cat	Any	Adult	1.2E-04	2.2E-07
2596-50, 62: Dog	Small		2.1E-04	3.8E-07
	Medium, Large		3.5E-04	6.4E-07
2596-63: Cat	Small		1.6E-04	3.0E-07
	Medium, Large		1.8E-04	3.4E-07
2596-83: Cat	Small		1.3E-04	2.4E-07
	Medium, Large		2.7E-04	5.0E-07
2596-84: Dog	Small		2.1E-04	3.8E-07
	Medium, Large		3.5E-04	6.4E-07
2596-139: Cat	Any		1.1E-04	2.0E-07
2596-139: Dog	Any		5.4E-04	9.9E-07
11556-164: Dog	Any		2.4E-04	4.5E-07
11556-165: Cat	Any		1.5E-04	2.8E-07

1 Total Lifetime Average Daily Dose (mg/kg/day) = Dermal LADD (mg/kg/day) + Inhalation LADD (mg/kg/day).

2 Dermal and Inhalation LADD equations provided in Appendix A of D426984.

3 Cancer risk estimates = Total LADD × Q_1^*, where $Q_1^* = 1.83 \times 10^{-3}$ $(mg/kg/day)^{-1}$

Table G.2. Residential Handler Cancer Exposure and Risk Estimates from TCVP Pet Products				
Reg No./ Animal Type	**Animal Size**	**Lifestage**	**LADD[1,2]**	**Cancer Risk Estimate[3]**
Dust/Powder				
47000-123: Dog	Small	Adult	1.9E-05	3.5E-08
	Medium		4.7E-05	8.7E-08
	Large		7.6E-05	1.4E-07
47000-123: Cat	Small		4.7E-06	8.7E-09
	Medium		1.1E-05	2.1E-08
	Large		1.7E-05	3.1E-08
2596-78: Cat	Small		3.1E-05	5.7E-08
	Medium		5.2E-05	9.6E-08
2596-79: Dog	Small		5.2E-05	9.6E-08
	Medium		1.0E-04	1.9E-07
	Large		1.3E-04	2.4E-07
67517-82: Dog	Small		5.7E-05	1.0E-07
	Medium		1.4E-04	2.6E-07
	Large		2.3E-04	4.2E-07
67517-82: Cat	Small		1.4E-05	2.6E-08
	Medium		3.4E-05	6.2E-08
	Large		5.1E-05	9.4E-08
Pump/Trigger Sprays				
2596-126: -140: Cat (Trigger)	Small	Adult	1.4E-05	2.5E-08
	Large		1.9E-05	3.5E-08
2596-140: Cat (Pump)	Small		2.8E-06	5.1E-09
	Large		3.9E-06	7.2E-09
2596-125, -140: Dog (Trigger)	Small		1.9E-05	3.5E-08
	Medium		2.2E-05	4.0E-08
	Large		3.9E-05	7.0E-08

1 Total Lifetime Average Daily Dose (mg/kg/day) = Dermal LADD (mg/kg/day) + Inhalation LADD (mg/kg/day).

2 Dermal and Inhalation LADD equations provided in Appendix A of D426984.

3 Cancer risk estimates = Total LADD × Q_1^*, where $Q_1^* = 1.83 \times 10^{-3}$ $(mg/kg/day)^{-1}$

Appendix H. Summary of Residential Post-Application Non-Cancer Exposure and Risk Estimates

Table H.1. Residential Post-Application Non-Cancer (Steady State) Exposure and Risk Estimates from TCVP Pet Collars (Liquid Formulation). Incidental Oral LOC is an MOE = 1,000.

EPA Reg. No./ Animal	Lifestage	Post-application Exposure Scenario / Route of Exposure	Application Rate (mg ai)[1]	Animal Size	Dose (mg/kg/day)[2]	MOEs[3]
Amitraz Exposure Data (MRID 49468801)						
2596-49: Cat	Adult	Dermal	1,650	Small	0.0086	X
				Medium	0.0051	X
				Large	0.0032	X
	Children 1 < 2	Dermal		Small	0.019	X
		Incidental Oral			0.0020	4,100
		Dermal		Medium	0.011	X
		Incidental Oral			0.0012	6,800
		Dermal		Large	0.0070	X
		Incidental Oral			0.00074	11,000
2596-50, 62: Dog	Adult	Dermal	2,770	Small	0.0072	X
			4,670	Large	0.0033	X
	Children 1 < 2	Dermal	2,770	Small	0.016	X
		Incidental Oral			0.0016	4,900
		Dermal	4,670	Large	0.0072	X
		Incidental Oral			0.00076	11,000
2596-83: Cat	Adult	Dermal	1,750	Small	0.0091	X
			3,650	Large	0.0071	X
	Children 1 < 2	Dermal	1,750	Small	0.020	X
		Incidental Oral			0.0021	3,800
		Dermal	3,650	Large	0.016	X
		Incidental Oral			0.0016	4,900
2596-139: Cat	Adult	Dermal	1,460	Small	0.0076	X
				Medium	0.0045	X
				Large	0.0028	X
	Children 1 < 2	Dermal		Small	0.017	X
		Incidental Oral			0.0017	4,600
		Dermal		Medium	0.010	X
		Incidental Oral			0.0010	7,700
		Dermal		Large	0.0062	X
		Incidental Oral			0.00065	12,000
11556-164: Dog	Adult	Dermal	3,290	Small	0.0085	X
				Medium	0.0037	X
				Large	0.0023	X
	Children 1 < 2	Dermal		Small	0.020	X
		Incidental Oral			0.0019	4,100
		Dermal		Medium	0.0080	X
		Incidental Oral			0.00084	9,600

Table H.1. Residential Post-Application Non-Cancer (Steady State) Exposure and Risk Estimates from TCVP Pet Collars (Liquid Formulation). Incidental Oral LOC is an MOE = 1,000.

EPA Reg. No./ Animal	Lifestage	Post-application Exposure Scenario / Route of Exposure	Application Rate (mg ai)[1]	Animal Size	Dose (mg/kg/day)[2]	MOEs[3]
		Dermal		Large	0.0051	X
		Incidental Oral			0.00053	15,000
11556-165: Cat	Adult	Dermal	2,060	Small	0.011	X
				Medium	0.0064	X
				Large	0.0040	X
	Children 1 < 2	Dermal		Small	0.023	X
		Incidental Oral			0.0024	3,300
		Dermal		Medium	0.014	X
		Incidental Oral			0.0015	5,500
		Dermal		Large	0.0088	X
		Incidental Oral			0.00092	8,700
2596-84: Dog	Adult	Dermal	2,770	Small	0.0072	X
			4,670	Large	0.0033	X
	Children 1 < 2	Dermal	2,770	Small	0.016	X
		Incidental Oral			0.0016	4,900
		Dermal	4,670	Large	0.0072	X
		Incidental Oral			0.00076	11,000
2596-139: Dog	Adult	Dermal	7,300	Small	0.019	X
				Medium	0.0081	X
				Large	0.0052	X
	Children 1 < 2	Dermal		Small	0.041	X
		Incidental Oral			0.0043	1,800
		Dermal		Medium	0.018	X
		Incidental Oral			0.0019	4,300
		Dermal		Large	0.011	X
		Incidental Oral			0.0012	6,800
2596-63: Cat	Adult	Dermal	2,190	Small	0.011	X
			2,480	Large	0.0048	X
	Children 1 < 2	Dermal	2,190	Small	0.025	X
		Incidental Oral			0.0026	3,100
		Dermal	2,480	Large	0.011	X
		Incidental Oral			0.0011	7,200

1 Based on registered TCVP pet products as detailed in Table 4.0 of D426984.

2 Dose (mg/kg/day) equations provided in Appendix A of D426984.

3 MOE = Incidental Oral PoD (8.0 mg/kg/day) ÷ Dose (mg/kg/day).

Table H.2. Residential Post-Application Non-Cancer (Steady State) Exposure and Risk Estimates from TCVP Pet Collars (Liquid Formulation). Incidental Oral LOC is an MOE = 1,000.						
EPA Reg. No./ Animal	**Lifestage**	**Post-application Exposure Scenario / Route of Exposure**	**Application Rate (mg ai)[1]**	**Animal Size**	**Dose (mg/kg/day)[2]**	**MOEs[3]**
Davis, M., et al (2008)						
2596-49: Cat	Adult	Dermal	1,650	Small	0.024	X
				Medium	0.015	X
				Large	0.0091	X
	Children 1 < 2	Dermal		Small	0.053	X
		Incidental Oral			0.0056	1,400
		Dermal		Medium	0.032	X
		Incidental Oral			0.0033	2,400
		Dermal		Large	0.020	X
		Incidental Oral			0.0021	3,800
2596-50, 62: Dog	Adult	Dermal	2,770	Small	0.020	X
			4,670	Large	0.0094	X
	Children 1 < 2	Dermal	2,770	Small	0.045	X
		Incidental Oral			0.0047	1,700
		Dermal	4,670	Large	0.021	X
		Incidental Oral			0.0021	3,700
2596-83: Cat	Adult	Dermal	1,750	Small	0.026	X
			3,650	Large	0.020	X
	Children 1 < 2	Dermal	1,750	Small	0.057	X
		Incidental Oral			0.0059	1,400
		Dermal	3,650	Large	0.044	X
		Incidental Oral			0.0046	1,700
2596-139: Cat	Adult	Dermal	1,460	Small	0.021	X
				Medium	0.013	X
				Large	0.0081	X
	Children 1 < 2	Dermal		Small	0.047	X
		Incidental Oral			0.0049	1,600
		Dermal		Medium	0.028	X
		Incidental Oral			0.0030	2,700
		Dermal		Large	0.018	X
		Incidental Oral			0.0018	4,300
11556-164: Dog	Adult	Dermal	3,290	Small	0.024	X
				Medium	0.010	X
				Large	0.0066	X
	Children 1 < 2	Dermal		Small	0.053	X
		Incidental Oral			0.0055	1,400
		Dermal		Medium	0.023	X
		Incidental Oral			0.0024	3,400
		Dermal		Large	0.015	X
		Incidental Oral			0.0015	5,300
11556-165:	Adult	Dermal	2,060	Small	0.030	X

Table H.2. Residential Post-Application Non-Cancer (Steady State) Exposure and Risk Estimates from TCVP Pet Collars (Liquid Formulation). Incidental Oral LOC is an MOE = 1,000.

EPA Reg. No./ Animal	Lifestage	Post-application Exposure Scenario / Route of Exposure	Application Rate (mg ai)[1]	Animal Size	Dose (mg/kg/day)[2]	MOEs[3]
Cat				Medium	0.018	X
				Large	0.011	X
	Children 1 < 2	Dermal		Small	0.066	X
		Incidental Oral			0.0069	1,200
		Dermal		Medium	0.040	X
		Incidental Oral			0.0042	1,900
		Dermal		Large	0.025	X
		Incidental Oral			0.0026	3,100
2596-84: Dog	Adult	Dermal	2,770	Small	0.020	X
			4,670	Large	0.0094	X
	Children 1 < 2	Dermal	2,770	Small	0.045	X
		Incidental Oral			0.0047	1,700
		Dermal	4,670	Large	0.021	X
		Incidental Oral			0.0021	3,700
2596-139: Dog	Adult	Dermal	7,300	Small	0.054	X
				Medium	0.023	X
				Large	0.015	X
	Children 1 < 2	Dermal		Small	0.12	X
		Incidental Oral			0.012	**650**
		Dermal		Medium	0.050	X
		Incidental Oral			0.0053	1,500
		Dermal		Large	0.032	X
		Incidental Oral			0.0034	2,400
2596-63: Cat	Adult	Dermal	2,190	Small	0.032	X
			2,480	Large	0.014	X
	Children 1 < 2	Dermal	2,190	Small	0.071	X
		Incidental Oral			0.0074	1,100
		Dermal	2,480	Large	0.030	X
		Incidental Oral			0.0031	2,500

1 Based on registered TCVP pet products as detailed in Table 4.0 of D426984.

2 Dose (mg/kg/day) equations provided in Appendix A of D426984.

3 MOE = Incidental Oral PoD (8.0 mg/kg/day) ÷ Dose (mg/kg/day).

Table H.3. Residential Post-Application Non-Cancer (Steady State) Exposure and Risk Estimates from TCVP Pet Collars (Solid Formulation). Incidental Oral LOC is an MOE = 1,000.						
EPA Reg. No./ Animal	**Lifestage**	**Post-application Exposure Scenario / Route of Exposure**	**Application Rate (mg ai)[1]**	**Animal Size**	**Dose (mg/kg/day)[2]**	**MOEs[3]**
Amitraz Exposure Data (MRID 49468801)						
2596-49: Cat	Adult	Dermal	1,650	Small	0.23	X
				Medium	0.14	X
				Large	0.086	X
	Children 1 < 2	Dermal		Small	0.51	X
		Incidental Oral			0.49	**16**
		Dermal		Medium	0.31	X
		Incidental Oral			0.30	**27**
		Dermal		Large	0.19	X
		Incidental Oral			0.18	**43**
2596-50 and 2596-62: Dog	Adult	Dermal	2,770	Small	0.19	X
			4,670	Large	0.089	X
	Children 1 < 2	Dermal	2,770	Small	0.43	X
		Incidental Oral			0.41	**19**
		Dermal	4,670	Large	0.20	X
		Incidental Oral			0.19	**42**
2596-83: Cat	Adult	Dermal	1,750	Small	0.24	X
			3,650	Large	0.19	X
	Children 1 < 2	Dermal	1,750	Small	0.54	X
		Incidental Oral			0.52	**15**
		Dermal	3,650	Large	0.42	X
		Incidental Oral			0.41	**20**
2596-139: Cat	Adult	Dermal	1,460	Small	0.20	X
				Medium	0.12	X
				Large	0.076	X
	Children 1 < 2	Dermal		Small	0.45	X
		Incidental Oral			0.44	**18**
		Dermal		Medium	0.27	X
		Incidental Oral			0.26	**31**
		Dermal		Large	0.17	X
		Incidental Oral			0.16	**49**
11556-164: Dog	Adult	Dermal	3,290	Small	0.23	X
				Medium	0.098	X
				Large	0.063	X
	Children 1 < 2	Dermal		Small	0.51	X
		Incidental Oral			0.49	**16**
		Dermal		Medium	0.22	X
		Incidental Oral			0.21	**38**
		Dermal		Large	0.14	X
		Incidental Oral			0.13	**60**
11556-165:	Adult	Dermal	2,060	Small	0.29	X

Table H.3. Residential Post-Application Non-Cancer (Steady State) Exposure and Risk Estimates from TCVP Pet Collars (Solid Formulation). Incidental Oral LOC is an MOE = 1,000.

EPA Reg. No./ Animal	Lifestage	Post-application Exposure Scenario / Route of Exposure	Application Rate (mg ai)[1]	Animal Size	Dose (mg/kg/day)[2]	MOEs[3]
Cat				Medium	0.17	X
				Large	0.11	X
	Children 1 < 2	Dermal		Small	0.63	X
		Incidental Oral			0.61	**13**
		Dermal		Medium	0.38	X
		Incidental Oral			0.37	**22**
		Dermal		Large	0.24	X
		Incidental Oral			0.23	**35**
2596-84: Dog	Adult	Dermal	2,770	Small	0.19	X
			4,670	Large	0.089	X
	Children 1 < 2	Dermal	2,770	Small	0.43	X
		Incidental Oral			0.41	**19**
		Dermal	4,670	Large	0.20	X
		Incidental Oral			0.19	**42**
2596-139: Dog	Adult	Dermal	7,300	Small	0.51	X
				Medium	0.22	X
				Large	0.14	X
	Children 1 < 2	Dermal		Small	1.1	X
		Incidental Oral			1.1	**7.3**
		Dermal		Medium	0.48	X
		Incidental Oral			0.47	**17**
		Dermal		Large	0.31	X
		Incidental Oral			0.30	**27**
2596-63: Cat	Adult	Dermal	2,190	Small	0.31	X
			2,480	Large	0.13	X
	Children 1 < 2	Dermal	2,190	Small	0.68	X
		Incidental Oral			0.65	**12**
		Dermal	2,480	Large	0.29	X
		Incidental Oral			0.28	**29**

1 Based on registered TCVP pet products as detailed in Table 4.0 of D426984.

2 Dose (mg/kg/day) equations provided in Appendix A of D426984.

3 MOE = Incidental Oral PoD (8.0 mg/kg/day) ÷ Dose (mg/kg/day).

Table H.4. Residential Post-Application Non-Cancer (Steady State) Exposure and Risk Estimates from TCVP Dust/Powder and Pump/Trigger Spray Formulations. Incidental Oral LOC is an MOE = 1,000.

EPA Reg. No./ Animal	Lifestage	Post-application Exposure Scenario / Route of Exposure	Application Rate (mg ai)[1]	Animal Size	Dose (mg/kg/day)[2]	MOEs[3]
Dusts/Powders						
47000-123: Dog	Adult	Dermal	170	Small	0.0041	X
			430	Medium	0.0044	X
			680	Large	0.0044	X
	Children 1 < 2	Dermal	170	Small	0.0090	X
		Incidental Oral			0.0087	**920**
		Dermal	430	Medium	0.0096	X
		Incidental Oral			0.0093	**860**
		Dermal	680	Large	0.0098	X
		Incidental Oral			0.0095	**840**
47000-123: Cat	Adult	Dermal	43	Small	0.0020	X
			100	Medium	0.0029	X
			150	Large	0.0027	X
	Children 1 < 2	Dermal	43	Small	0.0045	X
		Incidental Oral			0.0043	1,800
		Dermal	100	Medium	0.0065	X
		Incidental Oral			0.0063	1,300
		Dermal	150	Large	0.0061	X
		Incidental Oral			0.0059	1,400
2596-78: Cat	Adult	Dermal	280	Small	0.013	X
			470	Large	0.0084	X
	Children 1 < 2	Dermal	280	Small	0.030	X
		Incidental Oral			0.029	**280**
		Dermal	470	Large	0.019	X
		Incidental Oral			0.018	**450**
2596-79: Dog	Adult	Dermal	470	Small	0.011	X
			940	Medium	0.0096	X
			1,200	Large	0.0076	X
	Children 1 < 2	Dermal	470	Small	0.025	X
		Incidental Oral			0.024	**330**
		Dermal	940	Medium	0.021	X
		Incidental Oral			0.021	**390**
		Dermal	1,200	Large	0.017	X
		Incidental Oral			0.016	**490**
67517-82: Dog	Adult	Dermal	510	Small	0.012	X
			1,300	Medium	0.013	X
			2,000	Large	0.013	X
	Children 1 < 2	Dermal	510	Small	0.027	X
		Incidental Oral			0.026	**310**
		Dermal	1,300	Medium	0.029	X

Table H.4. Residential Post-Application Non-Cancer (Steady State) Exposure and Risk Estimates from TCVP Dust/Powder and Pump/Trigger Spray Formulations. Incidental Oral LOC is an MOE = 1,000.

EPA Reg. No./ Animal	Lifestage	Post-application Exposure Scenario / Route of Exposure	Application Rate (mg ai)[1]	Animal Size	Dose (mg/kg/day)[2]	MOEs[3]
		Incidental Oral			0.028	**290**
		Dermal	2,000	Large	0.029	X
		Incidental Oral			0.028	**280**
67517-82: Cat	Adult	Dermal	130	Small	0.0061	X
			310	Medium	0.0088	X
			460	Large	0.0082	X
	Children 1 < 2	Dermal	130	Small	0.013	X
		Incidental Oral			0.013	**610**
		Dermal	310	Medium	0.019	X
		Incidental Oral			0.019	**430**
		Dermal	460	Large	0.018	X
		Incidental Oral			0.018	**450**
Pump/Trigger Spray						
2596-126, 140: Cat (Trigger)	Adult	Dermal	250	Small	0.0075	X
			350	Large	0.0039	X
	Children 1 < 2	Dermal	250	Small	0.016	X
		Incidental Oral			0.0017	4,700
		Dermal	350	Large	0.0086	X
		Incidental Oral			0.00090	8,900
2596-140: Cat (Pump)	Adult	Dermal	51	Small	0.0015	X
			71	Large	0.00080	X
	Children 1 < 2	Dermal	51	Small	0.0034	X
		Incidental Oral			0.00035	23,000
		Dermal	71	Large	0.0018	X
		Incidental Oral			0.00018	43,000
2596-125, -140: Dog (Trigger)	Adult	Dermal	350	Small	0.0052	X
			400	Medium	0.0026	X
			700	Large	0.0029	X
	Children 1 < 2	Dermal	350	Small	0.012	X
		Incidental Oral			0.0012	6,600
		Dermal	400	Medium	0.0056	X
		Incidental Oral			0.00059	14,000
		Dermal	700	Large	0.0063	X
		Incidental Oral			0.00066	12,000

1 Based on registered TCVP pet products as detailed in Table 4.0 of D426984.
2 Dose (mg/kg/day) equations provided in Appendix A of D426984.
3 MOE = Incidental Oral PoD (8.0 mg/kg/day) ÷ Dose (mg/kg/day).

Appendix I. Summary of Residential Post-Application Cancer Exposure and Risks

Table I.1 Residential Post-Application Cancer Exposure and Risk Estimates from TCVP Pet Collar - Liquid Formulation				
Animal Type	**Animal Size**	**Lifestage**	**LADD[1,2]**	**Cancer Risk Estimate[3]**
Amitraz Exposure Data (MRID 49468801)				
2596-49: Cat	Small	Adult	9.1E-04	1.7E-06
	Medium		5.4E-04	1.0E-06
	Large		3.4E-04	6.2E-07
2596-50,62: Dog	Small		7.6E-04	1.4E-06
	Large		3.5E-04	6.4E-07
2596-83: Cat	Small		9.6E-04	1.8E-06
	Large		7.5E-04	1.4E-06
2596-139: Cat	Small		8.0E-04	1.5E-06
	Medium		4.8E-04	8.8E-07
	Large		3.0E-04	5.5E-07
11556-164: Dog	Small		9.0E-04	1.7E-06
	Medium		3.9E-04	7.1E-07
	Large		2.5E-04	4.5E-07
11556-165: Cat	Small		1.1E-03	2.1E-06
	Medium		6.8E-04	1.2E-06
	Large		4.2E-04	7.8E-07
2596-84: Dog	Small		7.6E-04	1.4E-06
	Large		3.5E-04	6.4E-07
2596-139: Dog	Small		2.0E-03	3.7E-06
	Medium		8.6E-04	1.6E-06
	Large		5.5E-04	1.0E-06
2596-63: Cat	Small		1.2E-03	2.2E-06
	Large		5.1E-04	9.4E-07
Davis, M., et al (2008)				
2596-49: Cat	Small		5.8E-03	1.1E-05
	Medium		3.5E-03	6.4E-06
	Large		2.2E-03	4.0E-06
2596-50,62: Dog	Small		4.9E-03	8.9E-06
	Large		2.2E-03	4.1E-06
2596-83: Cat	Small		6.2E-03	1.1E-05
	Large		4.8E-03	8.8E-06

Table I.1 Residential Post-Application Cancer Exposure and Risk Estimates from TCVP Pet Collar - Liquid Formulation				
Animal Type	**Animal Size**	**Lifestage**	**LADD[1,2]**	**Cancer Risk Estimate[3]**
2596-139: Cat	Small		5.1E-03	9.4E-06
	Medium		3.1E-03	5.6E-06
	Large		1.9E-03	3.5E-06
11556-164: Dog	Small		5.8E-03	1.1E-05
	Medium		2.5E-03	4.5E-06
	Large		1.6E-03	2.9E-06
11556-165: Cat	Small		7.2E-03	1.3E-05
	Medium		4.3E-03	7.9E-06
	Large		2.7E-03	5.0E-06
2596-84: Dog	Small		4.9E-03	8.9E-06
	Large		2.2E-03	4.1E-06
2596-139: Dog	Small		1.3E-02	2.3E-05
	Medium		5.5E-03	1.0E-05
	Large		3.5E-03	6.4E-06
2596-63: Cat	Small		7.7E-03	1.4E-05
	Large		3.3E-03	6.0E-06

Table I.2 Residential Post-Application Cancer Exposure and Risk Estimates from TCVP Pet Collar - Solid Formulation				
Animal Type	**Animal Size**	**Lifestage**	**LADD[1,2]**	**Cancer Risk Estimate[3]**
Amitraz Exposure Data (MRID 49468801)				
2596-49: Cat	Small	Adult	2.4E-02	4.5E-05
	Medium		1.5E-02	2.7E-05
	Large		9.2E-03	1.7E-05
2596-50,62: Dog	Small		2.1E-02	3.8E-05
	Large		9.4E-03	1.7E-05
2596-83: Cat	Small		2.6E-02	4.7E-05
	Large		2.0E-02	3.7E-05
2596-139: Cat	Small		2.2E-02	4.0E-05
	Medium		1.3E-02	2.4E-05
	Large		8.1E-03	1.5E-05
11556-164: Dog	Small		2.4E-02	4.5E-05
	Medium		1.0E-02	1.9E-05
	Large		6.6E-03	1.2E-05
11556-165: Cat	Small		3.0E-02	5.6E-05
	Medium		1.8E-02	3.3E-05
	Large		1.1E-02	2.1E-05
2596-84: Dog	Small		2.1E-02	3.8E-05
	Large		9.4E-03	1.7E-05
2596-139: Dog	Small		5.4E-02	9.9E-05
	Medium		2.3E-02	4.2E-05
	Large		1.5E-02	2.7E-05
2596-63: Cat	Small		3.2E-02	5.9E-05
	Large		1.4E-02	2.5E-05

Table I.3 Residential Post-Application Cancer Exposure and Risk Estimates from TCVP Pet Products				
Animal Type	**Animal Size**	**Lifestage**	**LADD[1,2]**	**Cancer Risk Estimate[3]**
Dust/Powder				
47000-123: Dog	Small	Adult	5.9E-04	1.1E-06
	Medium		6.3E-04	1.2E-06
	Large		6.4E-04	1.2E-06
47000-123: Cat	Small		2.9E-04	5.4E-07
	Medium		4.2E-04	7.8E-07
	Large		4.0E-04	7.3E-07
2596-78: Cat	Small		1.9E-03	3.6E-06
	Large		1.2E-03	2.2E-06
2596-79: Dog	Small		1.6E-03	3.0E-06
	Medium		1.4E-03	2.5E-06
	Large		1.1E-03	2.0E-06
67517-82: Dog	Small		1.8E-03	3.2E-06
	Medium		1.9E-03	3.5E-06
	Large		1.9E-03	3.5E-06
67517-82: Cat	Small		8.8E-04	1.6E-06
	Medium		1.3E-03	2.3E-06
	Large		1.2E-03	2.2E-06
Pump/Trigger Spray				
2596-126, 140: Cat (Trigger)	Small	Adult	5.3E-04	9.6E-07
	Large		2.8E-04	5.1E-07
2596-140: Cat (Pump)	Small		1.1E-04	2.0E-07
	Large		5.6E-05	1.0E-07
2596-125, -140: Dog (Trigger)	Small		3.7E-04	6.7E-07
	Medium		1.8E-04	3.3E-07
	Large		2.0E-04	3.7E-07

1 Total Lifetime Average Daily Dose (mg/kg/day) = Dermal LADD (mg/kg/day) + Inhalation LADD (mg/kg/day).
2 Dermal and Inhalation LADD equations provided in Appendix A of D426984.
3 Cancer risk estimates = Total LADD × Q1*, where Q1* = 1.83×10^{-3} $(mg/kg/day)^{-1}$

Appendix J. Summary of Occupational Handler Exposures and Risks

Table J.1. TCVP Occupational Handler Non-Cancer (Steady State) Risk Estimates.											
Exposure Scenario	**Crop or Target**	**App. Rate[a] (lb ai/ unit)**	**Area Treated[b] (units/ day)**	**Inhalation Dose (mg/kg/day)**				**Inhalation MOEs (LOC is an MOE = 300)**			
				No R	**PF5 R**	**PF10 R**	**EC**	**No R**	**PF5 R**	**PF10 R**	**EC**
Mixer/Loaders											
(1a) Mixing/ Loading Liquids for Groundboom Applications	Poultry Buildings (Floors)	0.00077 (lb ai/ sq ft)	100,000 (sq ft/day)	2.5E-04	4.9E-05	2.5E-05	9.3E-05	20,000	100,000	200,000	94,000
	Poultry Buildings (Floor Management, Fowl Tick)	0.00064		2.0E-04	4.1E-05	2.0E-05	7.7E-05	2,5000	120,000	250,000	110,000
	Poultry Buildings (Flies Residual)	0.00013		4.1E-05	8.3E-06	4.1E-06	1.6E-05	120,000	600,000	1,200,000	550,000
	Poultry Floor Management	0.000064		2.0E-05	4.1E-06	2.0E-06	7.7E-06	250,000	1,200,000	2,500,000	1,100,000
(1b) Mixing/ Loading Liquids for Paint Applications	Poultry Buildings (Roost)	0.077	2 gallons	4.9E-07	9.8E-08	4.9E-08	1.9E-07	1.0E+07	5.1E+07	1.0E+08	4.7E+07
		0.064 (lb ai/ gallon)		4.1E-07	8.1E-08	4.1E-08	1.5E-07	1.2E+07	6.1E+07	1.2E+08	5.6E+07
(2a) Mixing/ Loading Wettable Powders for Groundboom Applications	Poultry Buildings (Including: Droppings, Floor Management Litter, Fowl Tick)	0.00080 (lb ai/ sq ft)	100,000 sq ft	0.050	0.010	0.0050	0.00028	**170**	870	1,700	31,000
	Dairy Barns, Poultry Houses, Swine Barns, or Other Animal Buildings	0.00032		0.0200	0.040	0.0020	0.00011	430	2,200	4,300	78,000
(2b, 2c) Mixing/ Loading Wettable Powders for Handheld fogger, and Stationary Fogger Applications	Poultry (Floor Management - Litter)	0.0016 (lb ai/ bird)	20,000 birds	0.020	0.0040	0.0020	0.00011	430	2,200	4,300	78,000
		0.00078 (lb ai/ sq ft)	100,000 sq ft	0.049	0.0097	0.0049	0.00027	**180**	890	1,800	32,000
		0.00023		0.014	0.0029	0.0014	0.000080	610	3,000	6,100	110,000
(2d) Mixing/		0.080	2 gallons	1.0E-04	2.0E-05	1.0E-05	5.6E-07	87,000	430,000	870,000	16,000,000

Table J.1. TCVP Occupational Handler Non-Cancer (Steady State) Risk Estimates.											
Exposure Scenario	**Crop or Target**	**App. Rate[a] (lb ai/ unit)**	**Area Treated[b] (units/ day)**	**Inhalation Dose (mg/kg/day)**				**Inhalation MOEs (LOC is an MOE = 300)**			
				No R	**PF5 R**	**PF10 R**	**EC**	**No R**	**PF5 R**	**PF10 R**	**EC**
Loading Wettable Powders for Paint Applications	Poultry (Floor Management – Roost)	(lb ai/ gallon)									
(3a) Mixing/ Loading Dusts for Paint Applications (WP Data as Surrogate)		0.030 (lb ai/ gallon)		3.7E-05	7.5E-06	3.7E-06	2.1E-07	230,000	1,200,000	2,300,000	41,000,000
Applicators											
(4) Groundboom Applications	Poultry Buildings (Including: Droppings, Floor Management Litter, Fowl Tick, Garbage Piles, Manure Piles, Under Feed Troughs)	0.00080 (lb ai/ sq ft)	100,000 sq ft	3.9E-04	7.9E-05	3.9E-05	5.0E-05	6,300	31,000	63,000	170,000
	Poultry Buildings (Including: Ceilings, Floors, Larvicide, Walls)	0.00077		3.8E-04	7.6E-05	3.8E-05	4.8E-05	6,500	33,000	65,000	180,000
	Poultry Buildings (Including: Floor Management, Fowl Tick, Larvicide)	0.00064		3.2E-04	6.3E-05	3.2E-05	4.0E-05	7,800	39,000	78,000	220,000
	Dairy Barns, Poultry Houses, Swine Barns, or Other Animal Buildings	0.00032		1.6E-04	3.2E-05	1.6E-05	2.0E-05	1,6000	78,000	160,000	430,000
	Poultry Buildings (Flies Residual)	0.00013		6.4E-05	1.3E-05	6.4E-06	8.1E-06	39,000	190,000	390,000	1,100,000

Table J.1. TCVP Occupational Handler Non-Cancer (Steady State) Risk Estimates.											
Exposure Scenario	**Crop or Target**	**App. Rate[a] (lb ai/ unit)**	**Area Treated[b] (units/ day)**	**Inhalation Dose (mg/kg/day)**				**Inhalation MOEs (LOC is an MOE = 300)**			
				No R	**PF5 R**	**PF10 R**	**EC**	**No R**	**PF5 R**	**PF10 R**	**EC**
	Poultry (Floor Management)	0.000064		3.2E-05	6.3E-06	3.2E-06	4.0E-06	78,000	390,000	780,000	2,200,000
(5) Open Pour Liquid Additive for Feed Through Applications	Cattle Feed (Concentrate)	0.0039 (lb ai/ animal)	1,000 cows	1.2E-05	2.5E-06	1.2E-06	No Data	400,000	2,000,000	4,000,000	No Data
	Cattle Feed (Concentrate)	0.0022		7.0E-06	1.4E-06	7.0E-07	No Data	710,000	3,600,000	7,100,000	No Data
	Horse Feed	0.0017	500 horses	2.7E-06	5.4E-07	2.7E-07	No Data	1,800,000	9,300,000	18,000,000	No Data
	Swine Feed	0.00060	6,250 pigs	1.2E-05	2.4E-06	1.2E-06	No Data	420,000	2,100,000	4,200,000	No Data
(6a) RTU Pet Collar Applications[1] - Liquid Formulation	Cat (2596-49)	0.0036	8 animals	Inhalation exposures for the application of pet collar products are negligible.							
	Dog (2596-50,62) - Small	0.0061									
	Dog (2596-50,62) - Large	0.010									
	Cat (2596-63) - Small	0.0048									
	Cat (2596-63) - Large	0.0055									
	Cat (2596-83) - Small	0.0039									
	Cat (2596-83) - Large	0.0080									
	Dog (2596-84) – Small	0.0061									
	Dog (2596-84) – Large	0.010									
	Cat (2596-139) - All	0.0032									
	Dog (2596-139) - All	0.016									
	Dog (11556-164) - All	0.0072									
	Cat (11556-165) - All	0.0045									
	Cat (2596-49)	0.0036		0.504	0.101	0.0504	No Data	680	3400	6800	No Data

Table J.1. TCVP Occupational Handler Non-Cancer (Steady State) Risk Estimates.											
Exposure Scenario	**Crop or Target**	**App. Rate[a] (lb ai/ unit)**	**Area Treated[b] (units/ day)**	**Inhalation Dose (mg/kg/day)**				**Inhalation MOEs (LOC is an MOE = 300)**			
				No R	**PF5 R**	**PF10 R**	**EC**	**No R**	**PF5 R**	**PF10 R**	**EC**
(6b) RTU Pet Collar Applications - Dust Formulation	Dog (2596-50,62) - Small	0.0061		0.854	0.171	0.0854	No Data	400	2000	4000	No Data
	Dog (2596-50,62) - Large	0.010		1.4	0.28	0.14	No Data	**250**	1200	2500	No Data
	Cat (2596-63) - Small	0.0048		0.672	0.134	0.0672	No Data	510	2600	5100	No Data
	Cat (2596-63) - Large	0.0055		0.77	0.154	0.077	No Data	450	2200	4500	No Data
	Cat (2596-83) - Small	0.0039		0.546	0.109	0.0546	No Data	630	3200	6300	No Data
	Cat (2596-83) - Large	0.0080		1.12	0.224	0.112	No Data	310	1500	3100	No Data
	Dog (2596-84) – Small	0.0061		0.854	0.171	0.0854	No Data	400	2000	4000	No Data
	Dog (2596-84) – Large	0.010		1.4	0.28	0.14	No Data	**250**	1200	2500	No Data
	Cat (2596-139) - All	0.0032		0.448	0.0896	0.0448	No Data	770	3800	7700	No Data
	Dog (2596-139) - All	0.016		2.24	0.448	0.224	No Data	**150**	770	1500	No Data
	Dog (11556-164) - All	0.0072		1.01	0.202	0.101	No Data	340	1700	3400	No Data
	Cat (11556-165) - All	0.0045		0.63	0.126	0.063	No Data	550	2700	5500	No Data
(7) RTU Dust/Powder Applications	Dog (47000-123) - Small	0.00037		0.00075	0.00015	0.000075	No Data	6,600	33,000	66,000	No Data
	Dog (47000-123) - Medium	0.00094		0.0019	0.00038	0.00019	No Data	2,600	13,000	26,000	No Data
	Dog (47000-123) - Large	0.0015		0.0030	0.00061	0.00030	No Data	1,600	8,200	16,000	No Data
	Cat (47000-123) - Small	0.000090		0.00018	0.000037	0.000018	No Data	27,000	140,000	270,000	No Data
	Cat (47000-123) - Medium	0.00022		0.00045	0.000089	0.000045	No Data	11,000	56,000	110,000	No Data
	Cat (47000-123) - Large	0.00034		0.00069	0.00014	0.000069	No Data	7,200	36,000	72,000	No Data
	Cat (2596-78) - Small	0.00062		0.0013	0.00025	0.00013	No Data	4,000	20,000	40,000	No Data

Table J.1. TCVP Occupational Handler Non-Cancer (Steady State) Risk Estimates.											
Exposure Scenario	**Crop or Target**	**App. Rate[a] (lb ai/ unit)**	**Area Treated[b] (units/ day)**	**Inhalation Dose (mg/kg/day)**				**Inhalation MOEs (LOC is an MOE = 300)**			
				No R	**PF5 R**	**PF10 R**	**EC**	**No R**	**PF5 R**	**PF10 R**	**EC**
	Cat (2596-78) - Large	0.0010		0.0020	0.00041	0.00020	No Data	2,500	12,000	25,000	No Data
	Dog (2596-79) - Small	0.0010		0.0020	0.00041	0.00020	No Data	2,500	12,000	25,000	No Data
	Dog (2596-79) - Medium	0.0021		0.0043	0.00085	0.00043	No Data	1,200	5,900	12,000	No Data
	Dog (2596-79) - Large	0.0026		0.0053	0.0011	0.00053	No Data	940	4,700	9,400	No Data
	Dog (67517-82) - Small	0.0011		0.0022	0.00045	0.00022	No Data	2,200	11,000	22,000	No Data
	Dog (67517-82) - Medium	0.0028		0.0057	0.0011	0.00057	No Data	880	4,400	8,800	No Data
	Dog (67517-82) - Large	0.0045		0.0091	0.0018	0.00091	No Data	550	2,700	5,500	No Data
	Cat (67517-82) - Small	0.00028		0.00057	0.00011	0.000057	No Data	8,800	44,000	88,000	No Data
	Cat (67517-82) - Medium	0.00067		0.0014	0.00027	0.00014	No Data	3,700	18,000	37,000	No Data
	Cat (67517-82) - Large	0.0010		0.0020	0.00041	0.00020	No Data	2,500	12,000	25,000	No Data
(8) RTU Pump/Trigger Spray Applications	Cat (2596-126,140) - Trigger -Small	0.00055		0.00021	0.000042	0.000021	No Data	24,000	120,000	240,000	No Data
	Cat (2596-126,140) - Trigger - Large	0.00077		0.00029	0.000059	0.000029	No Data	17,000	85,000	170,000	No Data
	Cat (2596-140) - Pump - Small	0.00011		0.000042	0.0000084	0.0000042	No Data	120,000	590,000	1,200,000	No Data
	Cat (2596-140) - Pump - Large	0.00016		0.000061	0.000012	0.0000061	No Data	82,000	410,000	820,000	No Data
	Dog (2596-125,-140) - Small	0.00077		0.00029	0.000059	0.000029	No Data	17,000	85,000	170,000	No Data
	Dog (2596-125,-140) - Medium	0.00088		0.00034	0.000067	0.000034	No Data	15,000	74,000	150,000	No Data
	Dog (2596-125,-140) - Large	0.0015		0.00057	0.00012	0.000057	No Data	8,700	43,000	87,000	No Data
Mixers/Loaders/Applicators											
	Beef Cattle - Direct Applied	0.039 (lb ai/	400 animals	0.0068	0.0014	0.00068	No Data	1,300	6,400	13,000	No Data

Table J.1. TCVP Occupational Handler Non-Cancer (Steady State) Risk Estimates.											
Exposure Scenario	**Crop or Target**	**App. Rate[a] (lb ai/ unit)**	**Area Treated[b] (units/ day)**	**Inhalation Dose (mg/kg/day)**				**Inhalation MOEs (LOC is an MOE = 300)**			
				No R	**PF5 R**	**PF10 R**	**EC**	**No R**	**PF5 R**	**PF10 R**	**EC**
		animal)									
		0.032		0.0056	0.0011	0.00056	No Data	1,600	7,800	16,000	No Data
	Woody Borders of Kennels, Yards, Campgrounds, Recreational Parks, Footpaths and Roadways	0.032 (lb ai/ sq ft)	1,000 sq ft (spot)	0.014	0.0028	0.0014	No Data	620	3,100	6,200	No Data
	Beef Cattle - Direct Applied	0.026 (lb ai/ animal)	400 animals	0.0045	0.00090	0.00045	No Data	1,900	9,600	19,000	No Data
	Swine - Direct Applied	0.049		0.0085	0.0017	0.00085	No Data	1,000	5,100	10,000	No Data
	Lactating Dairy Cattle - Direct Applied	0.0049		0.00085	0.00017	0.000085	No Data	10,000	51,000	100,000	No Data
		0.0013		0.00023	0.000045	0.000023	No Data	38,000	190,000	380,000	No Data
(9a) Liquid: Backpack Sprayer	Poultry Buildings (Walls, Ceilings, Floors, Larvicide)	0.00077 lb ai/ sq ft	20,000 sq ft	0.0067	0.0013	0.00067	No Data	1,300	6,500	13,000	No Data
	Poultry Buildings (Floor Management, Fowl Tick, Larvicide)	0.00064		0.0056	0.0011	0.00056	No Data	1,600	7,800	16,000	No Data
	Poultry (Caged) - Direct Applied	0.00032 lb ai/ bird	20,000 birds	0.0028	0.00056	0.00028	No Data	3,100	16,000	31,000	No Data
	Poultry Buildings (Flies Residual) -	0.00013	20,000 sq ft	0.0011	0.00023	0.00011	No Data	3,300	17,000	33,000	No Data
	Poultry (Chicken on Litter) - Direct Applied	0.000078 lb ai/ bird	20,000 birds	0.00068	0.00014	0.000068	No Data	7,700	38,000	77,000	No Data
	Poultry Floor Management	0.000064 lb ai/ sq ft	20,000 sq ft	0.00056	0.00011	0.000056	No Data	13,000	64,000	130,000	No Data
(9b) Liquid:	Beef Cattle - Direct Applied	0.039 (lb ai/	400 animals	0.0068	0.0014	0.00068	No Data	1,300	6,400	13,000	No Data

Table J.1. TCVP Occupational Handler Non-Cancer (Steady State) Risk Estimates.											
Exposure Scenario	**Crop or Target**	**App. Rate[a] (lb ai/ unit)**	**Area Treated[b] (units/ day)**	**Inhalation Dose (mg/kg/day)**				**Inhalation MOEs (LOC is an MOE = 300)**			
				No R	**PF5 R**	**PF10 R**	**EC**	**No R**	**PF5 R**	**PF10 R**	**EC**
Manually-Pressurized Handwand		animal)									
		0.032		0.0056	0.0011	0.00056	No Data	1,600	7,800	16,000	No Data
	Woody Borders of Kennels, Yards, Campgrounds, Recreational Parks, Footpaths and Roadways	0.032 (lb ai/ sq ft)	1,000 sq ft (spot)	0.0139	0.0028	0.0014	No Data	620	3,100	6,200	No Data
	Beef Cattle - Direct Applied	0.026 (lb ai/ animal)	400 animals	0.0045	0.00090	0.00045	No Data	1,900	9,600	19,000	No Data
	Swine - Direct Applied	0.049		0.0085	0.0017	0.00085	No Data	1,000	5,100	10,000	No Data
	Lactating Dairy Cattle - Direct Applied	0.0049		0.00085	0.00017	0.000085	No Data	10,000	51,000	100,000	No Data
		0.0013		0.00023	0.00045	0.000023	No Data	38,000	190,000	380,000	No Data
	Poultry Buildings (Walls, Ceilings, Floors, Larvicide) -	0.00077 lb ai/ sq ft	20,000 sq ft	0.0067	0.0013	0.00067	No Data	1,300	6,500	13,000	No Data
	Poultry Buildings (Floor Management, Fowl Tick, Larvicide)	0.00064		0.0056	0.0011	0.00056	No Data	1,600	7,800	16,000	No Data
	Poultry (Caged) - Direct Applied	0.00031 lb ai/ bird	20,000 birds	0.0027	0.00054	0.00027	No Data	3,200	16,000	32,000	No Data
	Poultry Buildings (Flies Residual) -	0.00013	20,000 sq ft	0.0011	0.00023	0.00011	No Data	7,700	38,000	77,000	No Data
	Poultry (Chicken on Litter) - Direct Applied	0.000078 lb ai/ bird	20,000 birds	0.00068	0.00014	0.000068	No Data	13,000	64,000	130,000	No Data
	Poultry Floor Management	0.000064 lb ai/ sq ft	20,000 sq ft	0.00056	0.00011	0.000056	No Data	16,000	78,000	160,000	No Data
(9c) Liquid:	Beef Cattle - Direct Applied	0.039 (lb ai/	400 animals	0.018	0.0036	0.0018	No Data	490	2,400	4,900	No Data

Table J.1. TCVP Occupational Handler Non-Cancer (Steady State) Risk Estimates.											
Exposure Scenario	**Crop or Target**	**App. Rate[a] (lb ai/ unit)**	**Area Treated[b] (units/ day)**	**Inhalation Dose (mg/kg/day)**				**Inhalation MOEs (LOC is an MOE = 300)**			
				No R	**PF5 R**	**PF10 R**	**EC**	**No R**	**PF5 R**	**PF10 R**	**EC**
Mechanically -Pressurized Handgun		animal)									
		0.032		0.015	0.0029	0.0015	No Data	590	3,000	5,900	No Data
	Woody Borders of Kennels, Yards, Campgrounds, Recreational Parks, Footpaths and Roadways	0.026 (lb ai/ animal)		0.012	0.0024	0.0012	No Data	730	3,600	7,300	No Data
	Beef Cattle - Direct Applied	0.049		0.023	0.0045	0.0023	No Data	380	1,900	3,800	No Data
	Swine - Direct Applied	0.0049		0.0023	0.00045	0.00023	No Data	3,800	19,000	38,000	No Data
	Lactating Dairy Cattle - Direct Applied	0.0013		0.00060	0.00012	0.000060	No Data	15,000	73,000	150,000	No Data
	Poultry Buildings (Walls, Ceilings, Floors, Larvicide) -	0.00077 lb ai/ sq ft	20,000 sq ft	0.018	0.0035	0.0018	No Data	490	2,500	4,900	No Data
	Poultry Buildings (Floor Management, Fowl Tick, Larvicide)	0.00064		0.015	0.0029	0.0015	No Data	590	3,000	5,900	No Data
	Poultry (Caged) - Direct Applied	0.00032 lb ai/ bird	20,000 birds	0.0073	0.0015	0.00073	No Data	1,200	5,900	12,000	No Data
	Poultry Buildings (Flies Residual)	0.00013	20,000 sq ft	0.0030	0.00060	0.00023	No Data	2,900	15,000	29,000	No Data
	Poultry (Chicken on Litter) - Direct Applied	0.000078 lb ai/ bird	20,000 birds	0.0018	0.00036	0.00018	No Data	4,900	24,000	49,000	No Data
	Poultry Floor Management	0.000064 lb ai/ sq ft	20,000 sq ft	0.0015	0.00029	0.00015	No Data	5,900	30,000	59,000	No Data
(9d) Liquid: Backrubber or Facerubber	Cattle - Direct Applied	0.077 (lb ai/ gallon)	50 (gallons/ day)	0.000012	0.0000025	0.0000012	No Data	410,000	2,000,000	4,100,000	No Data

Table J.1. TCVP Occupational Handler Non-Cancer (Steady State) Risk Estimates.											
Exposure Scenario	**Crop or Target**	**App. Rate[a] (lb ai/ unit)**	**Area Treated[b] (units/ day)**	**Inhalation Dose (mg/kg/day)**				**Inhalation MOEs (LOC is an MOE = 300)**			
				No R	**PF5 R**	**PF10 R**	**EC**	**No R**	**PF5 R**	**PF10 R**	**EC**
		0.064		0.000010	0.0000020	0.0000010	No Data	490,000	2,500,000	4,900,000	No Data
(10a) Wettable Powder: Backpack Sprayer	Beef Cattle - Direct Spray	0.040	400 animals	0.0070	0.0014	0.00070	No Data	1,200	6,200	12,000	No Data
	Swine - Direct Spray	0.020		0.0035	0.00070	0.00035	No Data	2,500	12,000	25,000	No Data
	Poultry (Floor Management Litter, Fowl Tick), Poultry Droppings, Manure Piles, Garbage Piles, Under Feed Troughs	0.00080	20,000 sq ft	0.0070	0.0014	0.00070	No Data	1,200	6,200	12,000	No Data
	Poultry (Wire Cages) - Direct Spray	0.00040	20,000 birds	0.0035	0.00070	0.00035	No Data	2,500	12,000	25,000	No Data
	Dairy Barns, Poultry Houses, Swine Barns, or other Animal Buildings	0.00032	20,000 sq ft	0.0028	0.00056	0.00028	No Data	3,100	16,000	31,000	No Data
	Dairy Barns, Poultry Houses, Swine Barns, or other Animal Buildings	0.00016		0.0014	0.00028	0.00014	No Data	6,200	31,000	62,000	No Data
	Dairy Barns, Poultry Houses, Swine Barns, or other Animal Buildings	0.000080		0.00070	0.00014	0.000070	No Data	12,000	62,000	120,000	No Data
	Kennels, Yards, Campgrounds, Picnic Areas, and Recreational Parks	0.000040	1,000 sq ft (spot)	0.000017	0.0000035	0.0000017	No Data	500,000	2,500,000	5,000,000	No Data
(10b) Wettable Powder:	Beef Cattle - Direct Spray	0.040	400 animals	0.0067	0.0014	0.00070	No Data	1,200	6,200	12,000	No Data
	Swine - Direct Spray	0.020		0.0035	0.00070	0.00035	No Data	2,500	12,000	25,000	No Data

Table J.1. TCVP Occupational Handler Non-Cancer (Steady State) Risk Estimates.											
Exposure Scenario	**Crop or Target**	**App. Rate[a] (lb ai/ unit)**	**Area Treated[b] (units/ day)**	**Inhalation Dose (mg/kg/day)**				**Inhalation MOEs (LOC is an MOE = 300)**			
				No R	**PF5 R**	**PF10 R**	**EC**	**No R**	**PF5 R**	**PF10 R**	**EC**
Manually-Pressurized Handwand	Poultry (Floor Management Litter, Fowl Tick), Poultry Droppings, Manure Piles, Garbage Piles, Under Feed Troughs	0.00080	20,000 sq ft	0.0070	0.0014	0.00070	No Data	1,200	6,200	12,000	No Data
	Poultry (Wire Cages) - Direct Spray	0.00040	20,000 birds	0.0035	0.00070	0.00035	No Data	2,500	12,000	25,000	No Data
	Dairy Barns, Poultry Houses, Swine Barns, or other Animal Buildings	0.00032	20,000 sq ft	0.0028	0.00056	0.00028	No Data	3,100	16,000	31,000	No Data
		0.00016		0.0014	0.00028	0.00014	No Data	6,200	31,000	62,000	No Data
		0.000080		0.00070	0.00014	0.000070	No Data	12,000	62,000	120,000	No Data
	Kennels, Yards, Campgrounds, Picnic Areas, and Recreational Parks	0.000040	1,000 sq ft (spot)	0.000017	0.0000035	0.0000017	No Data	500,000	2,500,000	5,000,000	No Data
(10d and 10e) Wettable Powder: Handheld Fogger and Stationary Fogger	Poultry (Floor Management)	0.0016 lb ai/ bird	20,000 birds	No exposure data available for these use patterns.							
		0.00078 lb ai/ sq ft	20,000 sq ft								
	Poultry (Floor Management Litter)	0.00023									
(10f) Wettable Powder: Rotary Duster (Dust - Plunger Data as Surrogate)	Poultry (Floor Management Litter)	0.00023 lb ai/ sq ft	20,000 sq ft	0.11	0.023	0.011	No Data	44	220	440	No Data
(10g) Wettable Powder: Plunger Duster (Dust	Poultry (Floor Management)	0.0016 lb ai/ bird	1,000 birds	0.039	0.0078	0.0039	No Data	130	640	1,300	No Data
		0.00078 lb ai/	1,000 sq ft	0.019	0.0038	0.0019	No Data	260	1,300	2,600	No Data

Table J.1. TCVP Occupational Handler Non-Cancer (Steady State) Risk Estimates.											
Exposure Scenario	**Crop or Target**	**App. Rate[a] (lb ai/ unit)**	**Area Treated[b] (units/ day)**	**Inhalation Dose (mg/kg/day)**				**Inhalation MOEs (LOC is an MOE = 300)**			
				No R	**PF5 R**	**PF10 R**	**EC**	**No R**	**PF5 R**	**PF10 R**	**EC**
Data as Surrogate)		sq ft									
	Poultry (Floor Management Litter)	0.00023		0.0056	0.0011	0.00056	No Data	880	4,400	8,800	No Data
(11a) Dust: Self-Treating Dust Bag	Cattle	0.75 lb ai/ dust bag	10 dust bags	0.18	0.037	0.018	No Data	**27**	140	270	No Data
		0.38		0.093	0.019	0.0093	No Data	**54**	270	540	No Data
		0.13		0.032	0.0064	0.0032	No Data	**160**	780	1,600	No Data
(11b) Dust: Shaker Can	Cattle, Swine – Direct Applied	0.0075 (lb ai /animal)	400 animals	0.76	0.15	0.076	No Data	**6.6**	33	66	No Data
		0.0038		0.39	0.077	0.039	No Data	**13**	65	130	No Data
	Cattle – Direct Applied	0.0013		0.13	0.026	0.013	No Data	38	**190**	380	No Data
	Poultry (Dust Box) – Direct Applied	0.00060 (lb ai/ bird)	1,000 birds	0.15	0.030	0.015	No Data	**33**	160	330	No Data
	Poultry (Floor Management)	0.00030 (lb ai/ sq ft)	1,000 sq ft	0.076	0.015	0.0076	No Data	**66**	330	660	No Data
	Swine - Bedding	0.00020		0.051	0.010	0.0051	No Data	**98**	490	980	No Data
	Poultry (Wire Cage) – Direct Applied	0.00010	1,000 birds	0.025	0.0051	0.0025	No Data	**200**	980	2,000	No Data
(11c) Dust: Rotary Duster (Plunger Data as Surrogate)	Cattle, Swine – Direct Applied	0.0075 (lb ai /animal)	400 animals	0.074	0.015	0.0074	No Data	**68**	340	680	No Data
		0.0038		0.037	0.0075	0.0037	No Data	**130**	670	1,300	No Data
	Cattle – Direct Applied	0.0013		0.013	0.0026	0.0013	No Data	390	2,000	3,900	No Data
	Poultry (Dust Box) – Direct Applied	0.00060 lb ai/ bird	20,000 birds	0.29	0.060	0.029	No Data	**17**	85	170	No Data
	Poultry (Floor Management)	0.00030	20,000 sq ft	0.15	0.029	0.015	No Data	**34**	170	340	No Data
	Poultry (Wire Cage) – Direct Applied	0.00010	20,000 birds	0.049	0.0098	0.0049	No Data	**100**	510	1,000	No Data

Table J.1. TCVP Occupational Handler Non-Cancer (Steady State) Risk Estimates.											
Exposure Scenario	**Crop or Target**	**App. Rate[a] (lb ai/ unit)**	**Area Treated[b] (units/ day)**	**Inhalation Dose (mg/kg/day)**				**Inhalation MOEs (LOC is an MOE = 300)**			
				No R	**PF5 R**	**PF10 R**	**EC**	**No R**	**PF5 R**	**PF10 R**	**EC**
(11d) Dust: Plunger Duster	Poultry (Dust Box) – Direct Applied	0.00060 lb ai/ bird	1,000 birds	0.015	0.0029	0.0015	No Data	340	1,700	3,400	No Data
	Poultry (Floor Management)	0.00030	1,000 sq ft	0.0074	0.0015	0.00074	No Data	680	3,400	6,800	No Data
	Poultry (Wire Cage) – Direct Applied	0.00010	1,000 birds	0.0025	0.00049	0.00025	No Data	2,000	10,000	20,000	No Data
(12a) Paint: Brush or Roller	Poultry (Roost Paint)	0.08 lb ai/ gallon	2 gallons	0.00065	0.00013	0.000065	No Data	13,000	67,000	130,000	No Data
		0.077		0.00063	0.00013	0.000063	No Data	14,000	69,000	140,000	No Data
		0.064		0.00052	0.00010	0.000052	No Data	17,000	83,000	170,000	No Data
		0.03		0.00024	0.000049	0.000024	No Data	36,000	180,000	360,000	No Data
(12b) Paint: Airless	Poultry (Roost Paint)	0.08 lb ai/ gallon	2 gallons	0.0013	0.00026	0.00013	No Data	3,800	19,000	38,000	No Data
		0.077		0.0013	0.00025	0.00013	No Data	4,000	20,000	40,000	No Data
		0.064		0.0010	0.00021	0.00010	No Data	4,800	24,000	48,000	No Data
		0.03		0.00049	0.000097	0.000049	No Data	10,000	51,000	100,000	No Data
(13) Solid Feed Additive for Feed Through Applications via Cup (Granular Data as Surrogate)	Horse Feed	0.0015 (lb ai/ animal)	500 horses	0.00014	0.000027	0.000014	No Data	37,000	180,000	370,000	No Data
		0.00077		0.000070	0.000014	0.0000070	No Data	72,000	360,000	720,000	No Data
	Cattle Feed	0.0022	1,000 cows	0.00040	0.000080	0.000040	No Data	13,000	63,000	130,000	No Data
		0.0017		0.00031	0.000062	0.000031	No Data	16,000	81,000	160,000	No Data

Appendix K. Summary of Occupational Handler Cancer Risk Estimates

Table K.1. TCVP Occupational Handler Cancer Risk Estimates – Private/ Farmer													
Exposure Scenario	**Crop or Target**	**App. Rate[a] (lb ai/ unit)**	**Area Treated[b] (units/ day)**	**Private/Farmer**									
				SL/NoG No R	**SL/G NoR**	**DL/G No R**	**SL/NoG PF5 R**	**SL/G PF5 R**	**DL/G PF5 R**	**SL/No G PF10 R**	**SL.G PF10 R**	**DL/G PF10 R**	**EC**
Mixer/Loaders													
(1a) Mixing/ Loading Liquids for Groundboom Applications	Poultry Buildings (Including: Ceilings, Floors, Larvicide, Walls)	0.00077 (lb ai/ sq ft)	100,000 (sq ft/day)	5E-07	9E-08	7E-08	5E-07	9E-08	7E-08	5E-07	9E-08	7E-08	2E-08
	Poultry Buildings (Including: Floor Management, Fowl Tick, Larvicide)	0.00064		4E-07	8E-08	6E-08	4E-07	8E-08	6E-08	4E-07	7E-08	6E-08	2E-08
	Poultry Buildings (Flies Residual)	0.00013		9E-08	2E-08	1E-08	9E-08	2E-08	1E-08	9E-08	2E-08	1E-08	4E-09
	Poultry Floor Management	0.000064		4E-08	8E-09	6E-09	4E-08	8E-09	6E-09	4E-08	7E-09	6E-09	2E-09
(1b) Mixing/ Loading Liquids for Paint Applications	Poultry Buildings (Roost)	0.077	2 gallons	1E-09	2E-10	1E-10	1E-09	2E-10	1E-10	1E-09	2E-10	1E-10	5E-11
		0.064 (lb ai/ gallon)		9E-10	2E-10	1E-10	9E-10	2E-10	1E-10	9E-10	1E-10	1E-10	4E-11
(2a) Mixing/ Loading Wettable Powders for Groundboom Applications	Poultry Buildings (Including: Droppings, Floor Management Litter, Fowl Tick, Garbage Piles, Manure Piles, Under Feed Troughs)	0.00080 (lb ai/ sq ft)	100,000 sq ft	1E-05	2E-06	1E-06	9E-06	6E-07	5E-07	9E-06	5E-07	4E-07	3E-08
	Dairy Barns, Poultry Houses, Swine Barns, or Other Animal Buildings	0.00032		4E-06	6E-07	6E-07	4E-06	3E-07	2E-07	4E-06	2E-07	2E-07	1E-08
(2b, 2c) Mixing/ Loading Wettable Powders for Handheld	Poultry (Floor Management - Litter)	0.0016 (lb ai/ bird)	20,000 birds	4E-06	6E-07	6E-07	4E-06	3E-07	2E-07	4E-06	2E-07	2E-07	1E-08
		0.00078 (lb ai/ sq ft)	100,000 sq ft	1E-05	1E-06	1E-06	9E-06	6E-07	5E-07	9E-06	5E-07	4E-07	3E-08

Table K.1. TCVP Occupational Handler Cancer Risk Estimates – Private/ Farmer												
Exposure Scenario	**Crop or Target**	**App. Rate[a] (lb ai/ unit)**	**Area Treated[b] (units/ day)**	**Private/Farmer**									
				SL/NoG No R	**SL/G NoR**	**DL/G No R**	**SL/NoG PF5 R**	**SL/G PF5 R**	**DL/G PF5 R**	**SL/No G PF10 R**	**SL.G PF10 R**	**DL/G PF10 R**	**EC**
Fogger, and Stationary Fogger Applications		0.00023		3E-06	4E-07	4E-07	3E-06	2E-07	2E-07	3E-06	2E-07	1E-07	9E-09
(2d) Mixing/ Loading Wettable Powders for Paint Applications	Poultry (Floor Management – Roost)	0.080 (lb ai/ gallon)	2 gallons	2E-08	3E-09	3E-09	2E-08	1E-09	1E-09	2E-08	1E-09	9E-10	6E-11
(3a) Mixing/ Loading Dusts for Paint Applications (WP Data as Surrogate)		0.030 (lb ai/ gallon)		8E-09	1E-09	1E-09	7E-09	5E-10	4E-10	7E-09	4E-10	3E-10	2E-11
Applicators													
(4) Groundboom Applications	Poultry Buildings (Including: Droppings, Floor Management Litter, Fowl Tick, Garbage Piles, Manure Piles, Under Feed Troughs)	0.00080 (lb ai/ sq ft)	100,000 sq ft	2E-07	5E-08	4E-08	2E-07	4E-08	3E-08	2E-07	4E-08	3E-08	1E-08
	Poultry Buildings (Including: Ceilings, Floors, Larvicide, Walls)	0.00077		2E-07	5E-08	4E-08	2E-07	4E-08	3E-08	2E-07	4E-08	3E-08	1E-08
	Poultry Buildings (Including: Floor Management, Fowl Tick, Larvicide)	0.00064		2E-07	4E-08	3E-08	2E-07	3E-08	3E-08	2E-07	3E-08	3E-08	1E-08
	Dairy Barns, Poultry Houses,	0.00032		8E-08	2E-08	2E-08	8E-08	2E-08	1E-08	8E-08	2E-08	1E-08	5E-09

Table K.1. TCVP Occupational Handler Cancer Risk Estimates – Private/ Farmer												
Exposure Scenario	**Crop or Target**	**App. Rate[a] (lb ai/ unit)**	**Area Treated[b] (units/ day)**	**Private/Farmer**								
				SL/NoG No R	**SL/G NoR**	**DL/G No R**	**SL/NoG PF5 R**	**SL/G PF5 R**	**DL/G PF5 R**	**SL/No G PF10 R**	**SL.G PF10 R**	**DL/G PF10 R**	**EC**
	Swine Barns, or Other Animal Buildings												
	Poultry Buildings (Flies Residual)	0.00013		3E-08	8E-09	6E-09	3E-08	7E-09	5E-09	3E-08	7E-09	5E-09	2E-09
	Poultry (Floor Management)	0.000064		2E-08	4E-09	3E-09	2E-08	3E-09	3E-09	2E-08	3E-09	3E-09	1E-09
(5) Open Pour Liquid Additive for Feed Through Applications	Cattle Feed (Concentrate)	0.0039 (lb ai/ animal)	1,000 cows	3E-08	5E-09	4E-09	3E-08	5E-09	4E-09	3E-08	5E-09	3E-09	No Data
	Cattle Feed (Concentrate)	0.0022		2E-08	3E-09	2E-09	1E-08	3E-09	2E-09	1E-08	3E-09	2E-09	No Data
	Horse Feed	0.0017	500 horses	6E-09	1E-09	8E-10	6E-09	1E-09	8E-10	6E-09	1E-09	8E-10	No Data
	Swine Feed	0.00060	6,250 pigs	3E-08	5E-09	4E-09	3E-08	4E-09	3E-09	3E-08	4E-09	3E-09	No Data
(6a) RTU Pet Collar Applications - Liquid Formulation	Cat (2596-49)	0.0036	8 animals	1E-07	6E-08	4E-08	No Data	No Data	No Data	No Data	No Data	No Data	No Data
	Dog (2596-50,62) - Small	0.0061		2E-07	1E-07	6E-08	No Data	No Data	No Data	No Data	No Data	No Data	No Data
	Dog (2596-50,62) - Large	0.010		3E-07	2E-07	1E-07	No Data	No Data	No Data	No Data	No Data	No Data	No Data
	Cat (2596-63) - Small	0.0048		1E-07	8E-08	5E-08	No Data	No Data	No Data	No Data	No Data	No Data	No Data
	Cat (2596-63) - Large	0.0055		2E-07	9E-08	6E-08	No Data	No Data	No Data	No Data	No Data	No Data	No Data
	Cat (2596-83) - Small	0.0039		1E-07	7E-08	4E-08	No Data	No Data	No Data	No Data	No Data	No Data	No Data
	Cat (2596-83) - Large	0.0080		2E-07	1E-07	8E-08	No Data	No Data	No Data	No Data	No Data	No Data	No Data
	Dog (2596-84) – Small	0.0061		2E-07	1E-07	6E-08	No Data	No Data	No Data	No Data	No Data	No Data	No Data
	Dog (2596-84) – Large	0.010		3E-07	2E-07	1E-07	No Data	No Data	No Data	No Data	No Data	No Data	No Data
	Cat (2596-139) - All	0.0032		9E-08	5E-08	3E-08	No Data	No Data	No Data	No Data	No Data	No Data	No Data
	Dog (2596-139) - All	0.016		4E-07	3E-07	2E-07	No Data	No Data	No Data	No Data	No Data	No Data	No Data

Table K.1. TCVP Occupational Handler Cancer Risk Estimates – Private/ Farmer													
Exposure Scenario	**Crop or Target**	**App. Rate[a] (lb ai/ unit)**	**Area Treated[b] (units/ day)**	**Private/Farmer**									
				SL/NoG No R	**SL/G NoR**	**DL/G No R**	**SL/NoG PF5 R**	**SL/G PF5 R**	**DL/G PF5 R**	**SL/No G PF10 R**	**SL.G PF10 R**	**DL/G PF10 R**	**EC**
	Dog (11556-164) - All	0.0072		2E-07	1E-07	7E-08	No Data	No Data	No Data	No Data	No Data	No Data	No Data
	Cat (11556-165) - All	0.0045		1E-07	8E-08	5E-08	No Data	No Data	No Data	No Data	No Data	No Data	No Data
(6b) RTU Pet Collar Applications - Dust Formulation	Cat (2596-49)	0.0036		4E-06	3E-07	2E-07	4E-06	1E-07	1E-07	4E-06	1E-07	8E-08	No Data
	Dog (2596-50,62) - Small	0.0061		6E-06	4E-07	4E-07	6E-06	2E-07	2E-07	6E-06	2E-07	1E-07	No Data
	Dog (2596-50,62) - Large	0.010		1E-05	7E-07	6E-07	1E-05	4E-07	3E-07	1E-05	3E-07	2E-07	No Data
	Cat (2596-63) - Small	0.0048		5E-06	3E-07	3E-07	5E-06	2E-07	1E-07	5E-06	2E-07	1E-07	No Data
	Cat (2596-63) - Large	0.0055		6E-06	4E-07	3E-07	6E-06	2E-07	1E-07	6E-06	2E-07	1E-07	No Data
	Cat (2596-83) - Small	0.0039		4E-06	3E-07	2E-07	4E-06	1E-07	1E-07	4E-06	1E-07	9E-08	No Data
	Cat (2596-83) - Large	0.0080		8E-06	6E-07	5E-07	8E-06	3E-07	2E-07	8E-06	3E-07	2E-07	No Data
	Dog (2596-84) – Small	0.0061		6E-06	4E-07	4E-07	6E-06	2E-07	2E-07	6E-06	2E-07	1E-07	No Data
	Dog (2596-84) – Large	0.010		1E-05	7E-07	6E-07	1E-05	4E-07	3E-07	1E-05	3E-07	2E-07	No Data
	Cat (2596-139) - All	0.0032		3E-06	2E-07	2E-07	3E-06	1E-07	9E-08	3E-06	1E-07	7E-08	No Data
	Dog (2596-139) - All	0.016		2E-05	1E-06	1E-06	2E-05	6E-07	4E-07	2E-05	5E-07	4E-07	No Data
	Dog (11556-164) - All	0.0072		8E-06	5E-07	5E-07	7E-06	3E-07	2E-07	7E-06	2E-07	2E-07	No Data
	Cat (11556-165) - All	0.0045		5E-06	3E-07	3E-07	5E-06	2E-07	1E-07	5E-06	1E-07	1E-07	No Data
(7) RTU Dust/Powder Applications	Dog (47000-123) - Small	0.00037		4E-07	3E-08	2E-08	4E-07	1E-08	1E-08	4E-07	1E-08	8E-09	No Data
	Dog (47000-123) - Medium	0.00094		1E-06	7E-08	6E-08	9E-07	3E-08	3E-08	9E-07	3E-08	2E-08	No Data

Table K.1. TCVP Occupational Handler Cancer Risk Estimates – Private/ Farmer													
Exposure Scenario	**Crop or Target**	**App. Rate[a] (lb ai/ unit)**	**Area Treated[b] (units/ day)**	**Private/Farmer**									
				SL/NoG No R	**SL/G NoR**	**DL/G No R**	**SL/NoG PF5 R**	**SL/G PF5 R**	**DL/G PF5 R**	**SL/No G PF10 R**	**SL.G PF10 R**	**DL/G PF10 R**	**EC**
	Dog (47000-123) - Large	0.0015		2E-06	1E-07	9E-08	2E-06	5E-08	4E-08	2E-06	5E-08	3E-08	No Data
	Cat (47000-123) - Small	0.000090		9E-08	6E-09	6E-09	9E-08	3E-09	2E-09	9E-08	3E-09	2E-09	No Data
	Cat (47000-123) - Medium	0.00022		2E-07	2E-08	1E-08	2E-07	8E-09	6E-09	2E-07	7E-09	5E-09	No Data
	Cat (47000-123) - Large	0.00034		4E-07	2E-08	2E-08	3E-07	1E-08	9E-09	3E-07	1E-08	8E-09	No Data
	Cat (2596-78) - Small	0.00062		6E-07	4E-08	4E-08	6E-07	2E-08	2E-08	6E-07	2E-08	1E-08	No Data
	Cat (2596-78) - Large	0.0010		1E-06	7E-08	6E-08	1E-06	4E-08	3E-08	1E-06	3E-08	2E-08	No Data
	Dog (2596-79) - Small	0.0010		1E-06	7E-08	6E-08	1E-06	4E-08	3E-08	1E-06	3E-08	2E-08	No Data
	Dog (2596-79) - Medium	0.0021		2E-06	2E-07	1E-07	2E-06	8E-08	6E-08	2E-06	7E-08	5E-08	No Data
	Dog (2596-79) - Large	0.0026		3E-06	2E-07	2E-07	3E-06	9E-08	7E-08	3E-06	8E-08	6E-08	No Data
	Dog (67517-82) - Small	0.0011		1E-06	8E-08	7E-08	1E-06	4E-08	3E-08	1E-06	3E-08	2E-08	No Data
	Dog (67517-82) - Medium	0.0028		3E-06	2E-07	2E-07	3E-06	1E-07	8E-08	3E-06	9E-08	6E-08	No Data
	Dog (67517-82) - Large	0.0045		5E-06	3E-07	3E-07	5E-06	2E-07	1E-07	5E-06	1E-07	1E-07	No Data
	Cat (67517-82) - Small	0.00028		3E-07	2E-08	2E-08	3E-07	1E-08	8E-09	3E-07	9E-09	6E-09	No Data
	Cat (67517-82) - Medium	0.00067		7E-07	5E-08	4E-08	7E-07	2E-08	2E-08	7E-07	2E-08	2E-08	No Data
	Cat (67517-82) - Large	0.0010		1E-06	7E-08	6E-08	1E-06	4E-08	3E-08	1E-06	3E-08	2E-08	No Data
(8) RTU Pump/Trigger Spray Applications	Cat (2596-126,140) - Trigger -Small	0.00055		8E-08	7E-08	4E-08	7E-08	7E-08	4E-08	7E-08	7E-08	4E-08	No Data
	Cat (2596-126,140) - Trigger - Large	0.00077		1E-07	1E-07	6E-08	1E-07	1E-07	5E-08	1E-07	1E-07	5E-08	No Data
	Cat (2596-140) - Pump - Small	0.00011		2E-08	1E-08	8E-09	1E-08	1E-08	8E-09	1E-08	1E-08	7E-09	No Data

Table K.1. TCVP Occupational Handler Cancer Risk Estimates – Private/ Farmer												
Exposure Scenario	**Crop or Target**	**App. Rate[a] (lb ai/ unit)**	**Area Treated[b] (units/ day)**	**Private/Farmer**								
				SL/NoG No R	**SL/G NoR**	**DL/G No R**	**SL/NoG PF5 R**	**SL/G PF5 R**	**DL/G PF5 R**	**SL/No G PF10 R**	**SL.G PF10 R**	**DL/G PF10 R**	**EC**
	Cat (2596-140) - Pump - Large	0.00016		2E-08	2E-08	1E-08	2E-08	2E-08	1E-08	2E-08	2E-08	1E-08	No Data
	Dog (2596-125,-140) - Small	0.00077		1E-07	1E-07	6E-08	1E-07	1E-07	5E-08	1E-07	1E-07	5E-08	No Data
	Dog (2596-125,-140) - Medium	0.00088		1E-07	1E-07	7E-08	1E-07	1E-07	6E-08	1E-07	1E-07	6E-08	No Data
	Dog (2596-125,-140) - Large	0.0015		2E-07	2E-07	1E-07	2E-07	2E-07	1E-07	2E-07	2E-07	1E-07	No Data
Mixers/Loaders/Applicators													
(9a) Liquid: Backpack Sprayer	Beef Cattle - Direct Applied	0.039 (lb ai/ animal)	400 animals	4E-06	4E-06	2E-06	4E-06	4E-06	2E-06	4E-06	4E-06	2E-06	No Data
		0.032		1E-06	1E-06	8E-07	1E-06	1E-06	7E-07	1E-06	1E-06	6E-07	No Data
	Woody Borders of Kennels, Yards, Campgrounds, Recreational Parks, Footpaths and Roadways	0.032 (lb ai/ sq ft)	1,000 sq ft (spot)	3E-06	3E-06	2E-06	3E-06	3E-06	2E-06	3E-06	2E-06	2E-06	No Data
	Beef Cattle - Direct Applied	0.026 (lb ai/ animal)	400 animals	9E-07	9E-07	6E-07	8E-07	8E-07	5E-07	8E-07	8E-07	5E-07	No Data
	Swine - Direct Applied	0.049		2E-06	2E-06	1E-06	2E-06	2E-06	1E-06	2E-06	2E-06	1E-06	No Data
	Lactating Dairy Cattle - Direct Applied	0.0049		2E-07	2E-07	1E-07	2E-07	2E-07	1E-07	2E-07	2E-07	1E-07	No Data
		0.0013		5E-08	5E-08	3E-08	4E-08	4E-08	3E-08	4E-08	4E-08	3E-08	No Data
	Poultry Buildings (Walls, Ceilings, Floors, Larvicide)	0.00077 lb ai/ sq ft	20,000 sq ft	1E-06	1E-06	9E-07	1E-06	1E-06	8E-07	1E-06	1E-06	8E-07	No Data
	Poultry Buildings (Floor Management, Fowl Tick, Larvicide)	0.00064		1E-06	1E-06	8E-07	1E-06	1E-06	7E-07	1E-06	1E-06	6E-07	No Data
	Poultry (Caged) - Direct Applied	0.00031 lb ai/	20,000 birds	6E-07	6E-07	4E-07	5E-07	5E-07	3E-07	5E-07	5E-07	3E-07	No Data

Table K.1. TCVP Occupational Handler Cancer Risk Estimates – Private/ Farmer													
Exposure Scenario	**Crop or Target**	**App. Rate[a] (lb ai/ unit)**	**Area Treated[b] (units/ day)**	**Private/Farmer**									
				SL/NoG No R	**SL/G NoR**	**DL/G No R**	**SL/NoG PF5 R**	**SL/G PF5 R**	**DL/G PF5 R**	**SL/No G PF10 R**	**SL.G PF10 R**	**DL/G PF10 R**	**EC**
		bird											
	Poultry Buildings (Flies Residual) -	0.00013	20,000 sq ft	5E-07	5E-07	4E-07	5E-07	5E-07	3E-07	5E-07	5E-07	3E-07	No Data
	Poultry (Chicken on Litter) - Direct Applied	0.000078 lb ai/ bird	20,000 birds	2E-07	2E-07	2E-07	2E-07	2E-07	1E-07	2E-07	2E-07	1E-07	No Data
	Poultry Floor Management	0.000064 lb ai/ sq ft	20,000 sq ft	1E-07	1E-07	9E-08	1E-07	1E-07	8E-08	1E-07	1E-07	8E-08	No Data
(9b) Liquid: Manually-Pressurized Handwand	Beef Cattle - Direct Applied	0.039 (lb ai/ animal)	400 animals	5E-05	4E-07	3E-07	5E-05	2E-07	2E-07	5E-05	2E-07	2E-07	No Data
		0.032		4E-05	3E-07	3E-07	4E-05	2E-07	2E-07	4E-05	2E-07	2E-07	No Data
	Woody Borders of Kennels, Yards, Campgrounds, Recreational Parks, Footpaths and Roadways	0.032 (lb ai/ sq ft)	1,000 sq ft (spot)	1E-04	7E-07	7E-07	1E-04	5E-07	4E-07	1E-04	5E-07	4E-07	No Data
	Beef Cattle - Direct Applied	0.026 (lb ai/ animal)	400 animals	3E-05	2E-07	2E-07	3E-05	2E-07	1E-07	3E-05	1E-07	1E-07	No Data
	Swine - Direct Applied	0.049		6E-05	4E-07	4E-07	6E-05	3E-07	3E-07	6E-05	3E-07	2E-07	No Data
	Lactating Dairy Cattle - Direct Applied	0.0049		6E-06	4E-08	4E-08	6E-06	3E-08	3E-08	6E-06	3E-08	2E-08	No Data
		0.0013		2E-06	1E-08	1E-08	2E-06	8E-09	7E-09	2E-06	7E-09	6E-09	No Data
	Poultry Buildings (Walls, Ceilings, Floors, Larvicide) -	0.00077 lb ai/ sq ft	20,000 sq ft	5E-05	4E-07	3E-07	5E-05	2E-07	2E-07	5E-05	2E-07	2E-07	No Data
	Poultry Buildings (Floor Management, Fowl Tick, Larvicide)	0.00064		4E-05	3E-07	3E-07	4E-05	2E-07	2E-07	4E-05	2E-07	2E-07	No Data

Table K.1. TCVP Occupational Handler Cancer Risk Estimates – Private/ Farmer												
Exposure Scenario	**Crop or Target**	**App. Rate[a] (lb ai/ unit)**	**Area Treated[b] (units/ day)**	**Private/Farmer**								
				SL/NoG No R	**SL/G NoR**	**DL/G No R**	**SL/NoG PF5 R**	**SL/G PF5 R**	**DL/G PF5 R**	**SL/No G PF10 R**	**SL.G PF10 R**	**DL/G PF10 R**	**EC**
	Poultry (Caged) - Direct Applied	0.00031 lb ai/ bird	20,000 birds	2E-05	1E-07	1E-07	2E-05	1E-07	8E-08	2E-05	9E-08	8E-08	No Data
	Poultry Buildings (Flies Residual) -	0.00013	20,000 sq ft	2E-05	1E-07	1E-07	2E-05	9E-08	8E-08	2E-05	9E-08	7E-08	No Data
	Poultry (Chicken on Litter) - Direct Applied	0.000078 lb ai/ bird	20,000 birds	8E-06	6E-08	5E-08	8E-06	4E-08	3E-08	8E-06	4E-08	3E-08	No Data
	Poultry Floor Management	0.000064 lb ai/ sq ft	20,000 sq ft	5E-06	4E-08	3E-08	5E-06	2E-08	2E-08	5E-06	2E-08	2E-08	No Data
(9c) Liquid: Mechanically -Pressurized Handgun	Beef Cattle - Direct Applied	0.039 (lb ai/ animal)	400 animals	1E-06	7E-07	6E-07	9E-07	4E-07	3E-07	9E-07	3E-07	2E-07	No Data
		0.032		1E-06	6E-07	5E-07	8E-07	3E-07	2E-07	7E-07	3E-07	2E-07	No Data
	Woody Borders of Kennels, Yards, Campgrounds, Recreational Parks, Footpaths and Roadways	0.026 (lb ai/ animal)		8E-07	5E-07	4E-07	6E-07	3E-07	2E-07	6E-07	2E-07	1E-07	No Data
	Beef Cattle - Direct Applied	0.049		2E-06	9E-07	7E-07	1E-06	5E-07	3E-07	1E-06	4E-07	3E-07	No Data
	Swine - Direct Applied	0.0049		2E-07	9E-08	7E-08	1E-07	5E-08	3E-08	1E-07	4E-08	3E-08	No Data
	Lactating Dairy Cattle - Direct Applied	0.0013		4E-08	2E-08	2E-08	3E-08	1E-08	8E-09	3E-08	1E-08	7E-09	No Data
	Poultry Buildings (Walls, Ceilings, Floors, Larvicide) -	0.00077 lb ai/ sq ft	20,000 sq ft	1E-06	7E-07	6E-07	9E-07	4E-07	3E-07	9E-07	3E-07	2E-07	No Data
	Poultry Buildings (Floor Management, Fowl Tick, Larvicide)	0.00064		1E-06	6E-07	5E-07	8E-07	3E-07	2E-07	7E-07	3E-07	2E-07	No Data

Table K.1. TCVP Occupational Handler Cancer Risk Estimates – Private/ Farmer												
Exposure Scenario	**Crop or Target**	**App. Rate[a] (lb ai/ unit)**	**Area Treated[b] (units/ day)**	**Private/Farmer**								
				SL/NoG No R	**SL/G NoR**	**DL/G No R**	**SL/NoG PF5 R**	**SL/G PF5 R**	**DL/G PF5 R**	**SL/No G PF10 R**	**SL.G PF10 R**	**DL/G PF10 R**	**EC**
	Poultry (Caged) - Direct Applied	0.00031 lb ai/ bird	20,000 birds	5E-07	3E-07	2E-07	4E-07	2E-07	1E-07	4E-07	1E-07	9E-08	No Data
	Poultry Buildings (Flies Residual)	0.00013	20,000 sq ft	5E-07	3E-07	2E-07	4E-07	1E-07	1E-07	3E-07	1E-07	8E-08	No Data
	Poultry (Chicken on Litter) - Direct Applied	0.000078 lb ai/ bird	20,000 birds	2E-07	1E-07	9E-08	2E-07	6E-08	4E-08	2E-07	6E-08	4E-08	No Data
	Poultry Floor Management	0.000064 lb ai/ sq ft	20,000 sq ft	1E-07	7E-08	6E-08	9E-08	4E-08	3E-08	9E-08	3E-08	2E-08	No Data
(9d) Liquid: Backrubber or Facerubber	Cattle - Direct Applied	0.077 (lb ai/ gallon)	50 (gallons/ day)	3E-08	5E-09	4E-09	3E-08	5E-09	3E-09	3E-08	5E-09	3E-09	No Data
		0.064		2E-08	4E-09	3E-09	2E-08	4E-09	3E-09	2E-08	4E-09	3E-09	No Data
(10a) Wettable Powder: Backpack Sprayer	Beef Cattle - Direct Spray	0.040	400 animals	1E-06	1E-06	9E-07	1E-06	1E-06	8E-07	1E-06	1E-06	8E-07	No Data
	Swine - Direct Spray	0.020		7E-07	7E-07	5E-07	6E-07	6E-07	4E-07	6E-07	6E-07	4E-07	No Data
	Poultry (Floor Management Litter, Fowl Tick), Poultry Droppings, Manure Piles, Garbage Piles, Under Feed Troughs	0.00080	20,000 sq ft	1E-06	1E-06	9E-07	1E-06	1E-06	8E-07	1E-06	1E-06	8E-07	No Data
	Poultry (Wire Cages) - Direct Spray	0.00040	20,000 birds	7E-07	7E-07	5E-07	6E-07	6E-07	4E-07	6E-07	6E-07	4E-07	No Data
	Dairy Barns, Poultry Houses, Swine Barns, or other Animal Buildings	0.00032	20,000 sq ft	6E-07	6E-07	4E-07	5E-07	5E-07	3E-07	5E-07	5E-07	3E-07	No Data
	Dairy Barns, Poultry Houses, Swine Barns, or	0.00016		3E-07	3E-07	2E-07	3E-07	3E-07	2E-07	3E-07	2E-07	2E-07	No Data

Table K.1. TCVP Occupational Handler Cancer Risk Estimates – Private/ Farmer												
Exposure Scenario	**Crop or Target**	**App. Rate[a] (lb ai/ unit)**	**Area Treated[b] (units/ day)**	**Private/Farmer**								
				SL/NoG No R	**SL/G NoR**	**DL/G No R**	**SL/NoG PF5 R**	**SL/G PF5 R**	**DL/G PF5 R**	**SL/No G PF10 R**	**SL.G PF10 R**	**DL/G PF10 R**	**EC**
	other Animal Buildings												
	Dairy Barns, Poultry Houses, Swine Barns, or other Animal Buildings	0.000080		1E-07	1E-07	9E-08	1E-07	1E-07	8E-08	1E-07	1E-07	8E-08	No Data
	Kennels, Yards, Campgrounds, Picnic Areas, and Recreational Parks	0.000040	1,000 sq ft (spot)	3E-09	3E-09	2E-09	3E-09	3E-09	2E-09	3E-09	3E-09	2E-09	No Data
(10b) Wettable Powder: Manually-Pressurized Handwand	Beef Cattle - Direct Spray	0.040	400 animals	5E-05	4E-07	3E-07	5E-05	2E-07	2E-07	5E-05	2E-07	2E-07	No Data
	Swine - Direct Spray	0.020		2E-05	2E-07	2E-07	2E-05	1E-07	1E-07	2E-05	1E-07	1E-07	No Data
	Poultry (Floor Management Litter, Fowl Tick), Poultry Droppings, Manure Piles, Garbage Piles, Under Feed Troughs	0.00080	20,000 sq ft	5E-05	4E-07	3E-07	5E-05	2E-07	2E-07	5E-05	2E-07	2E-07	No Data
	Poultry (Wire Cages) - Direct Spray	0.00040	20,000 birds	2E-05	2E-07	2E-07	2E-05	1E-07	1E-07	2E-05	1E-07	1E-07	No Data
	Dairy Barns, Poultry Houses, Swine Barns, or other Animal Buildings	0.00032	20,000 sq ft	2E-05	1E-07	1E-07	2E-05	1E-07	8E-08	2E-05	9E-08	8E-08	No Data
		0.00016		1E-05	7E-08	7E-08	1E-05	5E-08	4E-08	1E-05	5E-08	4E-08	No Data
		0.000080		5E-06	4E-08	3E-08	5E-06	2E-08	2E-08	5E-06	2E-08	2E-08	No Data
	Kennels, Yards, Campgrounds, Picnic Areas, and Recreational Parks	0.000040	1,000 sq ft (spot)	1E-07	9E-10	8E-10	1E-07	6E-10	5E-10	1E-07	6E-10	5E-10	No Data
(10d and 10e) Wettable Powder: Handheld	Poultry (Floor Management)	0.0016 lb ai/ bird	20,000 birds	No exposure data available for these use patterns.									
		0.00078	20,000										

Table K.1. TCVP Occupational Handler Cancer Risk Estimates – Private/ Farmer													
Exposure Scenario	**Crop or Target**	**App. Rate[a] (lb ai/ unit)**	**Area Treated[b] (units/ day)**	**Private/Farmer**									
				SL/NoG No R	**SL/G NoR**	**DL/G No R**	**SL/NoG PF5 R**	**SL/G PF5 R**	**DL/G PF5 R**	**SL/No G PF10 R**	**SL.G PF10 R**	**DL/G PF10 R**	**EC**
Fogger and Stationary Fogger		lb ai/ sq ft	sq ft										
	Poultry (Floor Management Litter)	0.00023											
(10f) Wettable Powder: Rotary Duster (Dust - Plunger Data as Surrogate)	Poultry (Floor Management Litter)	0.00023 lb ai/ sq ft	20,000 sq ft	6E-04	9E-05	7E-05	6E-04	8E-05	7E-05	6E-04	8E-05	7E-05	No Data
(10g) Wettable Powder: Plunger Duster (Dust Data as Surrogate)	Poultry (Floor Management)	0.0016 lb ai/ bird	1,000 birds	9E-06	2E-06	2E-06	8E-06	1E-06	1E-06	8E-06	1E-06	1E-06	No Data
		0.00078 lb ai/ sq ft	1,000 sq ft	4E-06	1E-06	9E-07	4E-06	7E-07	6E-07	4E-06	6E-07	5E-07	No Data
	Poultry (Floor Management Litter)	0.00023		1E-06	3E-07	3E-07	1E-06	2E-07	2E-07	1E-06	2E-07	2E-07	No Data
(11a) Dust: Self-Treating Dust Bag	Cattle	0.75 lb ai/ dust bag	10 dust bags	4E-05	1E-05	9E-06	4E-05	7E-06	6E-06	4E-05	6E-06	5E-06	No Data
		0.38		2E-05	5E-06	4E-06	2E-05	3E-06	3E-06	2E-05	3E-06	3E-06	No Data
		0.13		7E-06	2E-06	2E-06	7E-06	1E-06	1E-06	7E-06	1E-06	9E-07	No Data
(11b) Dust: Shaker Can	Cattle, Swine – Direct Applied	0.0075 (lb ai /animal)	400 animals	4E-04	3E-05	2E-05	4E-04	1E-05	1E-05	4E-04	1E-05	8E-06	No Data
		0.0038		2E-04	1E-05	1E-05	2E-04	7E-06	5E-06	2E-04	6E-06	4E-06	No Data
	Cattle – Direct Applied	0.0013		7E-05	5E-06	4E-06	7E-05	2E-06	2E-06	6E-05	2E-06	1E-06	No Data
	Poultry (Dust Box) – Direct Applied	0.00060 (lb ai/ bird)	1,000 birds	8E-05	5E-06	5E-06	8E-05	3E-06	2E-06	8E-05	2E-06	2E-06	No Data
	Poultry (Floor Management)	0.00030 (lb ai/ sq ft)	1,000 sq ft	4E-05	3E-06	2E-06	4E-05	1E-06	1E-06	4E-05	1E-06	8E-07	No Data

Table K.1. TCVP Occupational Handler Cancer Risk Estimates – Private/ Farmer												
Exposure Scenario	**Crop or Target**	**App. Rate[a] (lb ai/ unit)**	**Area Treated[b] (units/ day)**	**Private/Farmer**								
				SL/NoG No R	**SL/G NoR**	**DL/G No R**	**SL/NoG PF5 R**	**SL/G PF5 R**	**DL/G PF5 R**	**SL/No G PF10 R**	**SL.G PF10 R**	**DL/G PF10 R**	**EC**
	Swine - Bedding	0.00020		3E-05	2E-06	2E-06	3E-05	9E-07	7E-07	3E-05	8E-07	6E-07	No Data
	Poultry (Wire Cage) – Direct Applied	0.00010	1,000 birds	1E-05	9E-07	8E-07	1E-05	5E-07	3E-07	1E-05	4E-07	3E-07	No Data
(11c) Dust: Rotary Duster (Plunger Data as Surrogate)	Cattle, Swine – Direct Applied	0.0075 (lb ai /animal)	400 animals	6E-04	9E-05	7E-05	6E-04	8E-05	7E-05	6E-04	8E-05	7E-05	No Data
		0.0038		6E-04	9E-05	7E-05	6E-04	8E-05	7E-05	6E-04	8E-05	7E-05	No Data
	Cattle – Direct Applied	0.0013		6E-04	9E-05	7E-05	6E-04	8E-05	7E-05	6E-04	8E-05	7E-05	No Data
	Poultry (Dust Box) – Direct Applied	0.00060 lb ai/ bird	20,000 birds	6E-04	9E-05	7E-05	6E-04	8E-05	7E-05	6E-04	8E-05	7E-05	No Data
	Poultry (Floor Management)	0.00030	20,000 sq ft	6E-04	9E-05	7E-05	6E-04	8E-05	7E-05	6E-04	8E-05	7E-05	No Data
	Poultry (Wire Cage) – Direct Applied	0.00010	20,000 birds	6E-04	9E-05	7E-05	6E-04	8E-05	7E-05	6E-04	8E-05	7E-05	No Data
(11d) Dust: Plunger Duster	Poultry (Dust Box) – Direct Applied	0.00060 lb ai/ bird	1,000 birds	6E-04	9E-05	7E-05	6E-04	8E-05	7E-05	6E-04	8E-05	7E-05	No Data
	Poultry (Floor Management)	0.00030	1,000 sq ft	1E-05	2E-06	1E-06	1E-05	2E-06	1E-06	1E-05	2E-06	1E-06	No Data
	Poultry (Wire Cage) – Direct Applied	0.00010	1,000 birds	3E-04	4E-05	4E-05	3E-04	4E-05	3E-05	3E-04	4E-05	3E-05	No Data
(12a) Paint: Brush or Roller	Poultry (Roost Paint)	0.08 lb ai/ gallon	2 gallons	9E-07	1E-07	1E-07	9E-07	1E-07	1E-07	9E-07	1E-07	1E-07	No Data
		0.077		9E-07	1E-07	1E-07	9E-07	1E-07	1E-07	9E-07	1E-07	1E-07	No Data
		0.064		7E-08	1E-08	1E-08	7E-08	1E-08	9E-09	7E-08	1E-08	9E-09	No Data
		0.03		3E-07	5E-08	5E-08	3E-07	5E-08	4E-08	3E-07	4E-08	4E-08	No Data
(12b) Paint: Airless	Poultry (Roost Paint)	0.08 lb ai/ gallon	2 gallons	2E-07	9E-08	8E-08	2E-07	6E-08	6E-08	2E-07	6E-08	6E-08	No Data
		0.077		2E-07	8E-08	8E-08	2E-07	6E-08	6E-08	2E-07	6E-08	5E-08	No Data
		0.064		2E-08	7E-09	6E-09	2E-08	5E-09	5E-09	2E-08	5E-09	4E-09	No Data

Table K.1. TCVP Occupational Handler Cancer Risk Estimates – Private/ Farmer												
Exposure Scenario	**Crop or Target**	**App. Rate[a] (lb ai/ unit)**	**Area Treated[b] (units/ day)**	**Private/Farmer**								
				SL/NoG No R	**SL/G NoR**	**DL/G No R**	**SL/NoG PF5 R**	**SL/G PF5 R**	**DL/G PF5 R**	**SL/No G PF10 R**	**SL.G PF10 R**	**DL/G PF10 R**	**EC**
		0.03		9E-08	3E-08	3E-08	8E-08	2E-08	2E-08	8E-08	2E-08	2E-08	No Data
(13) Solid Feed Additive for Feed Through Applications via Cup (Granular Data as Surrogate)	Horse Feed	0.0015 (lb ai/ animal)	500 horses	1E-09	7E-10	7E-10	6E-10	2E-10	2E-10	6E-10	1E-10	1E-10	No Data
		0.00077		6E-10	3E-10	3E-10	3E-10	9E-11	9E-11	3E-10	6E-11	6E-11	No Data
	Cattle Feed	0.0022	1,000 cows	2E-08	1E-08	1E-08	9E-09	3E-09	3E-09	8E-09	2E-09	2E-09	No Data
		0.0017		1E-08	7E-09	7E-09	7E-09	2E-09	2E-09	7E-09	1E-09	1E-09	No Data

Appendix L. Summary of TCVP Labels and Use Directions

Table L.1. Summary of TCVP Occupational Livestock Use					
EPA Reg. No.	**Use Site**	**Applic. Type/ Equipment**	**Applic. Rate (lb ai/A)**	**PPE**	**Use Directions and Limitations**
Feed Through (Solid Additive)					
270-164	Horse Oral Larvicide	Cup	1,100 lb horse: 0.0015 lb ai/animal/day (2.468% ai)	Baseline clothing and gloves	Feed to horses through top dress on grain or mixed with the horse's total ration. 300-500 lb horse: Feed 2/5 oz. per horse per day 500-700 lb horse: Feed 2/5 oz. per horse per day 700-900 lb horse: Feed 2/5 oz. per horse per day 900-1,100 lb horse: Feed 2/5 oz. per horse per day For larger horses over 1,00 lbs. of body weight feed ¼ oz. for each 250 lbs.
270-165			1,100 lb horse: 0.00077 lb ai/animal/day (1.234% ai)		Feed the recommended dosage to each horse separately to make certain he receives the full portion. Feed to horses through top dress on grain or mixed with the horse's total ration. 300-500 lb horse: Feed 2/5 oz. per horse per day 500-700 lb horse: Feed 2/5 oz. per horse per day 700-900 lb horse: Feed 2/5 oz. per horse per day 900-1,100 lb horse: Feed 2/5 oz. per horse per day For larger horses over 1,100 lbs. of body weight feed ¼ oz. for each 250 lbs.
7698-7	Beef Cattle Oral Larvicide		1,400 lb beef cow (estimated max): 0.0022 lb ai/animal/day		Mix uniformly with cattle feeds following standard mixing procedures. Common feed mixing equipment (i.e., vertical mixers, horizontal blenders, mixer/feeder truck) may be used to prepare formulated feeds. Can be offered by force-feeding or free-choice feeding, but not both. Feed 1/3 lb per 100 lbs. per month, or an average daily intake of 70 mg daily.
73600-4	Cattle and Horse Oral Larvicide		0.0017 lb ai/animal/day		To prepare a larvicidal ration, mix 1.5 lbs. of product per ton of complete mixed ration. Full feed this larvicidal ration to feeder cattle weighing from 400 – 1,400 lbs or to dairy cattle at a rate sustaining milk production, but not less than 2.6 lbs of the ration per 100 lbs of body weight daily.

Table L.1. Summary of TCVP Occupational Livestock Use					
EPA Reg. No.	**Use Site**	**Applic. Type/ Equipment**	**Applic. Rate (lb ai/A)**	**PPE**	**Use Directions and Limitations**
					Product can also be mixed with concentrate feeds that will provide 792 mg per animal per day.
Feed Through (Liquid Additive)					
6552-17	Cattle (concentrate feed)	Cup/Pour	1,700 lb cow (labeled max): 0.0039 lb ai/animal/day	Baseline clothing and gloves	This product can be used to prepare concentrate feeds that will provide 70 mgs. of ai/ 100 lbs. body weight daily. Feed the appropriate concentrate indicated to cattle weighing between 400 and 1,200 lbs. For large cattle weighing between 1,200 and 1,700 lbs, increase the amount of premix per ton of concentrate to 1.5 times that indicated.
	Cattle (complete ration)		1,400 lb cow (labeled max feeder cow): 0.0022 lb ai/animal/day		This product can be used to prepare rations containing 26.4 mg of ai/ pound of complete ration. Full feed the ration to feeder cattle weight from 400 to 1,400 lbs, but not less than 2.6 pounds of the ration per 100 lbs of body weight daily.
	Swine		0.00060 lb ai/animal/day		Mix 2.6 lbs of this product per ton of meal type feed and offer 4-6 lbs of feed per animal per day. This is equivalent to 45.4 mg of product per lb of feed.
	Horse		1,100 lb horse (estimated max): 0.0017 lb ai/animal/day		Use this product to prepare concentrate feeds/topdressings that will provide 70 mgs of ai per 100 lbs of weight daily.
11556-160	Cattle		1,700 lb cow (labeled max): 0.0039 lb ai/animal/day	Baseline clothing and gloves	Roughage fed separately: This product is used to prepare concentrate feeds that will provide 70 mg ai per 100 lbs body weight. Feed the appropriate larvicidal concentrate to cattle weighing between 400 and 1,200 lbs. For large cattle weighting between 1,200 and 1,700 lbs, increase the amount of premix per ton of concentrate to 1.5 times that indicated.
			1,400 lb cow (labeled max): 0.0022 lb ai/animal/day		No other roughage fed: Mix 1.5 lbs of product per ton of complete mixed ration containing both grain and roughage. Full feed this complete ration to feeder cattle weighing from 400 to 1,400 lbs or to dairy cattle at a rate to sustain milk production, but not less than 2.6 lbs of the ration per 100 lbs of body weight daily.
	Swine		0.00060 lb ai/animal/day		Mix 2.6 lbs of this product per ton of meal type feed and offer 4 to 6 lbs of

Table L.1. Summary of TCVP Occupational Livestock Use					
EPA Reg. No.	**Use Site**	**Applic. Type/ Equipment**	**Applic. Rate (lb ai/A)**	**PPE**	**Use Directions and Limitations**
					feed per animal per day. This is equivalent to 45.5 mg ai per pound of feed.
	Horse		1,100 lb horse (estimated max): 0.0017 lb ai/animal/day		Use this product to prepare concentrate feeds that will provide 70 mg ai per 100 lbs body weight daily.
Feed Block					
6552-17	Cattle and Horse Oral Larvicide	Hand Dispersal	1,100 lb horse (estimated max): 0.0017 lb ai/animal/day 1,400 lb cow (estimated max): 0.0022 lb ai/animal/day (0.473% ai)	Baseline clothing and gloves	Provide 1 block per 5 head of cattle or horses. Feed at a daily rate of 0.07 grams of Larvicide in 0.5 ounces of block per 100 pounds of body weight.
7698-17			1,100 lb horse (estimated max): 0.0017 lb ai/animal/day 1,400 lb cow (estimated max): 0.0022 lb ai/animal/day		Place in dry spots near loafing and watering areas. Cattles (or horses) should consume 1.05 lbs of the product per 100 lbs of body weight per month. This will supply the recommended average daily intake of 70 mg per 100 lbs of body weight.
7698-18			1,100 lb horse (estimated max): 0.0017 lb ai/animal/day 1,400 lb cow (estimated max): 0.0022 lb ai/animal/day		Cattles (or horses) should consume 0.68 lbs of the product per 100 lbs of body weight per month. This will supply the recommended average daily intake of 70 mg per 100 lbs of body weight.
9078-12			1,100 lb horse (estimated max): 0.0017 lb ai/animal/day 1,400 lb cow (estimated max): 0.0022 lb ai/animal/day (0.31% ai)		Feed approximately ½ lb block per 1,000 lb animal daily.
9374-8			1,100 lb horse (estimated max):		Allow free choice for cattle and horses. Cattle and horses should consume an average of 0.8 oz of the product per 100

Table L.1. Summary of TCVP Occupational Livestock Use					
EPA Reg. No.	**Use Site**	**Applic. Type/ Equipment**	**Applic. Rate (lb ai/A)**	**PPE**	**Use Directions and Limitations**
			0.0017 lb ai/animal/day 1,400 lb cow (estimated max): 0.0022 lb ai/animal/day (0.30% ai)		lbs of body weight per day. This will supply the recommended average daily intake of 70 mg.
55392-3			1,100 lb horse (estimated max): 0.0017 lb ai/animal/day 1,400 lb cow (estimated max): 0.0022 lb ai/animal/day (0.30% ai)		Provide one block per 15-20 head of cattle or horses. Consumption should average 0.83 oz of the block per 100 lbs. This will supply the recommended average daily intake of 70 kg.
73600-1			1,100 lb horse (estimated max): 0.0017 lb ai/animal/day 1,400 lb cow (estimated max): 0.0022 lb ai/animal/day (0.49% ai)		Feed 1 block per 5 head of cattle or horses. Feed blocks at the rate of 0.5 oz per 100 lb of bodyweight per day. This intake will supply 0.07 g of larvicide per 100 lb. of bodyweight per day.
73600-3			1,100 lb horse (estimated max): 0.0017 lb ai/animal/day 1,400 lb cow (estimated max): 0.0022 lb ai/animal/day (0.49% ai)		Feed only as a free choice source of salt, other minerals or vitamins. The product should be fed at a level to provide 70 mg per 100 lb of bodyweight per day.
73600-5			1,100 lb horse (estimated max): 0.0017 lb ai/animal/day 1,400 lb cow		Feed one block per 10-15 head of cattle or horses. Feed blocks at the rate of 0.88 oz. per 100 lb. of body weight per day. This intake will supply 0.07 g of Larvicide per 100 lb. of bodyweight per day.

Table L.1. Summary of TCVP Occupational Livestock Use					
EPA Reg. No.	**Use Site**	**Applic. Type/ Equipment**	**Applic. Rate (lb ai/A)**	**PPE**	**Use Directions and Limitations**
73600-6			(estimated max): 0.0022 lb ai/animal/day (0.30% ai)		Feed 1 block per 5 head of cattle or horses. Feed blocks at the rate of 0.88 oz. per 100 lb. of bod weight per day. This intake will supply 0.7 g of Larvicide per 100 lb. of bodyweight per day.
Dust					
11556-158	Beef Cattle and Dairy Cattle	Shaker Can, Rotary Duster, Spoon	2 oz. dust: 0.0038 lb ai 4 oz dust: 0.0075 lb ai (3% ai)	M/L/A: Baseline clothing, gloves, and PF5 respirator	Hand dusting: apply 2 oz. of dust by shaker can, rotary duster or by spoon to the upper portions of the back, neck and poll, and to the face. Also can be used after grubs have encysted by applying 3-4 oz. of dust down the backline and rubbing in.
		Hand Pour	12.5 lbs (estimated max dust bag): 0.38 lb ai per dust bag	Loaders and others handling dust bags: Baseline clothing, gloves	Self-treating dust bag: put dust in a cotton cloth or double burlap bag or use prepacked weather proof cattle dust bags and hang in door exits or alleyways leading from animal buildings, salt or mineral blocks or watering holes. The dust bag can also be placed in a loafing shed, holding pens, feedlots, near watering holes or other areas where cattle gather.
	Swine	Hand, Power Duster, Shaker Can	4 oz dust/animal: 0.0075 lb ai/animal 1 lb. per 150 sq. ft: 0.00020 lb/ sq ft.	M/L/A: Baseline clothing, gloves, and PF5 respirator	Hand dusting: apply 3-4 oz of dust by hand or power duster to each animal. In severe infestations, both animals and bedding may be treated. One lb. of 3% dust should be applied per 150 sq. ft.
	Poultry	Plunger, Rotary Type Duster, Shaker can Duster	0.00010 lb ai/ b nird		Wire cage housing: Apply 1 lb dust/300 birds with plunger or rotary type duster or shaker can duster.
		Plunger, Rotary Type Duster	0.00030 lb ai/ sq ft		Floor management litter: Apply 1 lb/100 sq ft with plunger or rotary type duster. Or, apply 3 to 8 oz/ 100 sq ft with plunger or rotary type duster for treatment of darkling beetles.
		Plunger, Rotary Type Duster, Shaker can Duster	0.00060 lb ai/bird		Dust box: Apply 2 lbs/100 birds

Table L.1. Summary of TCVP Occupational Livestock Use					
EPA Reg. No.	**Use Site**	**Applic. Type/ Equipment**	**Applic. Rate (lb ai/A)**	**PPE**	**Use Directions and Limitations**
		Paint	0.030 lb ai/ gallon (1 gallon treats 800 sq ft)		Roost paint: Make a thick slurry by mixing 1 lb of dust with 1 pint of water. Apply 1 lb/100 sq ft.
11556-182	Beef Cattle and Dairy Cattle	Shaker can, Rotary Duster, Spoon	1 oz. dust: 0.0038 lb ai 2 oz dust: 0.0075 lb ai (6% ai)	M/L/A: Baseline clothing, gloves, and PF5 respirator	Hand dusting: apply 1 oz. of dust by shaker can, rotary duster or by spoon to the upper portions of the back, neck and poll, and to the face. Also can be used after grubs have encysted by applying 1.5-2 oz. of dust down the backline and rubbing in.
		Hand Pour	12.5 lbs (estimated max dust bag): 0.75 lb ai per dust bag	Loaders and others handling dust bags: Baseline clothing, gloves	Self-treating dust bag: put dust in a cotton cloth or double burlap bag or use prepacked weather proof cattle dust bags and hang in door exits or alleyways leading from animal buildings, salt or mineral blocks or watering holes. The dust bag can also be placed in a loafing shed, holding pens, feedlots, near watering holes or other areas where cattle gather.
	Swine	Hand, Power Duster, Shaker Can	2 oz dust/animal: 0.0075 lb ai/animal 0.5 lb. per 150 sq. ft: 0.00020 lb/ sq ft.	M/L/A: Baseline clothing, gloves, and PF5 respirator	Hand dusting: apply 1.5-2 oz of dust by hand or power duster to each animal. In severe infestations, both animals and bedding may be treated. One half lb. of 6% dust should be applied per 150 sq. ft.
	Poultry	Plunger, Rotary Type Duster, Shaker Can Duster	0.00010 lb ai/ bird		Wire cage housing: Apply 1 lb dust/600 birds with plunger or rotary type duster or shaker can duster.
		Plunger, Rotary Type Duster	0.00030 lb ai/ sq ft		Floor management litter: Apply 0.5 lb/100 sq ft with plunger or rotary type duster. Or, apply 1.5 to 4 oz/ 100 sq ft with plunger or rotary type duster for treatment of darkling beetles.
		Plunger, Rotary Type Duster, Shaker Can Duster	0.00060 lb ai/bird		Dust box: Apply 1 lbs/100 birds
		Paint	0.030 lb ai/ gallon		Roost paint: Make a thick slurry by mixing 1 lb of dust with 1 pint of water. Apply 0.5 lb/100 sq ft.

Table L.1. Summary of TCVP Occupational Livestock Use					
EPA Reg. No.	**Use Site**	**Applic. Type/ Equipment**	**Applic. Rate (lb ai/A)**	**PPE**	**Use Directions and Limitations**
			(1 gallon treats 800 sq ft)		
19713-340	Beef Cattle and Dairy Cattle	Shaker can, Rotary Duster, Spoon	2 oz. dust: 0.0038 lb ai 4 oz dust: 0.0075 lb ai (3% ai)	Baseline clothing and gloves	Hand dusting: apply approximately 2 oz. of dust by shaker can, rotary duster or by spoon to the upper portions of the back, neck and poll, and to the face.
		Hand Pour	12.5 lbs (estimated max dust bag): 0.38 lb ai per dust bag		Self-treating dust bag: put dust in a cotton cloth or durable bag or use pre-packed weather proof cattle dust bags and hang in barn door exits or alleyways leading from animal buildings, salt or mineral blocks or watering holes.
	Swine	Hand, Power Duster, Shaker Can	2 oz dust/animal: 0.0038 lb ai/animal 1 lb. per 150 sq. ft: 0.00020 lb/ sq ft		Hand dusting: apply 1.5-2 oz of dust by conventional hand or power duster to each animal with special attention given to the neck and around the ears. One lb of 3% dust should be applied per 150 sq ft of bedding.
47000-113	Beef Cattle and Dairy Cattle	Shaker can, Rotary Duster, Spoon	2 oz. dust: 0.0038 lb ai 4 oz dust: 0.0075 lb ai (3% ai)	Baseline clothing and gloves	Hand dusting: apply 2 oz. of dust by shaker can, rotary duster or by spoon to the upper portions of the back, neck and poll, and to the face. Also can be used after grubs have encysted by applying 3-4 oz. of dust down the backline and rubbing in.
		Hand Pour	12.5 lbs (estimated max dust bag): 0.38 lb ai per dust bag		Self-treating dust bag: put dust in a cotton cloth or double burlap bag or use prepacked weather proof cattle dust bags and hang in door exits or alleyways leading from animal buildings, salt or mineral blocks or watering holes. The dust bag can also be placed in a loafing shed, holding pens, feedlots, near watering holes or other areas where cattle gather.
	Swine	Hand, Power Duster, Shaker Can	4 oz dust/animal: 0.0075 lb ai/animal 1 lb. per 150 sq. ft: 0.00020 lb/ sq ft.		Hand dusting: apply 3-4 oz of dust by hand or power duster to each animal. In severe infestations, both animals and bedding may be treated. One lb. of 3% dust should be applied per 150 sq. ft.
	Poultry	Plunger, Rotary Type	0.00010 lb ai/ bird		Wire cage housing: Apply 1 lb dust/300 birds with plunger or rotary type duster or shaker can duster.

Table L.1. Summary of TCVP Occupational Livestock Use					
EPA Reg. No.	**Use Site**	**Applic. Type/ Equipment**	**Applic. Rate (lb ai/A)**	**PPE**	**Use Directions and Limitations**
		Duster, Shaker Can			
		Plunger, Rotary Type Duster	0.00030 lb ai/ sq ft		Floor management litter: Apply 1 lb/100 sq ft with plunger or rotary type duster. Or, apply 3 to 8 oz/ 100 sq ft with plunger or rotary type duster for treatment of darkling beetles.
		Plunger, Rotary Type Duster, Shaker Can Duster	0.00060 lb ai/bird		Dust box: Apply 2 lbs/100 birds
		Paint	0.030 lb ai/ gallon (1 gallon treats 800 sq ft)		Roost paint: Make a thick slurry by mixing 1 lb of dust with 1 pint of water. Apply 1 lb/100 sq ft.
47000-122	Beef Cattle and Dairy Cattle	Shaker Can, Rotary Duster, Spoon	2 oz. dust: 0.0038 lb ai (3% ai)	Baseline clothing and gloves	Hand dusting: apply 2 oz. of dust by shaker can, rotary duster or by spoon to the upper portions of the back, neck and poll, and to the face.
		Hand Pour	12.5 lbs (estimated max dust bag): 0.38 lb ai per dust bag		Self-treating dust bag: put dust in a cotton cloth or double burlap bag or use prepacked weather proof cattle dust bags and hang in door exits or alleyways leading from animal buildings, salt or mineral blocks or watering holes. The dust bag can also be placed in a loafing shed, holding pens, feedlots, near watering holes or other areas where cattle gather.
	Swine	Hand, Power Duster, Shaker Can	4 oz dust/animal: 0.0075 lb ai/animal 1 lb. per 150 sq. ft: 0.00020 lb/ sq ft.		Hand dusting: apply 3-4 oz of dust by hand or power duster to each animal. In severe infestations, both animals and bedding may be treated. One lb. of 3% dust should be applied per 150 sq. ft.
47000-123	Beef Cattle and Dairy Cattle	Shaker Can, Rotary Duster, Spoon	2 oz. dust: 0.0013 lb ai (1% ai)	Baseline clothing, coveralls, gloves and dust mist respriator	Hand dusting: apply 2 oz. of dust by shaker can, rotary duster or by spoon to the upper portions of the back, neck and poll, and to the face.
		Hand Pour	12.5 lbs (estimated max dust bag): 0.13 lb ai per dust bag		Self-treating dust bag: put dust in a cotton cloth or double burlap bag or use prepacked weather proof cattle dust bags. Suspend bags in gateways or lanes through which the animals pass daily for water, feed or minerals. The dust

Table L.1. Summary of TCVP Occupational Livestock Use					
EPA Reg. No.	**Use Site**	**Applic. Type/ Equipment**	**Applic. Rate (lb ai/A)**	**PPE**	**Use Directions and Limitations**
					bag can also be placed in a loafing shed, holding pens, feedlots, near watering holes or other areas where cattle gather.
		Hand, Power Duster	12 oz dust/animal: 0.0075 lb ai/animal 3 lb. per 150 sq. ft: 0.00020 lb/ sq ft.		Hand dusting: apply 9-12 oz of dust by hand or power duster to each animal. In severe infestations, both animals and bedding may be treated. Three lbs of 1% dust should be applied per 150 sq. ft.
	Horse	Hand, Shaker Can	6 oz. dust/animal: 0.0038 lb ai/animal No application rate defined for premise dusting.*		Apply 6 oz by shaker can, hand duster, grooming brush or dust mitt. Cover upper portions of the back, neck and to the face, mane and tail for added control of face flies. For premise dusting, apply to barn or stall area floors where manure accumulates.*
	Dogs (Kennels)	Plunger Duster, Shaker Can	No application rate defined.*		Occasional dusting in and around sleeping quarters and other areas will help free area of ticks and fleas. Dust bedding as well.*
47000-125	Beef Cattle and Dairy Cattle	Shaker Can, Rotary Duster, Spoon	2 oz. dust: 0.0038 lb ai (3% ai)	Baseline clothing and gloves	Hand dusting: apply 2 oz. of dust by shaker can, rotary duster or by spoon to the upper portions of the back, neck and poll, and to the face.
		Hand, Pour	12.5 lbs (estimated max dust bag): 0.38 lb ai per dust bag		Self-treating dust bag: put dust in a cotton cloth or double burlap bag or use prepacked weather proof cattle dust bags and hang in door exits or alleyways leading from animal buildings, salt or mineral blocks or watering holes. The dust bag can also be placed in a loafing shed, holding pens, feedlots, near watering holes or other areas where cattle gather.
	Swine	Hand, Power Duster, Shaker Can	4 oz dust/animal: 0.0075 lb ai/animal 1 lb. per 150 sq. ft: 0.00020 lb/ sq ft.		Hand dusting: apply 3-4 oz of dust by hand or power duster to each animal. In severe infestations, both animals and bedding may be treated. One lb. of 3% dust should be applied per 150 sq. ft.
	Poultry	Plunger, Rotary Type Duster, Shaker can Duster	0.00010 lb ai/ bird		Wire cage housing: Apply 1 lb dust/300 birds with plunger or rotary type duster or shaker can duster.

Table L.1. Summary of TCVP Occupational Livestock Use					
EPA Reg. No.	**Use Site**	**Applic. Type/ Equipment**	**Applic. Rate (lb ai/A)**	**PPE**	**Use Directions and Limitations**
		Plunger, Rotary Type Duster	0.00030 lb ai/ sq ft		Floor management litter: Apply 1 lb/100 sq ft with plunger or rotary type duster. Or, apply 3 to 8 oz/ 100 sq ft with plunger or rotary type duster for treatment of darkling beetles.
		Hand	0.00060 lb ai/bird		Dust box: Apply 2 lbs/100 birds
		Paint	0.030 lb ai/ gallon (1 gallon treats 800 sq ft)		Roost paint: Make a thick slurry by mixing 1 lb of dust with 1 pint of water. Apply 1 lb/100 sq ft.
Emulsifiable Concentrate Spray					
11556-162	Beef Cattle	Spray	0.026 lb ai/animal (23% ai)	Baseline clothing, coveralls, and gloves	Dilute 1 gallon of product in 75 gallons of water. Use between 0.5 and 1 gallon of diluted spray solution per animal.
			0.039 lb ai/animal		For severe tick infestations, dilution may be increased to 1 gallon in 50 gallons water.
	Lactating Dairy Cattle		0.0049 lb ai/animal		Dilute 1 gallon of product in 200 gallons of water. Direct spray to cover thoroughly with up to 0.5 gallon of the dilution per animal.
	Beef and Dairy Cattle	Backrubber or Facerubber	0.077 lb/gallon		Dilute 1 gallon of product in 25 gallons water. Pour diluted solution into oil reservoir of mechanical rubbing devices or pour 1 gallon per 20 feet on burlap or rope backrubbers.
	Poultry (Caged)	Spray	0.039 lb ai/100 birds 0.00031 lb ai/bird		Dilute 1 gallon product in 50 gallons of water. Apply 1 gallon of dilution/100 birds under high pressure. For individual bird treatment, apply 1 oz/ bird.
	Poultry (Chickens on Litter)		0.000078 lb ai/ sq ft		Dilute 1 gallon product in 50 gallons of water. Apply 1-2 gallons of dilution/1,000 square feet evenly with penetration of litter surface.
	Poultry	Roost Paint or Spray	0.077 lb ai/ gallon		Dilute 1 gallon of product in 25 gallons of water. Apply 1 pint of dilution/100 ft of roost area with brush or spray.
		Buildings	0.00077 lb ai/ sq ft		Dilute 1 gallon of product in 25 gallons of water. Apply 1 gallon of dilution/100-150 sq ft to thoroughly cover walls, ceilings, floors, cracks and crevices using high pressure spray.
	Poultry and Livestock Facilities	Spray	0.00015 lb ai/ sq ft		Residual surface spray: Dilute 1 gallon of product in 25 gallons of water. Apply 1 gallon of dilution/500-1,000 sq

Table L.1. Summary of TCVP Occupational Livestock Use					
EPA Reg. No.	**Use Site**	**Applic. Type/ Equipment**	**Applic. Rate (lb ai/A)**	**PPE**	**Use Directions and Limitations**
					ft. Extreme infestations may necessitate increasing the diluted spray to 1 gallon product per 12.5 gallon water.
			0.00077 lb ai/ sq ft		Larvicide: Dilute 1 gallon of product in 25 gallons of water. Apply 1 gallon of dilution/100 sq ft.
	Kennels		0.000078 lb ai/ sq ft		Dilute 1 gallon of product in 50 gallons of water. Apply 1 gallon of dilution/500-1,000 sq ft as a spot treatment only once per year.
67517-33	Beef Cattle	Spray	0.032 lb ai/animal (24% ai)	Baseline, gloves, and organic vapor respirator	Dilute to a 0.30% - 0.50% solution. Use between 0.5 to 1 gallon of spray per animal.
	Lactating Dairy Cattle		0.0013 lb ai/ animal		Dilute to a 0.040% solution. Use 0.50 gallon of spray per animal.
	Beef and Lactating Dairy Cattle	Backrubber	0.064 lb ai/gallon	Baseline, gloves, coveralls, and organic vapor respirator	Dilute to a 1.0% solution. Mix with #2 diesel oil or any approved backrubber base oil.
	Swine	Spray, High Pressure Sprayer	0.016 lb ai/animal	Baseline, gloves, and organic vapor respirator	Dilute to a 0.5% solution. Apply a coarse spray using 0.25 to 0.5 gallon per head to thoroughly wet the animal.
	Poultry (Wire Cage)		0.032 lb ai/100 birds (gallon) 0.00025 lb ai/bird		Dilute to a 0.5% solution. Apply 1 gallon/100 birds directly to birds, spray vent and fluff areas from below. For individual bird treatment, apply 1 oz of mixture per bird.
	Poultry (Floor Management)		0.000064 lb ai/ sq ft (2 gallons)		Dilute to 0.5% solution. Apply 1-2 gallons/1,000 sq ft evenly for penetration to litter surface.
	Poultry (Roost Paint)	Paint	0.064 lb ai/ gallon		Dilute to 1.0% solution. Apply 1 pint solution/100 sq ft. Treat with a brush or spray thoroughly.
	Poultry (Fowl Tick)	Power Sprayer	0.00064 lb ai/ sq ft		Dilute to 1.0% solution. Apply 1 gallon solution/100-150 sq ft to walls, ceiling, floors, cracks and crevices with a power sprayer.
	Poultry (Flies Residual)	Spray	0.00013 lb ai/ sq ft		Dilute to 1.0% solution. Apply 1 gallon/500-1,000 sq ft thoroughly to point of runoff to walls, ceilings, and where flies congregate and feed.
	Poultry (Larvicide)		0.00064 lb ai/ sq ft		Dilute to 1.0% solution. Apply 1 gallon solution/100 sq ft of droppings.
	Woody Borders of Kennels, Yards, Campgrounds, Recreational		0.032 lb ai/ sq ft		Dilute to 0.5% solution. Apply as a spot spray.

Table L.1. Summary of TCVP Occupational Livestock Use					
EPA Reg. No.	**Use Site**	**Applic. Type/ Equipment**	**Applic. Rate (lb ai/A)**	**PPE**	**Use Directions and Limitations**
	Parks, Footpaths and Roadways				
Wettable Powder					
11556-156	Beef Cattle	Spray	0.040 lb ai/animal (1 gallon)	MLA for dusting, low pressure handwand and paint applications: Baseline clothing, gloves, coveralls, dust mist respirator All other MLA and other handlers: Baseline clothing and gloves	Dilute to a 0.35-0.50% solution. Use a low pressure coarse spray and apply to point before runoff. Use between 0.5 to 1 gallon of spray solution per animal.
	Swine		0.020 lb ai/animal (0.5 gallon)		Dilute to a 0.50% solution. Apply as a low pressure coarse spray and apply only to point before runoff. Use 0.25 to 0.50 gallon maximum solution per head to treat.
	Poultry (Wire Cages)		0.00040 lb ai/ bird (gallon) 0.00031 lb ai/bird (1 oz)		Dilute to a 0.50% solution. Apply directly to birds (1 gallon solution/100 birds). For individual bird treatment apply 1 oz of the mixture per bird. Use power sprayer.
	Poultry (Floor Management Dusting)	Handheld Fogger, Plunger Duster, Stationary Fogger	0.0016 lb ai/ bird		Apply 2.5 oz wettable powder/50 birds.
	Poultry (Floor Management Roost Paint)	Paint	0.080 lb ai/ gallon (1 gallon treats 800 sq ft)		Dilute to a 1.0% solution. Treat with brush or spray thoroughly using 1 pint/100 ft.
	Poultry (Floor Management Litter)	Spray	0.00080 lb ai/ sq ft (2 gallons)		Dilute to a 0.50% solution. Apply 1-2 gallons solution/100 sq ft for penetration of litter surface.
		Handheld Fogger, Rotary Duster, Stationary Fogger	0.00023 lb ai/ sq ft (0.75 oz)		Treat evenly using 0.75 oz wettable powder/100 sq ft. Use rotary, mechanical or electrostatic duster.
	Poultry (Fowl Tick)	Spray	0.00080 lb ai/ sq ft (1 gallon)		Dilute to a 1.0% solution. Apply 1 gallon solution/100-150 sq ft to walls, ceiling, floor cracks, and crevices with power sprayer.
	Dairy Barns, Poultry Houses, Swine Barns, or other Animal Buildings		0.00032 lb ai/ sq ft (1 gallon)		Dilute to a 2.0% solution. For dry whitewashed wood or concrete block surfaces use 1 gallon of solution/500 sq ft.
			0.00016 lb ai/ sq ft (1 gallon)		Dilute to a 1.0% solution. For unpainted wood or painted concrete block surfaces, use 1 gallon of solution/500 sq ft.

Table L.1. Summary of TCVP Occupational Livestock Use					
EPA Reg. No.	**Use Site**	**Applic. Type/ Equipment**	**Applic. Rate (lb ai/A)**	**PPE**	**Use Directions and Limitations**
			0.000080 lb ai/ sq ft (0.5 gallon)		Dilute to a 1.0% solution. For Masonite or galvanized sheet metal surfaces, use 0.5 gallon of solution/ 500 sq ft.
	Poultry Droppings, Manure Piles, Garbage Piles, Under Feed Troughs		0.0008 lb ai/ sq ft (1 gallon)		Dilute to a 1.0% solution. Apply 1 gallon of solution/100 sq ft.
	Kennels, Yards, Campgrounds, Picnic Areas, and Recreational Parks		0.000040 lb ai/ sq ft (spot)		Dilute to a 0.5% solution. Apply as a spot treatment using a low pressure handwand sprayer only. Apply woody borders.
47000-126	Beef Cattle	Spray	0.040 lb ai/gallon	MLA for dusting and paint applications: Baseline clothing, gloves, coveralls, dust mist respirator All other MLA: Baseline clothing, gloves	Dilute to a 0.35-0.50% solution. Use a low pressure coarse spray and apply to point before runoff. Use between 0.5 to 1 gallon of spray solution per animal.
	Swine		0.020 lb ai/animal (0.5 gallon)		Dilute to a 0.50% solution. Apply as a coarse spray. Use 0.25 to 0.50 gallon maximum solution per head to treat.
	Poultry (Wire Cages)		0.00040 lb ai/ bird (gallon) 0.00031 lb ai/bird (1 oz)		Dilute to a 0.50% solution. Apply directly to birds (1 gallon solution/100 birds). For individual bird treatment apply 1 oz of the mixture per bird. Use power sprayer.
	Poultry (Floor Management – Litter)	Handheld Fogger, Plunger Duster, Stationary Fogger	0.00078 lb ai/ sq ft		Treat evenly and thoroughly using 2.5 oz/100 sq ft.
	Poultry (Floor Management - Dusting)		0.0016 lb ai/ bird		Apply 2.5 oz wettable powder/50 birds.
	Poultry (Floor Management Roost Paint)	Paint	0.080 lb ai/ gallon (1 gallon treats 800 sq ft)		Dilute to a 1.0% solution. Treat with brush or spray thoroughly using 1 pint/100 ft.
	Poultry (Fowl Tick)	Spray**	0.00080 lb ai/ sq ft (1 gallon)		Dilute to a 1.0% solution. Apply 1 gallon solution/100-150 sq ft to walls, ceiling, floor cracks, and crevices with power sprayer.
	Dairy Barns, Poultry Houses, Swine Barns, or other Animal Buildings		0.00032 lb ai/ sq ft (1 gallon)		Dilute to a 2.0% solution. For dry whitewashed wood or concrete block surfaces use 1 gallon of solution/500 sq ft.
			0.00016 lb ai/ sq ft (1 gallon)		Dilute to a 1.0% solution. For unpainted wood or painted concrete block surfaces, use 1 gallon of solution/500 sq ft.

Table L.1. Summary of TCVP Occupational Livestock Use					
EPA Reg. No.	**Use Site**	**Applic. Type/ Equipment**	**Applic. Rate (lb ai/A)**	**PPE**	**Use Directions and Limitations**
			0.000080 lb ai/ sq ft (0.5 gallon)		Dilute to a 1.0% solution. For Masonite or galvanized sheet metal surfaces, use 0.5 gallon of solution/ 500 sq ft.
	Poultry Droppings, Manure Piles, Garbage Piles, Under Feed Troughs		0.000080 lb ai/ sq ft (1 gallon)		Dilute to a 1.0% solution. Apply 1 gallon of solution/100 sq ft.

Table L.2. Summary of TCVP Occupational Pet Products			
EPA Reg. No.	**Use Site**	**Application Rate**	**Use Restrictions**
Collars			
2596-49	Cats	1,650 mg ai 11.3 gram collar (14.6% ai)	Do not use in kittens under 12 weeks of age. Place the collar around the cat's neck, adjust for proper fit, and buckle in place. Leave 2 or 3 inches on the collar for extra adjustment and cut off and dispose of the extra length. Replace the collar every 3 months, every 2 months for severe infestation.
2596-50	Dogs	2,770 mg ai 19 gram collar (14.6 % ai)	Do not use on puppies less than 6 weeks of age. Place the collar around the dog's neck, adjust for proper fit, and buckle in place. Leave 2 or 3 inches on the collar for extra adjustment and cut off and dispose of the extra length. Replace the collar every 3 months, every 2 months for severe infestation.
2596-62		4,670 mg ai 32 gram collar (14.6% ai)	Do not use on puppies less than 12 weeks of age. Place the collar around the dog's neck, adjust for proper fit, and buckle in place. Leave 2 or 3 inches on the collar for extra adjustment and cut off and dispose of the extra length. Replace the collar every 5 months, every 4 months for severe infestation.
2596-63	Cats	2,190 mg ai 15 gram collar (14.6% ai) 2,480 mg ai 17 gram collar (14.6% ai)	Do not use on kittens less than 12 weeks of age. Place the collar around the cat's neck, adjust for proper fit, and buckle in place. Leave 2 or 3 inches on the collar for extra adjustment and cut off and dispose of the extra length. Replace the collar every 5 months, every 4 months for severe infestation.
2596-83	Cats	1,750 mg ai 12 gram collar (14.6% ai) 3,650 mg ai 25 gram collar (14.6% ai)	Do not use on kittens less than 12 weeks of age. Place the collar around the cat's neck, adjust for proper fit, and buckle in place. Leave 2 or 3 inches on the collar for extra adjustment and cut off and dispose of the extra length. Replace the collar every 7 months, every 5 months for severe infestation.

Table L.2. Summary of TCVP Occupational Pet Products			
EPA Reg. No.	**Use Site**	**Application Rate**	**Use Restrictions**
2596-84	Dogs	2,770 mg ai 19 gram collar (14.6% ai) 4,670 mg ai 32 gram collar (14.6% ai)	Do not use on puppies under 6 weeks of age. Place the collar around the dog's neck, adjust for proper fit, and buckle in place. Leave 2 or 3 inches on the collar for extra adjustment and cut off and dispose of the extra length. Replace the collar every 7 months, every 5 months for severe infestation.
2596-139	Cats/ Dogs	1,460 mg ai 10 gram collar (14.6% ai) 7,300 mg ai 50 gram collar (14.6% ai)	Do not use on puppies under 6 weeks old/ kittens under 12 weeks old. Place the collar around the cat's/dog's neck, adjust for proper fit, and buckle in place. Leave 2 or 3 inches on the collar for extra adjustment and cut off and dispose of the extra length. Replace the collar every 7 months, or more frequently for severe infestation.
11556-164	Dogs	3,290 mg ai 24 gram collar (13.7% ai)	Do not use on puppies under 6 weeks. Place the collar around the dog's neck, adjust for proper fit, and buckle in place. Leave 2 or 3 inches on the collar for extra adjustment and cut off and dispose of the extra length. Replace the collar every 5 months, every 4 months for severe infestation.
11556-165	Cats	2,060 mg ai 15 gram collar (13.7% ai)	Do not use on kittens less than 12 weeks of age. Place the collar around the cat's neck, adjust for proper fit, and buckle in place. Leave 2 or 3 inches on the collar for extra adjustment and cut off and dispose of the extra length. Replace the collar every 5 months, every 4 months for severe infestation.
Dusts/Powders			
2596-78	Cats	280 mg ai (3.3% ai) 0.30 ounce per small cat 470 mg ai (3.3% ai) 0.5 ounce per large cat	Not for use on kittens less than 12 weeks of age. Dust entire cat beginning at head and working back. Use approximately 1/3 ounce of powder for a small cat or ½ ounce for a large cat. Repeat at weekly intervals if necessary.
2596-79	Dogs	470 mg ai (3.3% ai) ½ ounce per small dog 940 mg ai 1 ounce per medium dog 1,200 mg ai 1 ¼ ounce per large dog	Not for use on puppies less than 12 weeks of age. Dust entire dog beginning at the head and working back. Make sure powder gets down to the skin. Lightly dust the dog's bedding with approximately the same amount of powder. Repeat treatment of dog and bedding at weekly intervals if necessary. Use ½ ounce of powder for a small dog; 1 oz for a medium dog; and 1 ¼ oz for large dogs.
47000-123	Cats	Estimated Range: 43 mg ai, small 100 mg ai, medium 150 mg ai, large (1.0% ai)	Do not apply to kittens or puppies under 12 weeks old. Dust powder evenly over the animal and rub thoroughly through the hair coat to skin. Use 1/3 oz of powder per every 10 pounds of body weight of your cat or dog. Do not reapply product for 30 days. *PPE: Baseline clothing, coveralls, gloves and dust mist respirator.
	Dogs	Estimated Range: 170 mg ai, small 430 mg ai, medium	

Table L.2. Summary of TCVP Occupational Pet Products			
EPA Reg. No.	**Use Site**	**Application Rate**	**Use Restrictions**
		680 mg ai, large	
67517-82	Cats	Estimated Range: 130 mg ai, small 310 mg ai, medium 460 mg ai, large (3% ai)	Do not use on puppies under 12 weeks of age. Dust powder liberally over the animal and rub thoroughly through hair coat to skin. Use 1/3 oz of powder per every 10 pounds of body weight of your cat or dog. To control fleas, reapply every 16 days. To control brown dog ticks, reapply every 7 days.
	Dogs	Estimated Range: 510 mg ai, small 1,300 mg ai, medium 2,000 mg ai, large	
Pump/Trigger Sprays			
2596-125	Dogs	300 mg ai, small 400 mg ai, medium 700 mg ai, large (1.1% ai)	Do not apply to pets (puppies) less than 6 weeks old. Hold bottle upright about 6 inches from pet. Spray lightly until the tips of the pet's hair are moist. Rub spray into animal's coat. Repeat once per week. Recommended dosage: Spray 25-30 strokes for a small dog. Spray 30-40 strokes for a medium dog. Spray 40-70 strokes for a large dog. More spray may be needed for longhaired dogs. [1]
2596-126	Cats	250 mg ai, small 350 mg ai, large (1.1% ai)	Do not apply to pets (kittens) less than 6 weeks old. Hold bottle upright about 6 inches from pet. Spray lightly until the tips of the pet's hair are moist. Rub spray into animal's coat. Repeat once per week. Recommended dosage: Spray 15-25 strokes for a small cat. Spray 25-35 strokes for a large cat. More spray may be needed for longhaired cats. [1]
2596-140	Cats[3] (Pump)	51 mg ai, small 71 mg ai, large (1.1% ai)	Do not use on puppies or kittens less than 12 weeks old. Hold bottle upright about 6 inches from pet. Spray lightly until the tips of the pet's hair are moist. Rub spray into animal's coat. Repeat once per week. Recommended dosage: Spray 15-25 strokes for a small cat. Spray 25-35 strokes for a large cat.[2] Recommended dosage: Spray 25-35 strokes for a small dog. Spray 30-40 strokes for a medium dog. Spray 40-70 strokes for a large dog.[2]
	Cats[3] (Trigger)	250 mg ai, small 350 mg ai, large (1.1% ai)	
	Dogs (Trigger)	350 mg ai, small 400 mg ai, medium 700 mg ai, large (1.1% ai)	
2596-136	A "Cancellation Order for Section 3 Pesticide Product Registration(s)" was finalized on July 31, 2013 pertaining to EPA Reg. No. 2596-136, Hartz 2 in 1 Flea and Tick Spray for Cats and Dogs.		
2596-122, -123	EPA Reg. Nos. 2596-122 and -123 have been voluntarily cancelled.		

Appendix M. Calculation of Inhalation Human-Equivalent Concentrations (HECs) and Human-Equivalent Doses

The calculation of HECs accounts for pharmacokinetic (not pharmacodynamic) interspecies differences. HECs for residential and occupational scenarios were derived using the POD from the route-specific inhalation study and the regional deposited-dose ratio (RDDR). The RDDR accounts for the particulate diameter [mass median aerodynamic diameter (MMAD) and geometric standard deviation (GSD)] and estimates the different dose fractions deposited along the respiratory tract. Table M.1 summarizes the inputs used to obtain the TCVP RDDR for HEC calculations.

Table M.1. Summary of RDDR Inputs for TCVP

Study MRID	Species and Strain	Animal Body Weight (g)[1]	Duration of Exposure		BMDL (mg/L)	BMD (mg/L)	MMAD (μm)[3]	GSD (μm)[3]	Respiratory Region for Effect[4]	RDDR
			hours/day	days/week[2]						
48803501	Sprague Dawley Rats	267	6	5.5	0.022	0.12	2.57	3.785	ER	2.525

NOAEL = no-observed adverse-effect level. LOAEL = lowest-observed adverse-effect level. MMAD = mass median aerodynamic diameter. GSD = geometric standard deviation. RDDR = regional deposited-dose ratio.
[1] Default Sprague Dawley rat body weight for males (sensitive sex).
[2] Rats were exposed 5 days a week for 3 weeks and 7 days a week for the last week resulting in an average of 5.5 days/week.
[3] MMAD and GSD selected from the dose closest to the BMD and BMDL values (0.05 mg/L).
[4] ET = extrathoracic, TB = tracheobronchial, PU = pulmonary, TH = thoracic, TR = total respiratory tract, ER = extrarespiratory (systemic).

The POD from the route-specific inhalation study was adjusted for expected human exposure duration. Duration adjustment is performed based on Haber's law, which assumes that a toxicological effect is proportional to the product of exposure level and duration. Animal-to-human ratios of daily (hours/day) and weekly (days/week) exposures are applied to the animal inhalation study POD to result in a duration-adjusted animal POD for HEC conversion. For example, expected human exposure for occupational exposures is 8 hours/day and 5 days/week. Therefore, the adjusted POD is 0.0165 mg/L.

$$POD_{adjusted} = \frac{0.02\ mg}{L} \times \frac{6\ hr/day}{8\ hr/day} \times \frac{5.5\ days/week}{5\ days/week} = \frac{0.0165\ mg}{L}$$

For residential handler and outdoor post-application exposures, no duration adjustment was applied. For residential indoor post-application exposures, a duration adjustment to 7 days/week was applied with no daily exposure adjustment resulting in a duration-adjusted POD of 0.0157 mg/L. For residential bystander exposures, duration adjustments to 24 hours/day and 7 days/week were applied resulting in a duration-adjusted POD of 0.0039 mg/L.

The RDDR was applied to the duration-adjusted POD (except residential handler and outdoor post-application exposures with no duration adjustment where the RDDR is applied directly to the POD) to calculate HECs (presented in Table M.3 below).

$$HEC = POD_{adjusted} \times RDDR$$

Human-equivalent doses were subsequently calculated from the HECs for residential and occupational handler scenarios. The following equation describes the conversion from HECs to human-equivalent doses:

Human-Equivalent Dose ≈ HEC (mg/L) × CF (L/hr-kg BW) × A × AF × D (hr/day)

HED = Human-Equivalent Dose (mg/kg BW/day).
HEC = Human-Equivalent Concentration (mg/L).
CF = Human-specific value that accounts for volume respired per unit time. CF equals 11.8 L/hr-kg based on the default-breathing rate assumed for a typical human (body weight of 70 kg) in the HEC calculation.
A = Absorption ratio through the respiratory tract as compared to the oral route – assumed to be unity.
AF = Relative ratio that accounts for relative changes in respiratory rate due to activity level. Different AF values should be used for different occupational and residential scenarios.
D = Duration of daily exposure in hours: 8 hours assumed for occupational exposures; 24 hours assumed for bystanders/residential exposure; and 2 hours is often assumed for residential handler exposures.

The conversion to human-equivalent doses is an approximation involving the application of a conversion factor (CF) that takes into account the typical human volume respired per unit time. As the default breathing rate in the HEC calculation is 13.8 L/min for a typical human (body weight of 70 kg) under light activity conditions, the corresponding CF is 11.8 L/hr-kg. Absorption differences through the respiratory tract as compared to the oral route are expressed in the ratio "A." In current practice, HED customarily assumes "A" to be unity (i.e., the entire animal orally administered dose is assumed to be absorbed via the inhalation route). Because the inhaled dose depends on activity level which directly impacts breathing parameters (at least until blood steady state levels are reached), the activity factor (AF) is a relative ratio that attempts to account for differences in respiratory rate due to activity level. Table M.2 lists the different exposure scenarios, the corresponding breathing rates associated with these activities, and the AF values that should be used for different occupational handler scenarios being assessed. Also listed in Table M.2 is the AF value assigned to residential handlers, which is assumed to be equal to occupational handlers in non-agricultural settings. The daily exposure duration (D) is equivalent to the "hours/day" value used in POD duration adjustment calculations. A summary of duration adjustments, HECs, and human-equivalent doses for all potential occupational and residential scenarios is presented in Table M.3.

Table M.2. Assigned Activity Factor (AF) Values Based on Different Handler Exposure Scenarios

Exposure Scenario		Human Breathing Rate (L/min)	HED Calculation Inputs
			AF[1]
Occupational	Pilots, tractor drivers (groundboom, airblast)	8.3	0.6
	Mixer/loaders, lawn care operators (non-agriculture)	16.7	1.2
	Handheld spray applications (e.g., backpacks, handgun, etc.)	29	2.1
Residential	Handlers	16.7	1.2

[1] AF = Exposure scenario-specific human breathing rate (L/min) ÷ 13.8 L/min (the rate assumed in HEC calculation). Body weight is assumed to be 70 kg for all calculations.

Table M.3. Summary of Inhalation Calculations for Human-Equivalent Concentrations and Doses for TCVP								
Population	Scenario	Toxicity Duration Adjustment		Human-Equivalent Concentration		Human-Equivalent Dose (mg/kg/day; breathing rate specific)		
		hours/day	days/week	mg/L	mg/m^3	8.3 L/min	16.7 L/min	29 L/min
Occupational	Handler	8	5	0.04166	41.66	2.371	4.771	8.285
Residential	Handler	NA	NA	0.05555	55.55	NA	1.590	NA
	Outdoor post-application	NA	NA	0.05050	50.50	NA	NA	NA
	Indoor post-application	NA	7	0.03968	39.68	NA		
	Bystander	24	7	0.00992	9.92	NA		

NA = not applicable (the expected duration of the exposure scenario is less than the duration of available inhalation toxicity studies; downward adjustments are not permitted). Note: for all exposure scenarios, the rounded value of 0.02 mg/L was used as the POD, except residential handler which used the unrounded value of 0.022 mg/L.