J

6

UNITED STATES ENVIRONMENTAL PROTECTION AGENCY

WASHINGTON, D.C. 20460

OPP OFFICIAL RECORD
HEALTH EFFECTS DIVISION
SCIENTIFIC DATA REVIEWS
EPA SERIES 361

OFFICE OF
CHEMICAL SAFETY AND
POLLUTION PREVENTION

Date: May 31, 2011

MEMORANDUM

SUBJECT: **Dinotefuran** ID#: 11VA02 Section 18 Emergency Exemption for Use on Pome Fruits and Stone Fruits in Virginia, New Jersey, Pennsylvania, Maryland, Delaware, West Virginia, and North Carolina to Control Stink Bugs.

PC Code: 044312
MRID No.: None
Petition No.: None
Assessment Type: Single Chemical Aggregate
TXR No.: NA

DP Barcode: 388993
Registration No.: 59639-135, 10163-317
Regulatory Action: Section 18
Reregistration Case No.: NA

CAS No.: 165252-70-0
40 CFR: 180.603

FROM: Barry O'Keefe, Risk Assessor/Senior Biologist B. O'Keefe
Leung Cheng, Ph.D., Senior Chemist Leung Cheng
Registration Action Branch 3
Health Effects Division (7509P)

THROUGH: Paula Deschamp, Branch Chief P M Deschamp
Registration Action Branch 3
Health Effects Division (7509P)

TO: Marcel Howard
Section 18 Team
Minor Use, Inerts and Emergency Response Branch
Registration Division (7505P)

The Registration Division (RD) of the Office of Pesticide Programs (OPP) has requested that HED evaluate the Section 18 Emergency Exemption request for the use of the insecticide dinotefuran to control stink bugs on pome fruits and stone fruits.

INTRODUCTION

A Section 18 Emergency Exemption request has been received for use of the insecticide dinotefuran to control rice stink bug on pome fruits and stone fruits in seven eastern states (i.e., Virginia, New Jersey, Pennsylvania, Maryland, Delaware, West Virginia, and North Carolina), on up to a total of 65,000 acres. The proposed use season on pome fruits and stone fruits would be from the April 15th through October 15th, 2011 time period, but would be spread over the acreage

Received 12RC
6/8/2011
EC

of the seven states. The dinotefuran products to be used are Venom Insecticide (EPA Reg. No. 59639-135), or Scorpion 35SL (EPA Reg. No. 10163-317).

EXECUTIVE SUMMARY

General Information

Dinotefuran ((RS)-1-methyl-2-nitro-3-(tetrahydro-3-furylmethyl) guanidine) is a broad-spectrum insecticide belonging to the nitroguanidine sub-class of the neonicotiniod class of insecticides. It is insecticidal by contact and ingestion, resulting in the cessation of insect feeding within hours of contact and death shortly thereafter by interfering with the acetylcholine receptor on the post-synaptic side of the nerve cells.

Dinotefuran is currently registered for use on leafy vegetables (except *Brassica*), cotton, fruiting vegetables, cucurbits, potatoes, grapes, head and stem *Brassica* vegetables, and leafy *Brassica* vegetables as well as professional turf management, professional ornamental production, in the residential lawn and garden markets, and as pet spot on products. There is potential for exposure from agricultural, commercial operator, and residential uses.

The proposed Section 18 use pattern is as follows:

The Virginia Department of Agriculture and Consumer Services requested an emergency specific exemption to use dinotefuran to control stink bugs on pome fruit and stone fruit. This request is on behalf of Virginia and six other eastern states in the following specific counties of Virginia (statewide), New Jersey (Hunterdon, Warren, Sussex, Burlington, Middlesex, Mercer, Monmouth, Atlantic, Camden, Cumberland, Gloucester, Salem, Bergen, Somerset and Ocean), Pennsylvania (statewide), Maryland (statewide), Delaware (New Castle, Kent and Sussex), West Virginia (Berkeley, Hampshire, Jefferson, Morgan and Monroe), and North Carolina(Henderson, Polk Cleveland, Lincoln, Wilkes, Alexander, Moore, Montgomery and Anson). The total acreage to be treated is up to 65,000 acres. The dinotefuran products to be used are Venom Insecticide (EPA Reg. No. 59639-135/Valent), or Scorpion 35SL (EPA Reg. No. 10163-317/Gowan). Dinotefuran is to be applied at a maximum application rate of 0.304 lb ai/A by foliar application by ground airblast equipment. Two applications are proposed with a retreatment interval of seven (7) days. The proposed use season on pome fruits and stone fruits would be from the April 15th through October 15th, 2011 time period, but would be spread over the acreage of the seven states. This is the first Section 18 request for this use. Applications may not be made within three (3) days of harvest. The restricted entry interval (REI) for workers is 12 hours.

Toxicology

The toxicology database for dinotefuran is complete for the purposes of this Section 18. Details of the toxicology of dinotefuran are available in the HED memo, "Dinotefuran – Report of the Hazard Identification Assessment Review Committee (HIARC), HED TXR No. 0052409, 03/05/2004". Additionally, further characterization of the toxicology database and HED decisions are included in another HED risk assessment document for dinotefuran (DP309412, B. O'Keefe, 12/08/04). The most recent updated characterization of the toxicological database can be found in another recent HED memorandum (i.e., DP371573, B. O'Keefe, 11/27/09). A summary of the

toxicology findings, dose and endpoints selections, and uncertainty factor selections are presented in the detailed discussion section of this document.

Dietary Exposure

For acute and non-cancer chronic exposures, HED is concerned when estimated dietary risk exceeds 100% of the population adjusted dose (PAD). Dinotefuran is classified as "not likely to be a carcinogen," so no dietary assessment was performed for cancer. For acute dietary exposures an unrefined assessment was conducted, assuming 100% crop treated, and tolerance level residues. For chronic dietary exposures limited refined assessments were conducted, assuming 100% crop treated, and tolerance level residues with the exception of pome and stone fruit, and grape commodities with some refinements. These are considered conservative residues nonetheless. Nevertheless, the acute and chronic dietary risk estimates are below the Agency's level of concern for the general U.S. population and all population subgroups (5.4% aPAD and 84% cPAD for the most highly exposed subgroups all infants (<1 year old) and children 1-2 years old, respectively).

Non-Dietary, Non-Occupational Exposure

There is potential for exposure in residential settings during the application of currently registered products containing dinotefuran, and from entering areas previously treated with dinotefuran, such as lawns where children might play, pets children might play with, or golf courses and home gardens that could lead to exposures for adults. As a result, risk assessments were previously completed for both residential handler and postapplication scenarios (DP285650, J. Arthur, 4/27/2004, DP318728, B. O'Keefe, 8/2/04, and DP347177, S. Recore, 5/7/08). The proposed Section 18 uses of dinotefuran do not add any additional residential exposures or risks.

Aggregate Risk

The aggregate acute and chronic dietary risk estimates for all populations, resulting from aggregate exposure to dinotefuran in food and drinking water are below HED's level of concern.

For children, short- and intermediate-term aggregate risk assessments were performed. For the short-term aggregate assessment MOEs ranged from 300 to 1,400 which are greater than 100, and therefore do not exceed HED's level of concern. For the intermediate-term aggregate risk assessment MOEs ranged from 160 to 400 which are greater than 100, and therefore do not exceed HED's level of concern.

For adults, a short-term aggregate risk assessment was not performed, because no systemic toxicity was seen at the limit dose in a 28-day dermal toxicity study, and because an intermediate-term aggregate assessment was performed that would be protective. The intermediate-term aggregate risk assessment provided a total aggregate ARI of 2.2 which is greater than 1, and therefore does not exceed HED's level of concern.

Occupational Exposure

Occupational handlers may be exposed dermally and by inhalation during mixing, loading and application of dinotefuran for both short- and intermediate-term durations. Since a short-term dermal endpoint was not identified, and because the short- and intermediate-term inhalation

endpoints are the same, only intermediate-term risks were assessed for handlers. Intermediate-term risk estimates should account for short-term risks, as well. Further, because common toxicity endpoints were identified for both dermal and inhalation routes, a combined risk from both routes of exposure was assessed. Combined risk was estimated by calculating an aggregate risk index (ARI) because, while dermal and inhalation endpoint effects are the same, they occur at different dose levels and have different associated levels of concern for the MOE. Calculated ARIs of ≥ 1 do not cause concern to HED. Calculated ARIs for all occupational handler exposure scenarios are greater than 1 with workers wearing baseline clothing, and therefore, do not exceed HED's level of concern.

This proposed Section 18 action on dinotefuran involves foliar applications to pome fruit and stone fruit. Therefore, there is a potential for short- and intermediate-term exposure to workers entering dinotefuran-treated areas to perform a variety of agricultural tasks, and a risk assessment is required. Long-term postapplication exposure is not expected because of the infrequent application intervals, the relatively short half-life of dinotefuran and the concern for pest resistance from over-application.

Generally, inhalation exposure is expected to be negligible for these outdoor postapplication scenarios following application of such pesticides. The vapor pressure of dinotefuran is very low (1.0×10^{-9} mm Hg @ 30 deg C). In addition, because estimates of inhalation exposure to applicators did not exceed HED's level of concern, the potential postapplication exposure to any residual airborne concentration of dinotefuran also is not considered to be of concern.

Using the intermediate-term dermal toxicity endpoint (a short-term endpoint was not identified) and data from the leafy vegetables residue dissipation study, discussed in previous reviews (DP285650, J Arthur, 4/27/2004 and DP300464, B. O'Keefe, 6/9/04), the MOEs for all postapplication activities exceed an MOE of 100 on the day of treatment (i.e., day 0) for the proposed uses, and therefore, do not exceed HED's level of concern.

Technical dinotefuran has a Toxicity Category IV for acute dermal, acute inhalation, primary eye irritation and primary skin irritation. Therefore, the REI of 12 hours appearing on the Venom Insecticide and Scorpion 35SL dinotefuran labels should be sufficient.

Conclusion

The HED has no concerns regarding human health exposure and risk from the proposed Section 18 use of dinotefuran on stone fruit and pome fruit for control of stink bugs. In connection with this Section 18, temporary tolerances should be established at 1.0 ppm in or on fruit, pome, group 11 and fruit, stone, group 12.

DETAIL DISCUSSION

Toxicology Considerations

The quality of the toxicology database for dinotefuran is good and the confidence in the hazard and dose-response assessments is high. The toxicity database for dinotefuran is considered adequate to support toxicity endpoint selection for risk assessment and for FQPA evaluation. However, under the current 40 CFR §158.500 data requirement guidelines, immunotoxicity data (OPPTS

780.7800) are now required. In 2004, prior to this new requirement, the registrant was required to submit a developmental neurotoxicity study including immunotoxicity parameters as a condition of registration. In response, the registrant submitted a dose-range finding developmental neurotoxicity and immunotoxicity study on dinotefuran in rats (MRID 47677501). This study has been reviewed (W. Phang, DP# 366688, 8/5/09, TXR# 0055238). It was concluded that dinotefuran showed no evidence of an effect on the functionality of the immune system in rats that were exposed to dinotefuran during the prenatal, postnatal, and post-weaning periods. Although, this study was a dose-range-finding study for a developmental immunotoxicity study, it examined all the parameters which would have been required in a regular developmental immunotoxicity study and the highest tested dose (1035 mg/kg) was slightly greater than the limit dose (1000 mg/kg). Since the last registration action, the registrant has submitted an acceptable/guideline DNT study and two immunotoxicity studies which are currently in review.

No concerns for developmental neurotoxicity were seen in a guideline DNT study where the offspring NOAEL approached or exceeded the Limit Dose (784 mg/kg/day, gestation; 1643 mg/kg/day, lactation).

Dinotefuran has low acute toxicity by the oral, dermal, and inhalation routes. It is not a dermal sensitizer, but causes a low level of skin irritation. The main target tissues are the nervous system and the immune system, with effects seen in several species. Nervous system toxicity is manifested as changes in motor activity observed in acute and subchronic neurotoxicity studies in the rat, decreased grip strength in adult offspring in the 2-gen rat study and maternal clinical signs (prone position and tremor) in the rabbit developmental study. These effects occurred at doses ranging from ~300 to ~1500 mg/kg/day. Immune system toxicity is manifested as decreases in spleen and thymus weights, seen in multiple studies and species (including dogs, rats, and mice). There are also indications of endocrine-related toxicity, manifested in the reproductive toxicity study (in rats) as decreases in primordial follicles and altered cyclicity in females and abnormal sperm parameters in males at the Limit Dose; changes in testes or ovary weight were also seen in several species (mouse, dog, and rat). No adverse effects in fetuses were seen in the developmental toxicity studies in rats or rabbits, at maternally toxic doses, and offspring effects in the reproduction study occurred at the same doses causing parental effects. Review of acceptable oncogenicity and mutagenicity studies provide no indication that dinotefuran is carcinogenic or mutagenic. Dinotefuran is characterized as "not likely to be carcinogenic to humans" based on the absence of significant tumor increases in two adequate rodent carcinogenicity studies.

HED concluded that the toxicology database for dinotefuran is adequate for FQPA assessment. Available studies include developmental toxicity studies in rats and rabbits, a reproductive toxicity study in rats, and acute, subchronic, and developmental neurotoxicity studies in rats. Additionally, a dose-range finding developmental neurotoxicity and immunotoxicity study was also available. There was no evidence of increased susceptibility following *in utero* exposures in the prenatal developmental toxicity studies in rats and rabbits. In the reproduction toxicity study, there was evidence for increased qualitative susceptibility. The level of concern for the observed susceptibility is low since 1) clear NOAELs and LOAELs are established for the endpoints of concern for parental and offspring toxicity; 2) the effects in the offspring were seen in the presence of parental toxicity; and 3) the effects were seen only at the highest dose tested which was the Limit Dose (1000 mg/kg/day). In the range-finding developmental neurotoxicity and immunotoxicity study, dinotefuran showed no evidence of an effect on the functionality of the immune system in rats that were exposed to dinotefuran during the prenatal, postnatal, and post-

weaning periods. Further, no concerns for developmental neurotoxicity were seen in the guideline DNT study where the offspring NOAEL was the highest dose tested (784 mg/kg/day, gestation; 1643 mg/kg/day, lactation). These results are consistent with other compounds in this chemical class (i.e., neonicotinoids thiacloprid, imidacloprid, clothainadin) where neurotoxicity (in the presence of decreased pup body weight) was seen in only one compound (imidacloprid) and the DNT was not used in the imidacloprid risk assessment.

In the current risk assessment for dinotefuran, the lowest point of departure for neurotoxicity is a NOAEL of 33 mg/kg/day, which is used for assessment of short-term incidental oral risk. Lower points of departure for systemic toxicities are used for the other risk assessment scenarios: The chronic RfD an extrapolated NOAEL of 2.0 mg/kg/day based decreased thymus weight, the intermediate term incidental oral exposure is based on a NOAEL of 22 mg/kg/day based on changes in body weight/body weight gain, and the short and the intermediate inhalation exposure endpoints are based on an extrapolated NOAEL of 6.0 mg/kg/day based on decreased body weight and food consumption.

Based on these weight-of-evidence considerations, HED has concluded that there are no residual uncertainties for pre- and or post- natal toxicity and that the FQPA Safety Factor can be removed (i.e., 1X) for acute dietary and non-dietary (incidental oral, and dermal) risk assessments. For the chronic dietary and for short- and intermediate-term inhalation risk assessments, however, the 10X FQPA Safety Factor is retained for the use of a LOAEL (UF_L) (i.e., lack of a NOAEL in the critical studies).

A 10X Uncertainty Factor for the use of a LOAEL (UF_L) was retained in deriving the chronic Reference Dose (RfD) and the MOE for long-term inhalation exposure risks since a NOAEL was not established in the 1-year toxicity study in dogs selected for these exposure scenarios. The endpoint of concern for these scenarios is the decreased thymus weight in male dogs. The default 10X UF was deemed to be adequate based on the magnitude and the nature of response at the LOAEL in the study: 1) at the LOAEL, the decreased thymus weight was limited to one sex (males) with no corroborative histopathological lesions in the thymus glands; 2) this appears to be a species specific effect since no treatment-related effects on the thymus (weight or histopathology) was seen following chronic exposures to mice or rats; and 3) there is high confidence that the extrapolated NOAEL of 2.0 mg/kg/day (LOAEL 20 ÷ 10 UF = 2.0) will be protective of the systemic toxicity seen at higher doses in mice (LOAEL = 34 mg/kg/day) and rats (LOAEL = 991 mg/kg/day) following chronic exposures.

A 10X (UF_L) was also retained for the use of a LOAEL in deriving the MOEs for short and intermediate term inhalation exposures since a NOAEL was not established in the 28-day inhalation toxicity study in rats selected for these exposure scenarios. The default 10X UF is deemed to be adequate since: 1) Following exposures for 28-days, no toxicity to the target organ (respiratory system) was seen at any concentration; 2) the endpoint of concern was generalized systemic toxicity characterized by decreased body weight gain and food consumption in one sex (males); and 3) the extrapolated NOAEL of 6.0 mg/kg/day will be protective of the potential toxicity via this route of exposure.

Risk assessments were conducted for acute and chronic dietary, intermediate-term dermal, and short- and intermediate-term oral and inhalation exposures. The HED/RAB3 risk assessment team made recommendations for acute and chronic Reference Doses (RfDs), toxicological endpoint

selections, uncertainty factors (UFs), and appropriate margins of exposure (MOEs) for use as appropriate in occupational/residential exposure risk assessments. The endpoints that were selected for dinotefuran are presented in the endpoint summary tables, Tables 1 and 2.

As explained above, HED has concluded that the FQPA Safety Factor can be removed (i.e., 1X) for acute dietary and non-dietary (incidental oral, and dermal) risk assessments. For the chronic dietary and for short- and intermediate-term inhalation risk assessments, however, the 10X FQPA Safety Factor is retained for the use of a LOAEL (UF_L) (i.e., lack of a NOAEL in the critical studies). The recommendation is based on the following:

- The toxicity database is adequate and there are no residual uncertainties for pre- and/or postnatal toxicity. The doses chosen as quantitative risk estimates are adequately protective for infants and children.

- Exposure data are complete or are estimated based on data that reasonably account for potential exposures.

- The acute dietary analysis was based on tolerance level residues and 100% crop treated assumptions for all commodities. The contribution from drinking water is minimal. HED concludes that the acute exposure estimates in this analysis are unlikely to underestimate actual exposure.

- The chronic dietary analysis included tolerance level residues and 100% crop treated. The field trials represent maximum application rates and minimum PHIs. The contribution from drinking water is minimal. HED concludes that the chronic exposure estimates in this analysis are unlikely to underestimate actual exposure.

- The dietary drinking water assessment utilizes water concentration values generated by model and associated modeling parameters which are designed to provide conservative, health protective, high-end estimates of water concentrations which will not likely be exceeded.

- While there is potential for postapplication residential exposure, the best data and approaches currently available were used in the dinotefuran residential assessment. HED used the current conservative approaches for residential assessment. HED believes that the calculated risks represent conservative estimates of exposure because maximum application rates are used to define residue levels upon which the calculations are based. Exposures are unlikely to be underestimated because the assessment was a screening level assessment.

HED previously completed a comprehensive Section 3 human health risk assessment for the use of dinotefuran on many crops (DP309412, B. O'Keefe, 12/08/04). Since then The Agency has received and reviewed a developmental immunotoxicity range-finding study (MRID 47677501), DNT range-finding and guideline studies (MRIDS 47677502 and 48291601, respectively), as well as two guideline immunotoxicity studies (MRIDs 48442101 and 48442102) which are currently in review. This current assessment considers the results from these studies save immunotoxicity. Additionally, the FQPA safety factor terminology has been revised to reflect current policy. All other hazard characterization and endpoint selection information from the previous risk assessment are applied directly to this action.

Table 1. Summary of Toxicological Doses and Endpoints for Dinotefuran for Use in Dietary and Non-Occupational Human Health Risk Assessments

Exposure/ Scenario	Point of Departure	Uncertainty/FQPA Safety Factors	RfD, PAD, Level of Concern for Risk Assessment	Study and Toxicological Effects
Acute Dietary (General Population, including Infants and Children)	NOAEL=125 mg/kg/day	UF_A= 10x UF_H= 10x FQPA SF= 1x	Acute RfD = 1.25 mg/kg/day aPAD =1.25 mg/kg/day	Developmental Toxicity Study in Rabbits LOAEL = 300 mg/kg/day based on clinical signs in does (prone position, tremor, erythema) seen following a single dose.
Chronic Dietary (All Populations)	LOAEL=20 mg/kg/day	UF_A= 10x UF_H= 10x FQPA SF= 10x, which is a UF_L	Chronic RfD = 0.02 mg/kg/day cPAD = 0.02 mg/kg/day	Chronic Toxicity in Dogs LOAEL = 20 mg/kg/day based on decreased thymus weight in males.
Incidental Oral Short-Term (1-30 days)	NOAEL=33 mg/kg/day	UF_A= 10x UF_H= 10x FQPA SF= 1x	Residential LOC for MOE = 100	Subchronic Neurotoxicity Study in Rats LOAEL = 327 mg/kg/day based on increased motor activity during week two.
Incidental Oral Intermediate-Term (1-6 months)	NOAEL=22 mg/kg/day	UF_A= 10x UF_H= 10x FQPA SF= 1x	Residential LOC for MOE = 100	Chronic Toxicity in Dogs LOAEL = 108 mg/kg/day based on decreased body weight and body weight gains in females.
Dermal Short-Term (1-30 days)	No systemic toxicity was seen at the limit dose in a 28-day rat dermal toxicity study in which neurotoxicity was evaluated and there are no developmental toxicity concerns. No hazard was identified for this exposure scenario.			
Dermal Intermediate-Term (1-6 months)	NOAEL=22 mg/kg/day	UF_A= 10x UF_H= 10x FQPA SF= 1x	Residential LOC for MOE = 100	Chronic Toxicity in Dogs LOAEL = 108 mg/kg/day based on decreased body weight and body weight gains in females.
Inhalation Short- Term (1-30 days)	LOAEL=60 mg/kg/day	UF_A= 10x UF_H= 10x FQPA SF= 10x, which is a UF_L	Residential LOC for MOE = 1000	28-day Inhalation Toxicity Study in Rats LOAEL = 60 mg/kg/day based on decreased body weight gain in males.
Inhalation Intermediate-Term (1-6 months)	LOAEL=60 mg/kg/day	UF_A= 10x UF_H= 10x FQPA SF= 10x, which is a UF_L	Residential LOC for MOE = 1000	28-day Inhalation Toxicity Study in Rats LOAEL = 60 mg/kg/day based on decreased body weight gain in males.
Cancer (oral, dermal, inhalation)	Classification: "Not likely to be Carcinogenic to Humans" based on the absence of significant tumor increases in two adequate rodent carcinogenicity studies.			

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. UF_A = extrapolation from animal to human (intraspecies). UF_H = potential variation in sensitivity among members of the human population (interspecies). UF_L = use of a LOAEL to extrapolate a NOAEL. UF_S = use of a short-term study for long-term risk assessment. UF_{DB} = to account for the absence of key date (i.e., lack of a critical study). FQPA SF = FQPA Safety Factor. PAD = population adjusted dose (a = acute, c = chronic). RfD = reference dose. MOE = margin of exposure. LOC = level of concern. N/A = not applicable.

Table 2. Summary of Toxicological Doses and Endpoints for Dinotefuran 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 Short-Term (1-30 days)	NA	NA	NA	No systemic toxicity was seen at the limit dose in a 28-day rat dermal toxicity study in which neurotoxicity was evaluated and there are no developmental toxicity concerns. No hazard was identified for this exposure scenario
Dermal Intermediate-Term (1-6 months)	NOAEL=22 mg/kg/day	UF_A= 10x UF_H= 10x	Occupational LOC for MOE = 100	Chronic Toxicity in Dogs LOAEL = 108 mg/kg/day based on decreased body weight and body weight gains in females.
Inhalation Short-Term (1-30 days)	LOAEL=60 mg/kg/day	UF_A=10x UF_H=10x UF_L= 10x	Occupational LOC for MOE = 1000	28-day Inhalation Toxicity Study in Rats LOAEL = 60 mg/kg/day based on decreased body weight gain in males.
Inhalation Intermediate-term (1-6 months)	LOAEL=60 mg/kg/day	UF_A=10x UF_H=10x UF_L= 10x	Occupational LOC for MOE = 1000	28-day Inhalation Toxicity Study in Rats LOAEL = 60 mg/kg/day based on decreased body weight gain in males.
Cancer (oral, dermal, inhalation)	Classification: "Not likely to be Carcinogenic to Humans" based on the absence of significant tumor increases in two adequate rodent carcinogenicity studies.			

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. UF_A = extrapolation from animal to human (intraspecies). UF_H = potential variation in sensitivity among members of the human population (interspecies). UF_L = use of a LOAEL to extrapolate a NOAEL. UF_S = use of a short-term study for long-term risk assessment. UF_{DB} = to account for the absence of key date (i.e., lack of a critical study). MOE = margin of exposure. LOC = level of concern. N/A = not applicable.

Residue Chemistry Considerations

The nature of the residue in plants and livestock commodities is understood (MARC report, TXR #52304, DP293759, L. Cheng, 1/20/2004). In plants, parent dinotefuran and the metabolites DN and UF are the residues of concern for tolerance monitoring, and dinotefuran, DN, UF and PHP for risk assessment. In livestock, dinotefuran is the residue of concern for tolerance monitoring, and dinotefuran and metabolites UF and FNG in ruminants, and dinotefuran and the metabolite FNG in poultry for risk assessment. Adequate enforcement methods exist for the determination of residues of concern of dinotefuran and its metabolites in/on plant commodities and in livestock commodities.

The proposed Section 18 emergency use pattern requests a maximum of 2 applications made ≥7 days apart at 0.304 lb ai/A/application with a pre-harvest interval (PHI) of 3 days. There were no residue data submitted for the Section 18 request on pome and stone fruit. A one-page executive summary of the magnitude of the residue on peach presents a maximum combined residue of parent plus two metabolites (UF and DN) at 0.64 ppm at a PHI of two (2) or three (3) days following two applications at 0.179 lb ai/A/application. The submitted peach summary residue data are not appropriate for dietary exposure assessment for stone fruit primarily due to insufficient application rate.

For dietary exposure assessment for pome fruit and stone fruit, data from an apple metabolism study (see 45639804.der) are extrapolated to residues in pome fruit and stone fruit commodities. Two dose rates were used in the study and the results from the higher dose (1.79 versus 0.179 lb ai/A) will be the basis for deriving residues in apple with peel, peeled apple, apple juice, apple sauce, stone fruit, and stone fruit juices. Since the metabolism data reflect a 21-day sample collection, a correction factor based on the residue decline data for tomato and pepper has been applied to account for a shorter PHI of 3 days.

Moreover, for chronic assessment, average residues in grape and processed commodities have been entered into the R98 file for DEEM.

The ruminant dietary burdens need not be revised since cotton gin byproducts account for the bulk (86%) of beef and dairy cattle, and consequently need not revise the meat and milk input values for DEEM.

HED recommends Section 18 tolerances be established on the following crop groups, for residues of dinotefuran, (RS)-1-methyl-2-nitro-3-((tetrahydro-3-furanyl)methyl)guanidine, including its metabolites and degradates, in or on the commodities listed below. Compliance with the tolerance levels specified below is to be determined by measuring only the sum of dinotefuran and its metabolites DN, 1-methyl-3-(tetrahydro-3-furylmethyl)guanidine, and UF, 1-methyl-3-(tetrahydro-3-furylmethyl)urea, calculated as the stoichiometric equivalent of dinotefuran:

Fruit, pome, group 11.....1.0 ppm
Fruit, stone, group 12.....1.0 ppm

Drinking Water Considerations

There are no drinking water monitoring data available on the concentrations of parent dinotefuran, or any of its degradates. EFED provided a draft tier 1 dinotefuran drinking water assessment with estimated drinking water concentrations (EDWCs) for dinotefuran and its metabolites/degradates (MNG, DN, UF, DN-2-OH, and DN-3-OH) (email on 5/26/11, from R. Parker). The EDWCs for the metabolites/degradates were reported in parent dinotefuran equivalents. The degradates UF and DN-2-OH are photolysates and are not likely to be formed in the fields of most crops. The formation of these degradates would be a result of direct exposure of parent dinotefuran to surface waters through spray drift, or through direct application to water, followed by photolysis. The estimated values for DN, UF, and DN-2-OH+DN-3-OH photolysates are considered to be the upper bound estimates, since these degradates are likely to form only in puddles or small water pockets in the field through photolysis, and therefore, these EDWCs should be considered an unrefined assessment. The surface water EDWCs were derived using the FQPA Index Reservoir Screening Tool (FIRST) simulation model. The Screening Concentration in Ground Water (SCI-GROW) model was used to derive the ground water EDWCs.

For surface water, the acute (peak) and chronic (annual average) total EDWCs (parent + metabolites) are 91.31 ppb and 25.16 ppb, respectively. The acute and chronic ground water total EDWC (parent + metabolites) is 3.5 ppb.

Dietary Exposure Analysis and Risk Estimates

Dietary exposure and risk assessments were previously completed by HED to support the existing registered crops. In those risk assessments, acute and chronic (non-cancer) dietary exposure analyses were conducted using the Dietary Exposure Evaluation Model (DEEM-FCID™, Version 1.3), which incorporates consumption data from the United States Department of Agriculture's (USDA's) Continuing Surveys of Food Intakes by Individuals (CSFII), 1994-96/1998.. This current dietary exposure and risk analysis was conducted to include commodities from all registered crops and to include the proposed Section 18 Emergency Exemption use on pome fruit and stone fruit. Additionally, potential exposures from drinking water sources were included. EDWCs for surface water, provided by EFED (email on 6/30/08, from Jose Melendez), were incorporated directly into the acute and chronic DEEM analyses. Subsequently, EFED provided new EDWC estimates (email on 5/26/11, from R. Parker) using the proposed Section 18 uses on pome fruits and stone fruits that are considerably lower (91 ppb for acute and 25 ppb for chronic) than the values used in HED's dietary exposure and risk analysis (281 ppb for acute and 129 for chronic). Thus, HED's dietary assessment overestimates exposure and risk from surface water sources for this action. Ground water sources were not included, as the EDWCs for this water source are minimal in comparison to surface water.

The dietary assessment is a refined but conservative assessment. The residue data used in the analyses are tolerance level residues except for pome and stone fruit and grape commodities without factoring in percent crop treated information. For acute and non-cancer chronic exposures, HED is concerned when estimated dietary risk exceeds 100% of the population adjusted dose (PAD). Dinotefuran is classified as "not likely to be a carcinogen," so no dietary assessment was performed for cancer. For acute dietary exposures unrefined assessments were conducted, assuming 100% crop treated, and tolerance level residues. For chronic dietary exposures limited refined assessments were conducted, assuming 100% crop treated, and tolerance level residues with the exception of pome and stone fruit, and grape commodities with refinements as described above. These are considered conservative residues nonetheless. The acute and chronic dietary risk estimates are below the Agency's level of concern for the general U.S. population and all population subgroups (5.4% aPAD and 84% cPAD for the most highly exposed subgroup "all infants" and "children 1-2 years old", respectively); see Table 3.

Table 3. Summary of Dietary Exposure Including Drinking Water and Risk for Dinotefuran Using DEEM-FCID

	Acute Dietary (95 Percentile)		Chronic Dietary	
Population Subgroup*	Dietary Exposure (mg/kg/day)	% aPAD**	Dietary Exposure (mg/kg/day)	% cPAD**
General U.S. Population	0.031	2.4	0.0083	41
All Infants (< 1 year old)	**0.067**	**5.4**	0.015	77
Children 1-2 years old	0.060	4.8	**0.017**	**84**
Children 3-5 years old	0.048	3.8	0.014	72
Children 6-12 years old	0.032	2.5	0.0091	45

Table 3. Summary of Dietary Exposure Including Drinking Water and Risk for Dinotefuran Using DEEM-FCID				
	Acute Dietary (95 Percentile)		Chronic Dietary	
Population Subgroup*	Dietary Exposure (mg/kg/day)	% aPAD**	Dietary Exposure (mg/kg/day)	% cPAD**
Youth 13-19 years old	0.023	1.8	0.0065	33
Adults 20-49 years old	0.026	2.1	0.0073	37
Adults 50+ years old	0.025	2.0	0.0077	39
Females 13-49 years old	0.026	2.1	0.0073	36

**The values for the highest exposed population for each type of risk assessment are bolded.*
*** Report %PADs to 2 significant figures.*

Non-Dietary, Non-Occupational Exposure

There is potential for exposure in residential settings during the application of currently registered products containing dinotefuran, and from entering areas previously treated with dinotefuran, such as lawns where children might play, pets children might play with, or golf courses and home gardens that could lead to exposures for adults. As a result, risk assessments were previously completed for both residential handler and postapplication scenarios (DP285650, J. Arthur, 4/27/2004, DP318728, B. O'Keefe, 8/2/04, and DP347177, S. Recore, 5/7/08). The proposed Section 18 uses of dinotefuran do not add any additional residential exposures or risks.

Residential Bystander Post-Application Inhalation Exposure

Based on the Agency's current practices, a quantitative post-application inhalation exposure assessment was not performed for dinotefuran at this time. However, volatilization of pesticides may be a potential source of post-application inhalation exposure to individuals nearby to pesticide applications. The Agency sought expert advice and input on issues related to volatilization of pesticides from its Federal Insecticide, Fungicide, and Rodenticide Act Scientific Advisory Panel (SAP) in December 2009. The Agency received the SAP's final report on March 2, 2010 (http://www.epa.gov/scipoly/SAP/meetings/2009/120109meeting.html) and is in the process of evaluating the SAP report. The Agency may, as appropriate, develop policies and procedures to identify the need for and, subsequently, the way to incorporate post-application inhalation exposure into the Agency's risk assessments. If new policies or procedures are put into place, the Agency may revisit the need for a quantitative post-application inhalation exposure assessment for dinotefuran.

Spray Drift

Spray drift is always a potential source of exposure to residents nearby to spraying operations. This is particularly the case with aerial application, but, to a lesser extent, could also be a potential source of exposure from the ground application method employed for the previously-registered uses of dinotefuran. The Agency has been working with the Spray Drift Task Force, EPA Regional Offices, and State Lead Agencies for pesticide regulation and other parties to develop the best spray drift management practices. The Agency is now requiring interim mitigation measures for aerial applications that must be placed on product labels/labeling. The Agency has completed

its evaluation of the new data base submitted by the Spray Drift Task Force, a membership of U.S. pesticide registrants, and is developing a policy on how to appropriately apply the data and the AgDRIFT computer model to its risk assessments for pesticides applied by air, orchard airblast, and ground hydraulic methods. After the policy is in place, the Agency may impose further refinements in spray drift management practices to reduce off-target drift and risks associated with aerial as well as other application types where appropriate.

Aggregate Risk

In accordance with the FQPA, HED must consider and aggregate pesticide exposures and risks from three major sources: food, drinking water, and residential exposures. 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.

Based on the proposed Section 18 uses and the existing Section 3 uses, acute, short-term, intermediate-term and chronic aggregate exposures are anticipated. Aggregate exposure assessments were performed for acute aggregate dietary exposure (food + drinking water), chronic aggregate dietary exposure (food + drinking water), and residential intermediate-term exposure to children (from dermal and incidental oral exposures) and adults (from dermal and inhalation exposures). A cancer aggregate risk assessment was not performed because dinotefuran is not carcinogenic. All potential exposure pathways were assessed in the aggregate risk assessment. Dietary (food and drinking water) exposures were considered because there is a potential for individuals to be exposed concurrently through these routes.

Acute Aggregate Risk

The aggregate acute risk estimates include exposure to residues of dinotefuran in food and drinking water, and does not include dermal, inhalation or incidental oral exposure. Since the acute dietary exposure assessment already includes the highest acute exposure from the drinking water modeling data, no further calculations are necessary. The acute risk estimate for all populations, resulting from aggregate exposure to dinotefuran in food and drinking water is below HED's level of concern. The food and drinking water exposure estimates for the most highly exposed subgroup, all infants (< 1 year old), is 5.4% of the aPAD.

Chronic Aggregate Risk

The aggregate chronic risk estimates include exposure to residues of dinotefuran in food and drinking water, and does not include dermal, inhalation or incidental oral exposure. Since the chronic dietary exposure assessment already includes the highest chronic exposure from the drinking water modeling data, no further calculations are necessary. The chronic risk estimate for all populations, resulting from aggregate exposure to dinotefuran in food and drinking water is below HED's level of concern. The food and drinking water exposure estimates for the most highly exposed subgroup, children 1-2 yrs old, is 84% of the aPAD.

Short- & IntermediateTerm Aggregate Risk

Because there are existing residential uses of dinotefuran, short- and intermediate-term aggregate risk assessments based on exposure from oral, inhalation, and dermal routes were considered. However, the toxicological effects for short-term incidental oral and inhalation routes of exposure are different (i.e., neurotoxicity for oral and decrease in body weight for inhalation); and therefore, these exposure scenarios have not been combined. Also, because no systemic toxicity was seen at the limit dose in a 28-day dermal toxicity study, no quantification of short-term dermal risk is required. Therefore, only short-term oral residential hand-to-mouth exposures for small children need to be aggregated with chronic food and drinking water exposures. These exposures were aggregated and are presented in Table 4. Additionally, as a worse-case estimate of risk, intermediate-term dermal and oral residential hand-to-mouth exposures for small children were aggregated with chronic food and drinking water exposures. Also, the point of departure for intermediate-term dermal and oral exposures is a NOAEL of 22 mg/kg/day versus the point of departure for short-term oral exposures which is 33 mg/kg/day.

Table 4. Aggregate Risk for Short-Term Exposure of Children (1-2 yrs) to Dinotefuran

Residential Use Site	NOAEL mg/kg/day	Level of Concern	Average Food + Water Exposure	Oral Residential Exposure	Aggregate MOE (Food + Residential)
Turf	33	100	0.017	0.005827	1,400
Indoor Carpets	33	100	0.017	0.080	340
Pet (Cat)	33	100	0.017	0.0916	300

An intermediate-term aggregate risk assessment was performed as a screening level assessment. Intermediate-term aggregate risk assessments were performed for adults and children. For children, the subgroup with the highest estimated chronic dietary exposure (children 1-2 years old) was aggregated with residential exposures to children playing on treated lawns (dermal and oral hand-to-mouth exposures) in order to calculate the worst case intermediate-term aggregate risk to children. The reciprocal MOE method was used to conduct the intermediate-term aggregate risk assessment for children, since the levels of concern are identical for all MOEs in the calculation. For adults, the aggregate risk index (ARI) method was used, since levels of concern are not identical for all types of exposure in the calculation. For children, the aggregate MOEs range from 160 to 400 which are all greater than 100, and therefore do not exceed HED's level of concern. For adults, the total aggregate ARI is 2.2 which is greater than 1, and therefore does not exceed HED's level of concern. For adults, a short-term aggregate risk assessment was not performed, because no systemic toxicity was seen at the limit dose in a 28-day dermal toxicity study, and because an intermediate-term aggregate assessment was performed that would be protective.

Table 5. Aggregate Risk for Intermediate-Term Exposure of Children (1-2 yrs) to Dinotefuran

Population	NOAEL mg/kg/day	Level of Concern MOE[1]	Average Food + Water Exposure[2]	Oral Residential Exposure[3]	Dermal Residential Exposure[4]	Aggregate MOE (Food + Residential)[5]
Turf	22	100	0.017	0.005827	0.031	400
Indoor Carpets	22	100	0.017	0.080	0.041	160
Pet (Cat)	22	100	0.017	0.038	0.0536	200

[1]The level of concern MOE of 100 is based on the standard inter- and intra-species safety factors, 10x for intra-species variability and 10x for inter-species extrapolation.
[2]Average food and drinking water exposure
[3]Residential oral exposure to children playing on treated lawns (oral hand-to-mouth + oral object-to-mouth + oral soil ingestion)
[4]Residential dermal exposure to children playing on treated lawns
[5]Aggregate MOE = NOAEL/[(average food + drinking water exposure) + (residential oral exposure) + (residential dermal exposure)]

Table 6. Aggregate Risk for Intermediate-Term Exposure of Adults to Dinotefuran						
Population	Level of Concern ARI[1]	ARI (Food + Water)[2]	Residential ARIs			Total Aggregate ARI[4]
			Handlers		Post Application Dermal Exposure	
			Dermal Exposure	Inhalation Exposure		
General U.S. Population	1	26.5	12	77	3.1	2.2

[1] ARI (Aggregate Risk Index) = $MOE_{Calculated}$ / $MOE_{Acceptable}$
[2] $ARI_{Food + Water}$ = (22 mg/kg/day/0.0083 mg/kg/day) / 100 = 26.5
[3] ARI_{Dermal} =MOE / 100 and, $ARI_{Inhalation}$ = MOE / 1000
[4] $ARI_{Total\ Aggregate} = 1/[(1/ARI_{Food + water}) + (1/ARI_{Residential\ Handler\ Dermal}) + (1/ARI_{Residential\ Handler\ Inhalation}) + (1/ARI_{Post\ Application\ Dermal})]$

Occupational Considerations

The potential exposure and associated risks for handlers mixing, loading and applying dinotefuran to pome fruits and stone fruits were based on the proposed labels. The proposed use is to apply dinotefuran by airblast application only at a maximum application rate of 0.304 lb ai/A using Venom Insecticide, or Scorpion 35SL, products. Two applications are proposed with a retreatment interval of seven (7) days. Applications may not be made within three (3) days of harvest. The proposed restricted entry interval (REI) for workers is 12 hours.

Risk Estimates for Occupational Handlers

Based on the proposed Section 18 use of dinotefuran on pome fruits and stone fruits three occupational handler scenarios were identified for which exposure to dinotefuran is expected. These scenarios are as follows (Note: soluble granulars are essentially dry flowables):

(1) open mixing/loading of dry flowables for airblast applications,
(2) open mixing/loading of liquids for airblast applications, and
(3) applying sprays by airblast.

No chemical-specific handler exposure data were submitted in support of this Section 18 registration. To assess handler exposures for regulatory actions when chemical-specific monitoring data are not available, HED relies on the most scientifically-reliable surrogate data currently available from various sources such as the Pesticide Handler Exposure Database (PHED), the Agricultural Handler Exposure Task Force (AHETF), and the Outdoor Residential Exposure Task Force (ORETF). Some of this data, such as the industry task force data, is compensatory, subject to the data protection provisions of FIFRA. HED policy on use of surrogate data is described in more detail on the Agency's website (http://www.epa.gov/pesticides/science/handler-exposure-data.html). Scenario-specific surrogate exposure data, including their sources, are presented in the "Occupational Pesticide Handler Unit Exposure Surrogate Reference Table" (http://www.epa.gov/pesticides/science/handler-exposure-table.pdf). HED has developed a series of tables of standard unit exposure values for many occupational scenarios that can be utilized to ensure consistency in exposure.

The assumptions and factors used in the risk calculations include:

- Average body weight of an adult handler is 70 kg, because the toxicity endpoint effects identified by HED are not gender-specific.

- All analyses were completed using surrogate exposure data that were deemed to be acceptable for the scenario in question.

- Exposure factors used to calculate daily exposures to handlers are based on applicable data if available.

- The Agency uses the maximum application rates allowed by labels in its risk assessments in order to evaluate what is legally possible based on the labels.

- It is anticipated that occupational dinotefuran exposures will generally only occur in short- and intermediate-term durations. There are no chronic exposures (≥ 180 days per year) expected.

- 30% dermal absorption factor used because the dermal endpoint is based on an oral study.

Occupational handlers may be exposed dermally and by inhalation during mixing, loading and application of dinotefuran for both short- and intermediate-term durations. Since a short-term dermal endpoint was not identified, and because the short-and intermediate-term inhalation endpoints are the same, only intermediate-term risks were assessed for handlers. Intermediate-term risk estimates should account for short-term risks, as well. Further, because common toxicity endpoints were identified for both dermal and inhalation routes, a combined risk from both routes of exposure is assessed. Combined risk was estimated by calculating an aggregate risk index (ARI) because, while dermal and inhalation endpoint effects are the same, they occur at different dose levels and have different associated levels of concern for the MOE. Calculated ARIs of ≥ 1 do not cause concern to HED. The following formula is used to calculate the ARI:

$$ARI_{total} = 1/[(1/ARI_{dermal}) + (1/ARI_{inhal})]$$

where, $ARI_{dermal} = MOE_{dermal}/100$ and, $ARI_{inhal} = MOE_{inhal}/1000$

Table 7 below presents results of the occupational handler exposure/risk assessment. Calculated ARIs for all occupational handler exposure scenarios are greater than 1 with workers wearing baseline clothing, and therefore, do not exceed HED's level of concern.

Table 7. Occupational Handler Exposure and Risk Estimates for Dinotefuran

Exposure Scenario (Unit exposure from PHED unless otherwise indicated)	Personal Protective Equipment	Exposure Route	Application Rate	Amount Treated per day	Unit Exposure (mg/lb ai)	Daily Dose[1] (mg/kg/day)	MOE[2]	ARI[3]	Total ARI[4]
M/L Dry Flowable: Open mixing (Airblast)	long sleeves long pants no gloves	Dermal	0.304 lb ai/A	40 acres	0.227	0.0118	1,900	19	13
		Inhalation			0.00896	0.00156	39,000	39	
M/L Liquid: Open mixing (Airblast)	long sleeves long pants no gloves	Dermal	0.304 lb ai/A	40 acres	0.220	0.0115	1,900	19	19
		Inhalation			0.000219	0.000038	1,600,000	1,600	
Applicator, Open Cab Airblast	long sleeves long pants no gloves	Dermal	0.304 lb ai/A	40 acres	0.360	0.0188	1,200	12	10
		Inhalation			0.0045	0.000782	77,000	77	

[1] Daily Dose = [Application Rate * Amount Treated * Unit Exposure (mg/lb ai handled) * Absorption Factor (30% for dermal; 100% for inhalation)]/Body Weight (70 kg)

[2] MOE = NOAEL or LOAEL/Daily Dose. No short-term dermal NOAEL was identified since no systemic toxicity was seen at the limit dose (28-day dermal toxicity study). The intermediate-term dermal NOAEL = 22 mg/kg/day, was used for all calculations. The dermal level of concern is a MOE < 100. The short- and intermediate-term inhalation LOAEL = 60 mg/kg/day. The inhalation level of concern is a MOE < 1000, because a LOAEL was used.

[3] $ARI_{dermal} = MOE_{dermal}/100$ and, $ARI_{inhal} = MOE_{inhal}/1000$

[4] $ARI_{total} = 1/[(1/ARI_{dermal}) + (1/ARI_{inhal})]$

Risk Estimates for Post Application Workers

Dinotefuran has been proposed for use on pome fruits and stone fruits. Agricultural postapplication exposures may occur from a variety of activities following treatment of these crops.

No post-application data were submitted in support of this registration action; therefore, dermal exposures during post-application activities were estimated using dermal transfer coefficients from the Science Advisory Council for Exposure Policy Number 3 (http://www.epa.gov/pesticides/science/exposac_policy3.pdf). This policy reflects adoption of all Agricultural Re-Entry Exposure Task Force (ARTF) data. Use of the data in this policy requires compensation to the ARTF under FIFRA. Therefore, because Mitsui Chemicals, Inc. is not a member of the task force there may be data compensation issues with the use of ARTF data in this assessment. The transfer coefficients (TCs) used in this assessment were taken from the Agency's revised Agricultural Transfer Coefficient SOP. Many of the TCs in this SOP are based on work of the ARTF.

Data from chemical-specific residue dissipation studies were previously submitted for use in completing the postapplication risk assessments for ornamental, turf and agricultural (leafy vegetable) applications. These studies were summarized in the previous review (DP285650, J. Arthur, 4/27/04). Dissipation data from the study on leafy vegetables (DP300464, MRID 45640008, 4/21/04) were used in this risk assessment.

This proposed Section 18 action on dinotefuran involves foliar applications to pome fruits and stone fruits. Therefore, there is a potential for short- and intermediate-term exposure to workers entering dinotefuran-treated areas to perform a variety of agricultural tasks, and a risk assessment is required. Long-term postapplication exposure is not expected because of the infrequent application intervals, the relatively short half-life of dinotefuran and the concern for pest resistance from over-application.

Using the intermediate-term dermal toxicity endpoint (a short-term endpoint was not identified) and data from the leafy vegetables residue dissipation study, discussed in previous reviews (DP285650, J Arthur, 4/27/04 and DP300464, B. O'Keefe, 6/9/04), the MOEs for all postapplication activities exceed an MOE of 100 on the day of treatment (i.e., day 0) for the proposed uses, and therefore, do not pose a concern to HED. A summary of the postapplication exposure and risk assessment is seen in Table 7.

Technical dinotefuran has a Toxicity Category IV for acute dermal, acute inhalation, primary eye irritation and primary skin irritation. Therefore, the REI of 12 hours appearing on the Venom Insecticide and Scorpion 35SL dinotefuran labels should be sufficient.

Table 8. Exposure and Risk Assessment for Occupational Postapplication Activities

Crop Group	Max. Foliar Application Rate (lb ai/A)	Dermal Transfer Coefficient (cm^2/hr)	Postapplication Day (t)	Dislodgeable Foliar Residue ($\mu g/cm^2$)[1]	Daily Dose[2] (mg/kg/day)	Intermediate-Term Dermal MOE[3]
Stone Fruit & Pome Fruit	0.304	100 Orchard Maintenance, Propping	0	0.733	0.00251	8,800
		580 Hand Pruning, Training, Scouting			0.0146	1,500
		1400 Hand Harvesting			0.0352	625
		3600 Thinning Fruit			0.0905	240

[1] The estimated "day 0" residue value (0.323 $\mu g/cm^2$) from the leafy vegetables DFR study conducted in Pennsylvania (MRID 45640008) is the highest of the three sites studied and is used as a screen for estimated day "0" values. The 0.323 $\mu g/cm^2$ DFR value was adjusted for the difference in application rates, i.e. 0.304 lb ai/A versus 0.134 lb ai/A used on the leafy vegetables.
[2] Daily Dose = [Dislodgeable Foliar Residue * (0.001 mg/ug) * Dermal Transfer Coefficient * Dermal Absorption Factor (30%) * Exposure Time (8 hours)]/[Body weight (70 kg)]
[3] MOE = NOAEL/Daily Dose. Intermediate-Term Dermal NOAEL = 22 mg/kg/day.

Generally, inhalation exposure is expected to be negligible for all of these outdoor postapplication scenarios following application of such pesticides. In addition, because estimates of inhalation exposure to applicators did not exceed HED's level of concern, the potential postapplication exposure to any residual airborne concentration of dinotefuran also is not considered to be of concern.

Based on the Agency's current practices, a quantitative post-application inhalation exposure assessment was not performed for dinotefuran at this time primarily because of the low acute inhalation toxicity (Toxicity Category III and IV), low vapor pressure (1.0×10^{-9} mm Hg at 30 deg C), and the low proposed use rate (0. 304 lb ai/A). However, there are multiple potential sources of post-application inhalation exposure to individuals performing post-application activities in previously treated fields. These potential sources include volatilization of pesticides and resuspension of dusts and/or particulates that contain pesticides. The Agency sought expert advice and input on issues related to volatilization of pesticides from its Federal Insecticide, Fungicide, and Rodenticide Act Scientific Advisory Panel (SAP) in December 2009, and received the SAP's final report on March 2, 2010 (http://www.epa.gov/scipoly/SAP/meetings/2009/120109meeting.html). The Agency is in the process of evaluating the SAP report as well as available post-application inhalation exposure data generated by the Agricultural Reentry Task Force and may, as appropriate, develop policies and procedures, to identify the need for and, subsequently, the way to incorporate occupational post-application inhalation exposure into the Agency's risk assessments. If new policies or procedures are put into place, the Agency may revisit the need for a quantitative occupational post-application inhalation exposure assessment for dinotefuran.

Although a quantitative occupational postapplication inhalation exposure assessment was not performed, an inhalation exposure assessment was performed for occupational/commercial handlers. Handler exposure resulting from application of pesticides outdoors is likely to result in higher exposure than postapplication exposure. Therefore, it is expected that these handler inhalation exposure estimates would be protective of most occupational postapplication inhalation exposure scenarios."

Cumulative Risk

Unlike other pesticides for which EPA has followed a cumulative risk approach based on a common mechanism of toxicity, EPA has not made a common mechanism of toxicity finding as to dinotefuran and any other substances and dinotefuran does not appear to produce a toxic metabolite produced by other substances. For the purposes of this Section 18 action, therefore, EPA has not assumed that dinotefuran has a common mechanism of toxicity with other substances. For information regarding EPA's efforts to determine which chemicals have a common mechanism of toxicity and to evaluate the cumulative effects of such chemicals, see the policy statements released by EPA's Office of Pesticide Programs concerning common mechanism determinations and procedures for cumulating effects from substances found to have a common mechanism on EPA's website at http://www.epa.gov/pesticides/cumulative/.

Conclusion

The HED has no concerns regarding human health exposure and risk from the proposed Section 18 use of dinotefuran on pome fruits and stone fruits for control of stink bugs. In connection with this Section 18, temporary tolerances should be established at 1.0 ppm in or on fruit, pome, group 11 and fruit, stone, group 12.

13544

R192473

Chemical Name: Dinotefuran

PC Code: 044312
HED File Code: 11000 Chemistry Reviews
Memo Date: 5/31/2011
File ID: 00000000
Accession #: 000-00-0137

HED Records Reference Center
6/9/2011