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

OFFICE OF
PREVENTION, PESTICIDES, AND
TOXIC SUBSTANCES

MEMORANDUM

DATE: August 2, 2004

SUBJECT: **Human Health Risk Assessment for Proposed Section 3 Registration of Dinotefuran Spot-On Products on Domestic Cats and Dogs.** PC Code: 044312. DP Barcode: D318728 & D318908.

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The Health Effects Division (HED) of the Office of Pesticide Programs (OPP) is charged with estimating the risk to human health from exposure to pesticides. The Registration Division (RD) of OPP has requested that HED evaluate hazard and exposure data and conduct residential and aggregate exposure assessments, as needed, to estimate the risk to human health that will result from proposed and currently registered uses of dinotefuran ((RS)-1-methyl-2-nitro-3-(tetrahydro-3-furylmethyl)guanidine).

Hartz Mountain Corporation has submitted requests for new Section 3 registrations for topical spot-on treatments for cats and kittens, and dogs and puppies. This document is an assessment of the human exposure and health risks resulting from the registered and proposed uses for dinotefuran.

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1.0 EXECUTIVE SUMMARY

General Background

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, and head and stem *Brassica* vegetables, as well as professional turf management, professional ornamental production, and in the residential lawn and garden markets. HED assessed these uses this past year (B. O'Keefe, D285577, 4/30/04; and B. O'Keefe, D309412, 12/08/04)[1, 2].

Hartz Mountain Corporation has submitted requests for new Section 3 registrations for topical spot-on treatments for cats and kittens, and dogs and puppies. The Health Effects Division (HED) has conducted a human health risk assessment for dinotefuran for the purpose of making registration eligibility recommendations on these proposed new uses.

Hazard Assessment

The existing toxicological database for dinotefuran is adequate to support the decision regarding the proposed spot-on uses on cats and dogs.

On December 17, 2003, the Health Effects Division (HED) Hazard Identification Assessment Review Committee (HIARC) reviewed the recommendations of the toxicology reviewer for dinotefuran with regard to the acute and chronic Reference Doses (RfDs) and the toxicological endpoint selection for use as appropriate in occupational/residential exposure risk assessments. The potential for increased susceptibility of infants and children from exposure to dinotefuran was also evaluated as required by the Food Quality Protection Act (FQPA) of 1996. Details of the toxicology of dinotefuran are available in the HED memo, *Dinotefuran - Report of the Hazard Identification Assessment Review Committee.* K. Raffaele. 03/05/04, TXR# 0052409[3].

Based on the hazard data, the HIARC recommended the special FQPA Safety Factor (SF) be reduced to 1X. The dinotefuran risk assessment team evaluated the quality of the exposure data, and based on these data, also recommended that the special FQPA SF be reduced to 1X. Details of the recommendation for the FQPA Safety Factor for dinotefuran are available in the last HED risk assessment document (B. O'Keefe, 12/8/04, D309412)[2].

The HIARC 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. For the proposed companion animal spot-on uses short- and intermediate-term incidental oral and dermal

exposures are possible. However, a short-term dermal endpoint was not identified. Therefore, only intermediate-term incidental oral and dermal exposures are assessed in this document. For these intermediate-term dermal and incidental oral exposures the following endpoint is used: NOAEL of 22 mg/kg/day, from the one year toxicity study in dogs, with a LOAEL = 108 mg/kg/day, based on decreased body weight and body weight gain in females; and LOC for MOE = 100.

Dietary Exposure Estimates

For the currently registered uses of dinotefuran, the acute and chronic dietary exposure assessment was completed in a HED-memorandum dated November 26, 2004 (L. Cheng, D309936)[4]. The dietary assessment is an unrefined conservative assessment. 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 (<3% aPAD and <54% cPAD for the most highly exposed subgroup "children 1-2 years old").

Residential Exposure Estimates

There is potential for exposure to homeowners in residential settings during the application of currently registered products containing dinotefuran, or from entering areas previously treated with dinotefuran, such as lawns where children might play, 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 (J. Arthur, D285650, 4/27/2004)[5]. The proposed new pet spot-on uses of dinotefuran add to these non-occupational exposures or risks.

Potential residential handler exposures from applying spot-on treatments to pets were not assessed, since negligible exposure is expected from these products due to self-contained packaging and minimal handling requirements.

Individuals of varying ages can potentially be exposed from contact with treated companion animals. Potential routes of exposure include incidental ingestion (toddlers only) and dermal. While it is assumed that most residential uses of dinotefuran will result in short-term (1 to 30 days) postapplication exposures, it is also believed that intermediate-term exposures (> 30 days to 180 days) are possible. Further, it is assumed that toddler exposures result in the worst case risks, and therefore only toddler postapplication exposures to treated companion animals were assessed.

Instructions for pet spot-on treatments include a monthly re-treatment regimen. Residues are anticipated to dissipate between applications. Because only an intermediate-term dermal endpoint was identified for the assessment, a 31-day average residue level was used to estimate exposure, based on a residue dissipation rate of 5% per day, and a re-application on the 31st day. The calculation begins with the day of application, where the amount of residue available on the animal is equal to 5% of the application rate (20% was also calculated). It should be noted that the value used in this assessment for the percent of the application rate initially available to transfer from pet to human is 5%, and not the 20% standard value from HED's Residential

Exposure SOPs [5,6,7], even though results from using both values are presented in this risk assessment.

Children's dermal and incidental oral (i.e., hand-to-mouth activity) exposures from hugging treated pets have been combined to give a total MOE. Because the toxicity endpoint (i.e., NOAEL = 22 mg/kg/day, based on body weight gain) is the same for both dermal and incidental oral exposures, the total combined risk (i.e., total MOE) for children is calculated by adding the daily doses from all relevant exposure routes and activities and comparing this total to the common toxicity endpoint NOAEL. **Combined dermal and incidental oral exposures of children from hugging pets that have been treated with the proposed dinotefuran spot-on products result in MOEs ≥100, and therefore, do not exceed HED's level of concern.** However, as can be seen in the assessment, when using the standard value from HED's SOPs [6,7,8], for the amount of residue initially available to transfer from treated pets (20%), the MOE for combined dermal and incidental oral exposures from hugging cats treated at the maximum application rate results in an MOE of 60, which exceeds HED's level of concern. While HED has used the non-SOP 5% value in this assessment, the assumption that the proposed dinotefuran pet spot-on products are similar to the fipronil product may, or may not, be true. Therefore, **HED recommends that registration of the proposed dinotefuran pet spot-on products be conditional upon the completion of a dinotefuran transferrable residue study.** ***Note: Prior to initiating this study, a protocol should be submitted to the Agency for review.***

Drinking Water Exposure Estimates

The Environmental Fate and Effects Division (EFED) previously provided estimated drinking water concentrations (EDWCs) for dinotefuran and its metabolites (MNG, DN, UF, DN-2-OH, and DN-3-OH); January 21, 2004 (S. Dutta, D290192)[9]. For surface water, the acute (peak) and chronic (annual average) total EDWCs (parent + metabolites) are 76 ppb and 21 ppb, respectively. The acute and chronic ground water total EDWC (parent + metabolites) is 5.1 ppb.

Aggregate Exposure Scenarios and Risk Conclusions

For the existing uses, human health aggregate risk assessments have been conducted for acute aggregate exposure (food + drinking water), chronic aggregate exposure (food + drinking water), and intermediate-term aggregate scenarios. For the proposed and existing uses, an intermediate-term aggregate risk assessment was performed as a screening level assessment, since a short-term aggregate risk assessment could not be performed. This assessment was performed for children (from dermal and incidental oral exposures) as a screening level assessment, since children are believed to be the most highly exposed population. The child subgroup with the highest estimated chronic dietary exposure (children 1-2 years old) was aggregated with residential exposures (at the highest application rates) to children playing with companion animals (dermal and oral hand-to-mouth exposures), in order to calculate the worst case intermediate-term aggregate risks to children. Because HED does not have surface and ground water monitoring data to calculate a quantitative aggregate exposure, DWLOCs were calculated. A drinking water level of comparison (DWLOC) is a theoretical upper limit on a pesticide's concentration in drinking water in light of total aggregate exposure to a pesticide in food, drinking water, and through residential uses. **Compared with the EDWCs generated by**

EFED, HED's calculated aggregate intermediate-term DWLOCs do not exceed HED's level of concern for the subgroup population of children 1-2 years old.

Data Needs

HED emphasizes that the fipronil data cited in this document is proprietary information. There may be data compensation issues with the use of fipronil data in this assessment. HED recommends that a registration of the proposed dinotefuran pet spot-on products be conditional upon the completion of a dinotefuran transferrable residue study. ***Note: Prior to initiating this study, a protocol should be submitted to the Agency for review.***

2.0 HAZARD CHARACTERIZATION

The existing toxicological database for dinotefuran is adequate to support the decision regarding the proposed spot-on uses on cats and dogs.

On December 17, 2003, the Health Effects Division (HED) Hazard Identification Assessment Review Committee (HIARC) reviewed the recommendations of the toxicology reviewer for dinotefuran with regard to the acute and chronic Reference Doses (RfDs) and the toxicological endpoint selection for use as appropriate in occupational/residential exposure risk assessments. The potential for increased susceptibility of infants and children from exposure to dinotefuran was also evaluated as required by the Food Quality Protection Act (FQPA) of 1996.

2.1 Hazard Profile

Dinotefuran has low acute toxicity by the oral, dermal, and inhalation routes. It is not a dermal sensitizer, or eye irritant, but causes a low level of skin irritation. The acute toxicity of dinotefuran is summarized in Table 1.

Table 1. Acute Toxicity Profile

Guideline No.	Study Type	MRID #(s)	Results	Toxicity Category
81-1	Acute Oral – Rat	45639823	LD_{50}= 2804/2000 [M/F]	III
81-1	Acute Oral – Mouse	45639824	LD_{50}=2450/2275 [M/F]	III
81-2	Acute Dermal – Rat	45639901	LD_{50} > 2000 mg/kg	IV
81-3	Acute Inhalation – Rat	45639902	LC_{50} > 4.09 mg/L	IV
81-4	Primary Eye Irritation – Rabbit	46301601	no positive effects	IV
81-5	Primary Skin Irritation – Rabbit	45639904	low level of irritation	IV
81-6	Dermal Sensitization (Guinea Pig Maximization test)	45639905	not a sensitizer	

The main target tissues are the nervous system and the immune system, with effects seen

in several species. Nervous system toxicity is manifested as clinical signs and decreased motor activity seen after acute dosing (in both rats and rabbits) and increased motor activity seen after repeated dosing; these findings are consistent with effects on the nicotinic cholinergic nervous system. 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, abnormal sperm parameters in males; 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 (including decreased spleen and thymus weights, and decreased grip strength) effects in the reproduction study occurred at the same doses causing parental effects. There was a qualitative increase in sensitivity in rat pups in the reproductive toxicity study. Review of acceptable oncogenicity and mutagenicity studies provide no indication that dinotefuran is carcinogenic or mutagenic.

Details of the toxicology of dinotefuran are available in the HED memo, *Dinotefuran - Report of the Hazard Identification Assessment Review Committee.* K. Raffaele. 03/05/04, TXR# 0052409[3].

2.2 FQPA Considerations

On December 17, 2003, the HED HIARC evaluated the potential for increased susceptibility of infants and children from exposure to dinotefuran according to the February 2002 OPP 10X guidance document. The HIARC 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 and subchronic neurotoxicity studies in rats. The HIARC concluded the following: 1) There is low concern for pre- and/or postnatal toxicity resulting from exposure to dinotefuran; 2) There is a concern for neurotoxicity and developmental neurotoxicity resulting from exposure to dinotefuran; and 3) There is a concern for immunotoxicity following exposure to dinotefuran during the period of organogenesis.

Recommendation for the FQPA Safety Factor

Based on the hazard data, the HIARC recommended the special FQPA Safety Factor (SF) be reduced to 1X. The dinotefuran risk assessment team evaluated the quality of the exposure data, and based on these data, also recommended that the special FQPA SF be reduced to 1X. Details of the recommendation for the FQPA Safety Factor for dinotefuran are available in the last HED risk assessment document (B. O'Keefe, 12/8/04, D309412)[2].

2.3 Dose-Response Assessment

On December 17, 2003, the HIARC evaluated the toxicological database for dinotefuran. The HIARC made recommendations for acute and chronic Reference Doses (RfDs), toxicological endpoint selections, and appropriate margins of exposure (MOEs) for use as appropriate in occupational/residential exposure risk assessments. The doses, toxicological

endpoints, and margins of exposure (MOEs) selected for the various exposure scenarios are summarized in Table 2.

Table 2. Summary of Toxicological Dose and Endpoints for Dinotefuran

Exposure Scenario	Dose Used in Risk Assessment, UF	Special FQPA SF* and Level of Concern for Risk Assessment	Study and Toxicological Effects
Acute Dietary (General population including infants and children)	NOAEL = **125** mg/kg/day UF = **100** **Acute RfD = 1.25** mg/kg/day	FQPA SF = **1** **aPAD** = acute RfD / FQPA SF = **1.25** mg/kg/day	**Developmental Toxicity Study in Rabbits** LOAEL = **300** mg/kg/day based on **clinical signs in does (prone position, panting, tremor, erythema) seen following a single dose.**
Chronic Dietary (All populations)	LOAEL= **20** mg/kg/day UF = **1000** **Chronic RfD = 0.02** mg/kg/day	FQPA SF = **1** **cPAD** = chronic RfD / FQPA SF = **0.02** mg/kg/day	**Chronic Toxicity Study in Dogs** LOAEL = **20** mg/kg/day based on **decreased thymus weight in males**
Short-Term Incidental Oral (1 to 30 days)	NOAEL= **33** mg/kg/day	**Residential** LOC for MOE = **100** **Occupational** = NA	**Subchronic Neurotoxicity study in rats** LOAEL = **327** mg/kg/day based on **increased motor activity during week 2**
Intermediate-Term Incidental Oral (1 to 6 months)	NOAEL= **22** mg/kg/day	**Residential** LOC for MOE =**100** **Occupational** = NA	**Chronic Toxicity Study in Dogs** LOAEL = **108** mg/kg/day based on **decreased body weight and body weight gain in females**
Short-Term Dermal (1 to 30 days)	No quantitation required.	**Residential** LOC for MOE = **NA** **Occupational** LOC for MOE = **NA**	No quantitation required. No systemic toxicity was seen at the limit dose in a 28-day dermal toxicity study in which neurotoxicity was evaluated. No developmental toxicity concerns.
Intermediate-Term Dermal (1 to 6 months)	Oral study NOAEL= **22** mg/kg/day (dermal absorption rate = 30%)	**Residential** LOC for MOE =**100** **Occupational** LOC for MOE =**100**	**Chronic Toxicity Study in Dogs** LOAEL = **108** mg/kg/day based on **decreased body weight and body weight gain in females**
Long-Term Dermal (>6 months)	Oral study LOAEL= **20** mg/kg/day (dermal absorption rate = 30%)	**Residential** LOC for MOE = **1000** **Occupational** LOC for MOE = **1000**	**Chronic Toxicity Study in Dogs** LOAEL = **20** mg/kg/day based on **decreased thymus weight in males**

Exposure Scenario	Dose Used in Risk Assessment, UF	Special FQPA SF* and Level of Concern for Risk Assessment	Study and Toxicological Effects
Short-Term Inhalation (1 to 30 days)	Inhalation study LOAEL= 60 mg/kg/day	**Residential** LOC for MOE = **1000** **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**
Intermediate-Term Inhalation (1 to 6 months)	Inhalation study LOAEL= 60 mg/kg/day	**Residential** LOC for MOE =**1000** **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**
Long-Term Inhalation (>6 months)	Oral study LOAEL= **20** mg/kg/day (inhalation absorption rate = 100%)	**Residential** LOC for MOE = **1000** **Occupational** LOC for MOE = **1000**	**Chronic Toxicity Study in Dogs** LOAEL = **20** mg/kg/day based on **decreased thymus weight in males**
Cancer (oral, dermal, inhalation)			Not required; no evidence of carcinogenicity.

UF = uncertainty factor, FQPA SF = Special FQPA safety factor, NOAEL = no observed adverse effect level, LOAEL = lowest observed adverse effect level, PAD = population adjusted dose (a = acute, c = chronic) RfD = reference dose, MOE = margin of exposure, LOC = level of concern, NA = Not Applicable

Recommendation for Aggregate Exposure Risk Assessments

As per FQPA, 1996, when there are potential residential exposures to the pesticide, aggregate risk assessment must consider exposures from three major sources: oral, dermal and inhalation exposures. The toxicity endpoints selected for these routes of exposure may be aggregated as follows:

For short-term aggregate exposure assessment, incidental oral and inhalation cannot be combined due to differences in the endpoint, i.e. neurotoxicity for incidental oral and decreases in body weight for inhalation. No quantification of dermal risk is required.

For intermediate-term aggregate exposure, incidental oral, dermal and inhalation endpoints can be aggregated because of the use of a common endpoint (decreased body weight gain).

For long-term aggregate exposure, incidental oral, dermal and inhalation endpoints can be aggregated because of the use of oral equivalents and a common endpoint (decreased thymus weight).

3.0 EXPOSURE ASSESSMENT

3.1 Summary of Proposed Uses

Dinotefuran is a broad-spectrum insecticide belonging to the nitroguanidine sub-class of the neonicotiniod class of insecticides. Dinotefuran is currently registered for use on leafy vegetables (except *Brassica*), cotton, fruiting vegetables, cucurbits, potatoes, grapes. and head and stem *Brassica* vegetables, as well as professional turf management, professional ornamental production, and in the residential lawn and garden markets. HED assessed these uses this past year (B. O'Keefe, D285577, 4/30/04; and B. O'Keefe, D309412, 12/08/04)[1,2].

Hartz Mountain Corporation has submitted requests for new Section 3 registrations for topical spot-on treatments for cats and kittens, and dogs and puppies. Two end-use products are proposed: Hartz® Reference 121, a 14.85% ai RTU product formulated in a squeeze-tube applicator with permethrin (45% ai) and pyriproxyfen (1.48%) for use on dogs and puppies, and: Hartz® Reference 123, a 14.85% ai RTU product formulated in a squeeze-tube applicator (without permethrin or sunilarv) for use on cats and kittens. Proposed dinotefuran products are further described in Table 3.

Table 3. Dinotefuran Use Profile Summary for Homeowner Spot-on Treatment of Companion Animals

Product	Use Sites	Max. Application Rate	Handler Scenario	Number of Treatments	Use Instructions
Spot-On Treatments					
Hartz® Reference 123 (14.85% ai)	Cats and kittens	* Pets ≤ 9 lbs: 192 mg ai/treatment * Pets > 9 lbs: 320 mg ai/treatment	Apply Liquid: squeeze tube	1	* Using the tip of the applicator to part the cat's (kitten's) hair at skin level, apply evenly to one spot along the cat's (kitten's) back. * Do not get product in pet's eyes or mouth. * Do not reapply for 30 days. * Use only on cats or kittens older than 12 weeks of age.
Hartz® Reference 121 (14.85% ai. with 45% permethrin & 1.48% pyriproxyfen)	Dogs and puppies	* Pets ≤ 10 lbs: 40.3 mg ai/treatment * Pets 11 - 20 lbs: 80.7 mg ai/treatment * Pets 21 - 55 lbs: 161.6 mg ai/treatment * Pets > 55 lbs: 193.8 mg ai/treatment	Apply Liquid: squeeze tube	1	* Using the tip of the applicator to part the dog's hair at skin level, apply evenly along the dog's back from the shoulder blades to the base of the tail. Apply monthly . Do Not reapply for 30 days. Do Not use on puppies less than 7 weeks old. Do Not use on cats.

3.2 Dietary Exposure/Risk Pathway

Dinotefuran is currently registered for use on leafy vegetables, cotton, fruiting vegetables, cucurbits, potatoes, grapes, and head and stem *Brassica* vegetables. The tolerances for these crops are based on detectable residues that may be present in or on crops at harvest. Dinotefuran may also potentially be present in drinking water, given its high water solubility, high mobility in soils, and potential persistence in the environment. The exposures and risks from food and drinking water were previously assessed (B. O'Keefe, D285577, 4/30/04; and B. O'Keefe, D309412. 12/08/04)[1,2].

The residue chemistry data submitted in support of the use of dinotefuran on leafy vegetables, cotton, fruiting vegetables, cucurbits, potatoes, grapes, and head and stem *Brassica* vegetables were reviewed in the following HED-memoranda: #1) L. Cheng, *Dinotefuran. Petition for the Establishment of Permanent Tolerances for Use on Leafy Vegetables (except Brassica). Summary of Analytical Chemistry and Residue Data.* D285648[10]; and #2) L. Cheng, *Dinotefuran. Petition for the Establishment of Permanent Tolerances on Cotton (PP#2F6427), Fruiting Vegetables, Cucurbits, Head & Stem Brassica Vegetables, Grapes, Potato, Meat, Milk, and Meat Byproducts (PP#3F6566). Summary of Analytical Chemistry and Residue Data.* D290191[11]. The drinking water assessment was completed by EFED on January 21, 2004 (S. Dutta, D290192)[9]. The acute and chronic dietary exposure assessment was completed in a HED-memorandum dated November 26, 2004 (L. Cheng, D309936).

Table 4 lists the conclusions of the HED Metabolism Assessment Review Committee (MARC) concerning the dinotefuran residues of concern in crops, livestock, rotational crops and drinking water (MARC Report, TXR # 52304, D293759, L. Cheng, 1/20/04)[12].

Table 4. Residues of Concern in Crops, Livestock, Rotational Crops, and Water

Matrix	Tolerance Expression	Residues for Risk Assessment
Plants	Dinotefuran, DN, UF	Dinotefuran, DN, UF, and PHP
Ruminants	Dinotefuran	Dinotefuran, UF, FNG
Poultry	Dinotefuran	Dinotefuran, FNG
Rotational Crops	Not decided	Not decided
Water	Not applicable	Dinotefuran, MNG, DN, UF, DN-2-OH, and DN-3-OH

3.2.1 Residue Profile

Permanent tolerances exists for combined residues of dinotefuran [(RS)-1-methyl-2-nitro-3-(tetrahydro-3-furylmethyl)guanidine] and its major metabolites, DN [1-methyl-3-(tetrahydro-3-furylmethyl)guanidine] and UF [1-methyl-3-(tetrahydro-3-furylmethyl)urea], calculated as dinotefuran, in/on the following commodities: leafy vegetables; cotton, seed, undelinted; cotton, gin byproducts; fruiting vegetables; cucurbits; head and stem *Brassica*; grapes; potato; meat, milk, and byproducts; tomato paste; raisins; potato chips; and potato granules. There are no established Codex, Canadian or Mexican maximum residue limits (MRLs) for dinotefuran.

3.2.2 Dietary Exposure Analyses

For the currently registered uses of dinotefuran, the acute and chronic dietary exposure assessment was completed in a HED-memorandum dated November 26, 2004 (L. Cheng, D309936)[4]. The dietary assessment is an unrefined conservative assessment. The acute and chronic dietary exposure analyses were conducted using the Dietary Exposure Evaluation Model-Food Consumption Intake Database (DEEM-FCID™, version1.3) program and the Lifeline™ model (version 2.0), which both incorporate consumption data from the United States Department of Agriculture's (USDA's) Continuing Surveys of Food Intakes by Individuals (CSFII), 1994-96/1998. 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 (<3% aPAD and <54% cPAD for the most highly exposed subgroup "children 1-2 years old").

Table 5. Dinotefuran Dietary Exposure & Risk Using DEEM-FCID (Upper Row) & LifeLine (Lower Row) Software

Population Subgroup*	Acute Dietary (95 Percentile)		Chronic Dietary	
	Dietary Exposure (mg/kg/day)	% aPAD**	Dietary Exposure (mg/kg/day)	% cPAD**
General U.S. Population	0.015	1.2	0.0042	21
	0.015	1.2	0.0041	21
All Infants (< 1 year old)	0.016	1.3	0.0037	18
	0.016	1.3	0.0035	18
Children 1-2 years old	**0.037**	**2.9**	**0.011**	**54**
	0.035	**2.8**	**0.0091**	**46**
Children 3-5 years old	0.027	2.2	0.0082	41
	0.028	2.3	0.0081	40
Children 6-12 years old	0.017	1.4	0.0050	25
	0.016	1.2	0.0045	23
Youth 13-19 years old	0.012	0.93	0.0032	16
	0.011	0.89	0.0030	15
Adults 20-49 years old	0.013	1.0	0.0037	18
	0.014	1.1	0.0038	19
Adults 50+ years old	0.013	1.0	0.0038	19
	0.014	1.1	0.0040	20
Females 13-49 years old	0.013	1.1	0.0037	19
	0.015	1.2	0.0040	20

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

3.3 Water Exposure/Risk Pathway

Per the recommendations of the HED Metabolism Assessment Review Committee (MARC), EFED provided estimated drinking water concentrations (EDWCs) for dinotefuran and its metabolites (MNG, DN, UF, DN-2-OH, and DN-3-OH); January 21, 2004 (S. Dutta, D290192)[9]. However, the degradates UF and DN-2-OH are photolysates and are not likely to be formed in the crop field. The formation of these degradates would be a result of direct exposure of parent to surface waters through spray drift, 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 76 ppb and 21 ppb, respectively. The acute and chronic ground water total EDWC (parent + metabolites) is 5.1 ppb.

3.4 Residential (Non-Occupational) Exposure/Risk Pathway

There is potential for exposure to homeowners in residential settings during the application of currently registered products containing dinotefuran, or from entering areas previously treated with dinotefuran, such as lawns where children might play, 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. The proposed new pet spot-on uses of dinotefuran add to these non-occupational exposures or risks.

3.4.1 Residential Handler Exposures and Risks

Potential exposures from applying spot-on treatments to pets were not assessed. Negligible exposure is expected from these products due to self-contained packaging and minimal handling requirements.

3.4.2 Residential Postapplication Exposures and Risks

As previously assessed and documented, postapplication exposures to adults and children may occur due to registered uses on turf and ornamentals (HED Memo, J. Arthur; D285650)[5]. From the proposed spot-on flea treatment of companion animals (i.e., dogs and cats), individuals of varying ages can potentially be exposed from contact with treated companion animals. Potential routes of exposure include incidental ingestion (toddlers only) and dermal. While it is assumed that most residential uses of dinotefuran will result in short-term (1 to 30 days) postapplication exposures, it is also believed that intermediate-term exposures (> 30 days to 180 days) are possible. Further, it is assumed that toddler exposures result in the worst case risks, and therefore only toddler postapplication exposures to treated companion animals were assessed.

Instructions for pet spot-on treatments include a monthly re-treatment regimen. Residues are anticipated to dissipate between applications. Because only an intermediate-term dermal endpoint was identified for the assessment, a 31-day average residue level was used to estimate exposure, based on a residue dissipation rate of 5% per day, and a re-application on the 31st day. The calculation begins with the day of application, where the amount of residue available on the animal is equal to 5% of the application rate (20% was also calculated). On each of the next 30 days this amount is diminished by 5%. On the 31st day, a new application amount is added. Then the residue amounts for each day are added and divided by 31 days to estimate the 31-day average residue on the animal available for transfer to humans.

It should be noted that the value to be used in this assessment for the percent of the application rate initially available to transfer from pet to human is 5%, and not the 20% standard value from HED's Residential Exposure SOPs [6,7,8], even though results from using both values are presented in the risk Tables below. The rationale for using the 5% value includes the following:

- The 20% transferrability factor in the SOPs is a bounding value, determined from a study that employed a vigorous rubbing of the treated area for an extended period of time.

- The 20% value was derived from a study on a shampoo product, which is presumed to have more readily available surface residues for transfer to humans than the proposed spot-on treatments which are applied to the animals skin, and thought to migrate more along the skin of the animal (i.e., not the fur).

- The results from a study on the dislodgeability of fipronil from animals treated by a similar spot-on treatment product (MRID 44433303), where dislodgeable residues were determined to represent less than 2% of the applied dose, were cited as a basis for using a 5% value in a previous assessment of an imidacloprid spot-on product (D268562; 1/22/01)[13]. **HED emphasizes that the fipronil data cited above is proprietary information.** While HED has used the 5% value in this assessment, the assumption that the proposed dinotefuran pet spot-on products are similar to the fipronil product may, or may not, be true. Therefore, **HED recommends that registration of the proposed dinotefuran pet spot-on products be conditional upon the completion of a dinotefuran transferrable residue study.**

The assessment includes exposure/risk estimates for both proposed products, Hartz® Reference 121 (14.85% ai) for dogs and puppies, and Hartz® Reference 123 (14.85% ai) for cats and kittens. The algorithms used for pet exposure scenarios are presented below, with summaries of the estimated exposures and risks presented in Tables 6 through 9.

Dermal Exposure

$$D = [(AR * F_{AR})/(SA_{pet}) * (1 - DR)^{t} * (SA_{hug}) * (AB)]/BW$$

where:

D	=	daily dose from dermal pet contact (mg/day);
AR	=	application rate or amount applied to animal in a single treatment (mg ai/animal);
F_{AR}	=	fraction of the application rate available as transferable residue (0.05 and 0.20);
SA_{pet}	=	surface area of a treated dog (cm^2/animal);

t	=	time after application (days);
DR	=	fractional dissipation rate per day (0.05 per day);
SA_{hug}	=	surface area of a child hug (cm^2 contact/hug);
AB	=	absorption factor (30%)
BW	=	body weight of child (15 kg).

Table 6. Dermal Exposure and Risk to Children from Treated Cats/Kittens

AR[1]	F_{AR}	SA_{pet}	Ave. 31-day Residue	SA_{hug}	AB	BW	Dose	MOE[2]
192 mg	0.2	5986 cm^2	0.00344 mg/cm^2	1875 cm^2	0.3	15 kg	0.129 mg/kg/day	170
	0.05		0.000859 mg/cm^2				0.0322 mg/kg/day	680
320 mg	0.2	5986 cm^2	0.00573 mg/cm^2	1875 cm^2	0.3	15 kg	0.215 mg/kg/day	100
	0.05		0.00143 mg/cm^2				0.0536 mg/kg/day	410

[1] Application rate is based on information from registrant.
[2] MOE = NOAEL/Dose, where the intermediate-term dermal endpoint was used (NOAEL = 22 mg/kg/day)

Table 7. Dermal Exposure and Risk to Children from Treated Dogs/Puppies

AR[1]	F_{AR}	SA_{pet}	Ave. 31-day Residue	SA_{hug}	AB	BW	Dose	MOE[2]
40.3 mg	0.2	5986 cm^2	0.000722 mg/cm^2	1875 cm^2	0.3	15 kg	0.027 mg/kg/day	810
	0.05		0.00018 mg/cm^2				0.0068 mg/kg/day	3300
80.7 mg	0.2	5986 cm^2	0.00145 mg/cm^2	1875 cm^2	0.3	15 kg	0.054 mg/kg/day	410
	0.05		0.000361 mg/cm^2				0.014 mg/kg/day	1600
161.6 mg	0.2	5986 cm^2	0.00289 mg/cm^2	1875 cm^2	0.3	15 kg	0.11 mg/kg/day	200
	0.05		0.000722 mg/cm^2				0.027 mg/kg/day	810
193.8 mg	0.2	5986 cm^2	0.00347 mg/cm^2	1875 cm^2	0.3	15 kg	0.130 mg/kg/day	170
	0.05		0.000867 mg/cm^2				0.033 mg/kg/day	670

[1] Application rate is based on information from registrant.
[2] MOE = NOAEL/Dose, where the intermediate-term dermal endpoint was used (NOAEL = 22 mg/kg/day)

Hand-to-Mouth

$$D = [(AR * F_{AR})/SA_{pet}) * (1 - DR)^t * (SAL) * SA_{hands} * Freq * Hr)]/BW$$

where:

D	=	daily nondietary ingestion dose from with treated pets (mg/day);
AR	=	application rate or amount applied to animal in a single treatment (mg ai/animal);
F_{AR}	=	fraction of the application rate available as transferable residue (0.05 to 0.20);
SA_{pet}	=	surface area of a treated dog (cm^2/animal);
t	=	time after application (days);
DR	=	fractional dissipation rate per day (0.05 per day);
SAL	=	saliva extraction factor (50%);
SA_{hands}	=	surface area of the hands (20 cm^2);
Freq	=	frequency of hand-to-mouth events (20 events/hour);
Hr	=	exposure duration (2 hours); and
BW	=	body weight (15 kg).

Table 8. Hand-to-Mouth Exposure and Risk to Children from Treated Cats/Kittens

AR[1]	F_{AR}	SA_{pet}	Ave. 31-day Residue	SAL	SA_{hands}	Freq (events/hour)	ET (hours)	Dose (mg/kg/day)	MOE[2]
192 mg	0.2	5986 cm^2	0.00344 mg/cm^2	0.5	20 cm^2	20	2	0.092	240
	0.05		0.000859 mg/cm^2					0.023	960
320 mg	0.2	5986 cm^2	0.00573 mg/cm^2	0.5	20 cm^2	20	2	0.153	140
	0.05		0.00143 mg/cm^2					0.038	580

[1] Application rate is based on information from registrant.
[2] MOE = NOAEL/Dose, where the intermediate-term incidental oral endpoint was used (NOAEL = 22 mg/kg/day)

Table 9. Hand-to-Mouth Exposure and Risk to Children from Treated Dogs/Puppies

AR[1]	F_{AR}	SA_{pet}	Ave. 31-day Residue	SAL	SA_{hands}	Freq (events/hour)	ET (hours)	Dose (mg/kg/day)	MOE[2]
40.3 mg	0.2	5986 cm^2	0.000722 mg/cm^2	0.5	20 cm^2	20	2	0.0192	1100
	0.05		0.00018 mg/cm^2					0.0048	4600
80.7 mg	0.2	5986 cm^2	0.00145 mg/cm^2	0.5	20 cm^2	20	2	0.0387	570
	0.05		0.000361 mg/cm^2					0.00963	2300
161.6 mg	0.2	5986 cm^2	0.00289 mg/cm^2	0.5	20 cm^2	20	2	0.0771	290
	0.05		0.000722 mg/cm^2					0.0193	1100
193.8 mg	0.2	5986 cm^2	0.00347 mg/cm^2	0.5	20 cm^2	20	2	0.0925	240
	0.05		0.000867 mg/cm^2					0.023	960

[1] Application rate is based on information from registrant.
[2] MOE = NOAEL/Dose, where the intermediate-term incidental oral endpoint was used (NOAEL = 22 mg/kg/day)

The MOEs for **postapplication dermal and incidental oral hand-to-mouth exposures to children from hugging treated companion cats or dogs** are ≥ 100, and therefore **do not exceed HED's level of concern.**

3.4.3 Combined Residential Risks

The Agency combines residential risks resulting from exposures to individual chemicals when it is likely they can occur simultaneously based on the use pattern and the behavior associated with the exposed population. Typically, the Agency only combines exposures from different pesticide uses when risks from the individual uses are not already a concern. The risks from all routes of exposure (e.g., dermal, inhalation, incidental oral) for a given pesticide use and activity (e.g., hugging treated pets) can be added, as well as, the risks from all routes of exposure from different residential uses that can possibly co-occur (e.g., exposure from treating indoor areas for fleas and hugging treated pets).

HED believes it is possible that indoor areas may be treated for fleas at the same time that pets are treated for fleas. However, at this time there are no registered uses for indoor flea

treatment. If such indoor uses are to be registered, then combining of these uses with pet spot-on treatment will be considered.

Children's dermal and incidental oral (i.e., hand-to-mouth activity) exposures from hugging treated pets have been combined to give a total MOE. Because the toxicity endpoint (i.e., NOAEL = 22 mg/kg/day, based on body weight gain) is the same for both dermal and incidental oral exposures, the total combined risk (i.e., total MOE) for children is calculated by adding the daily doses from all relevant exposure routes and activities and comparing this total to the common toxicity endpoint NOAEL. The resulting risks are presented in Tables 10 and 11.

Table 10. Children's Residential Combined Risk from Hugging Cats/Kittens

Scenario	Route	Daily Dose (mg/kg/day)	MOE	Total MOE
192 mg/animal with 20% transferrable	Dermal	0.129	170	100
	HTM (Hand-to-Mouth)	0.092	240	
192 mg/animal with 5% transferrable	Dermal	0.032	680	400
	HTM (Hand-to-Mouth)	0.023	960	
320 mg/animal with 20% transferrable	Dermal	0.215	100	60
	HTM (Hand-to-Mouth)	0.153	140	
320 mg/animal with 5% transferrable	Dermal	0.0536	410	240
	HTM (Hand-to-Mouth)	0.038	580	

Table 11. Children's Residential Combined Risk from Hugging Dogs

Scenario	Route	Daily Dose (mg/kg/day)	MOE	Total MOE
40.3 mg/animal with 20% transferrable	Dermal	0.027	810	480
	HTM (Hand-to-Mouth)	0.0192	1100	
40.3 mg/animal with 5% transferrable	Dermal	0.0068	3300	1800
	HTM (Hand-to-Mouth)	0.0048	4600	
80.7 mg/animal with 20% transferrable	Dermal	0.054	410	240
	HTM (Hand-to-Mouth)	0.0387	570	
80.7 mg/animal with 5% transferrable	Dermal	0.014	1600	910
	HTM (Hand-to-Mouth)	0.00963	2300	
161.6 mg/animal with 20% transferrable	Dermal	0.11	200	120
	HTM (Hand-to-Mouth)	0.0771	290	

Table 11. Children's Residential Combined Risk from Hugging Dogs				
161.6 mg/animal with 5% transferrable	Dermal	0.027	810	480
	HTM (Hand-to-Mouth)	0.0193	1100	
193.8 mg/animal with 20% transferrable	Dermal	0.130	170	100
	HTM (Hand-to-Mouth)	0.0925	240	
193.8 mg/animal with 5% transferrable	Dermal	0.033	670	390
	HTM (Hand-to-Mouth)	0.023	960	

The total MOE for **children's combined risk from hugging pets** is ≥ 100 for all scenarios (using 5% of the application rate for residue initially available to transfer), and therefore, **does not exceed HED's level of concern.**

3.4.4 Summary/Characterization of Residential Risk and Data Gaps

The HIARC did not identify a short-term dermal toxicity endpoint; therefore, the intermediate-term endpoint was used for all dermal risk estimates, even for scenarios where the residential exposure duration is believed to be primarily short-term, based on the use pattern. Because the use of the intermediate-term endpoint NOAEL for short-term exposures is conservative, HED used average residue levels over a 31-day period in calculating postapplication risks.

Combined dermal and incidental oral exposures of children from hugging pets that have been treated with the proposed dinotefuran spot-on products result in MOEs ≥100, and therefore, do not exceed HED's level of concern. However, as can be seen in the assessment, when using the standard value from HED's SOPs [6,7,8], for the amount of residue initially available to transfer from treated pets (20%), the MOE for combined dermal and incidental oral exposures from hugging cats treated at the maximum application rate results in an MOE of 60, which exceeds HED's level of concern. While HED has provided a rationale for using the non-SOP value for initial available residue (5%) in a previous section, the most appropriate value for use in this assessment should come from a residue transferrability study with proposed dinotefuran pet spot-on treatments. For this reason, **HED recommends that a registration of the proposed dinotefuran pet spot-on products be conditional upon the completion of a transferrable residue study.** ***Note: Prior to initiating this study, a protocol should be submitted to the Agency for review.***

4.0 AGGREGATE RISK ASSESSMENTS AND RISK CHARACTERIZATION

Aggregate exposure assessments were performed for residential intermediate-term exposures to children (from dermal and incidental oral exposures).

Because HED does not have surface and ground water monitoring data to calculate a quantitative aggregate exposure, DWLOCs were calculated. A drinking water level of comparison (DWLOC) is a theoretical upper limit on a pesticide's concentration in drinking water in light of total aggregate exposure to a pesticide in food, drinking water, and through residential uses. A DWLOC will vary depending on the toxicity endpoint, drinking water consumption, body weights,

and pesticide uses. Different populations will have different DWLOCs. HED uses DWLOCs in the risk assessment process to assess potential concern for exposure associated with pesticides in drinking water. DWLOC values are not regulatory standards for drinking water. If estimated drinking water concentration (EDWC) values are less than DWLOCs, aggregate exposure to pesticides are below HED's level of concern.

To calculate DWLOCs, the dietary food estimates (from DEEM-FCID™) were subtracted from the PAD value to obtain the maximum water exposure level. DWLOCs were then calculated using the standard body weights and drinking water consumption figures: 70 kg/2 L (U.S. population, adult male 20-49 yrs, and adults >50 yrs), 60 kg/2 L (females 13-49 yrs and youths 13-19 yrs), and 10 kg/1 L (infants, children 1-2 yrs, children 3-5 yrs, and children 6-12 yrs).

4.1 Short- and Intermediate-Term Aggregate Risk Assessments

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 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, a short-term aggregate risk assessment was not performed.

An intermediate-term aggregate risk assessment was performed as a screening level assessment. Intermediate-term aggregate risk assessments were performed for children, since they are believed to be the most highly exposed population. The child subgroup with the highest estimated chronic dietary exposure (children 1-2 years old) was aggregated with residential exposures (at the highest application rates) to children playing on treated lawns (dermal and oral hand-to-mouth exposures) and playing with companion animals (dermal and oral hand-to-mouth exposures) in order to calculate the worst case intermediate-term aggregate risks to children. **Compared with the EDWCs generated by EFED, HED's calculated aggregate intermediate-term DWLOCs do not exceed HED's level of concern for the subgroup population of children 1-2 years old** (Table 12):

Table 12. Aggregate Risk Assessment for Intermediate-Term Exposure of Children to Dinotefuran.

Exposure Scenarios	NOAEL mg/kg/day	Level of Concern MOE[1]	Max Exposure[2] mg/kg/day	Average Food Exposure mg/kg/day	Residential Exposure[3] mg/kg/day	Aggregate MOE (food & residential)[4]	Max Water Exposure[5] mg/kg/day	Ground Water EDWC[6] µg/L	Surface Water EDWC[6] µg/L	Intermediate Term DWLOC[7] µg/L
Dogs	22	100	0.22	0.011	0.0560	330	0.1530	21	5.06	1500
Cats	22	100	0.22	0.011	0.0916	210	0.1174	21	5.06	1200

[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] Maximum exposure (mg/kg/day) = NOAEL/level of concern MOE
[3] Residential exposures (at the highest application rates) to children hugging companion animals (combined dermal + oral hand-to-mouth)
[4] Aggregate MOE = [NOAEL/(Avg. Food Exposure + Residential Exposure)]
[5] Maximum Water Exposure (mg/kg/day) = Target Maximum Exposure - (Food Exposure + Residential Exposure)
[6] The use site producing the highest level was used; i.e. turf.
[7] DWLOC (µg/L) = [Maximum water exposure (mg/kg/day) x body weight (10 kg)]/[Water exposure (1L) x 10^{-3} mg/µg]

5.0 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 tolerance 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/.

6.0 OCCUPATIONAL EXPOSURE

Hand application to pets by squeeze bottle was not assessed because only negligible handler exposure is expected due to the self-contained packaging and minimal handling requirements. Also, postapplication occupational exposure to treated animals is not expected. Companion animals are expected to be treated and immediately returned to their owners such that occupational postapplication contact will be negligible.

7.0 DATA NEEDS/LABEL REQUIREMENTS

HED emphasizes that the fipronil data cited above in this document is proprietary information. There may be data compensation issues with the use of fipronil data in this assessment.

HED recommends that a registration of the proposed dinotefuran pet spot-on products be conditional upon the completion of a dinotefuran transferrable residue study. ***Note: Prior to initiating this study, a protocol should be submitted to the Agency for review.***

8.0 REFERENCES

[1] *PP#: 2F6427 & 3F6566. Dinotefuran. Health Effects Division (HED) Risk Assessment.* B. O'Keefe, D285577, 4/30/04.

[2] *Petition Nos. 2F6427 & 3F6566. Dinotefuran Risk Assessment for Proposed New Uses.* B. O'Keefe, D309412, 12/8/04.

[3] *Dinotefuran - Report of the Hazard Identification Assessment Review Committee* (Memo, HED TXR No. 0052409, 03/05/2004).

[4] *Dinotefuran Acute and Chronic Dietary Exposure Assessments for the Section 3 Registration on Cotton, Fruiting Vegetables, Cucurbits, Head & Stem Brassica Vegetables, Grape, Potato, and Leafy Vegetables (except Brassica).* L. Cheng, D309936, 11/26/2004.

[5] *Occupational and Residential Exposure Assessment for Proposed Section # Registration of Dinotefuran on Leafy Vegetables and Residential (Non-Food) Use Sites.* J. Arthur, D285650. 4/27/2004.

[6] Draft Standard Operating Procedures (SOPs) for Residential Exposure Assessments: (OPP; December 18, 1997)

[7] Health Effects Division Science Advisory Council for Exposure *SOP 12: Recommended Revisions To The Standard Operating Procedures For Residential Exposure Assessment* which was completed on February 22, 2001.

[8] Draft: Part B - SOPs, Residential SOPs (Revisions of April 5, 2000)

[9] EFED Memo - *Tier I Estimated Drinking Water Concentrations of Dinotefuran (MTI446) and its major transformation products for use in Human Health Risk Assessment.* S Dutta, D290192. 01/21/2004.

[10] *Dinotefuran. Petition for the Establishment of permanent Tolerances for Use on Leafy vegetables (except Brassica). Summary of Analytical Chemistry and Residue Data.* L. Cheng, D285648, 02/26/2004.

[11] *Dinotefuran. Petition for the Establishment of Permanent Tolerances on Cotton (PP#2F6427), Fruiting Vegetables, Cucurbits, Head & Stem Brassica Vegetables, Grapes, Potato, Meat, Milk, and Meat Byproducts (PP#3F6566). Summary of Analytical Chemistry and Residue Data.* L. Cheng, D290191, 11/23/2004.

[12] *Dinotefuran. Report of the Metabolism Assessment Review Committee.* L Cheng, D293759, 12/22/2003.

[13] *Non-Occupational/Residential Exposure Assessment for Imidacloprid - Turf and Pet Uses.* Y. Donovan, D268562, 1/22/01.

cc: RAB3 file; B. O'Keefe; J. Arthur