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OFFICE OF PREVENTION, PESTICIDE AND TOXIC SUBSTANCES

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MEMORANDUM

Date: 4/2/2010

SUBJECT: Pymetrozine. Updated Aggregate Human Health Risk Assessment.

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Background

In 2001, the Office of Pesticide Programs (OPP) Health Effects Division (HED) completed a human health risk assessment for the insecticide pymetrozine based on proposed uses on a number of crops, including cotton, hops, pecans, leafy vegetables, head and stem Brassica, turnip greens, cucurbits, and fruiting vegetables (D. Dotson, D279321, 12/20/2001). The resulting Federal Register (FR) notice announcing the establishment of relevant tolerances (66 FR 66786, December 27, 2001) was the subject of objections filed by the Natural Resources Defense Council (NRDC) during 2002; pymetrozine was just one of 13 pesticides included in the objections, which were generally directed at children's safety factor issues, aggregate risk issues, and issues related to the use of the LOAEL (lowest observed adverse effects level) in risk assessment, in the absence of a NOAEL (no observed adverse effects level). For pymetrozine,

the NRDC objections were based on 1) EPA's use of a 3X uncertainty/FQPA factor to account for the lack of a developmental neurotoxicity (DNT) study; and 2) use of a LOAEL for dose selection for acute and short term risk assessments.

The Agency's final order denying the NRDC objections to tolerances covered a host of issues for the 13 relevant chemicals, including the specific issues raised for pymetrozine [OPP–2005–0190; FRL–7727–4, 8/10/2005]. Subsequently, NRDC petitioned for a review of the Agency's final order by the 9th Circuit Court of Appeals. The Court determined that EPA had not been arbitrary and capricious in issuing pymetrozine tolerances in the absence of the required DNT study. However, the Court was unable to determine whether or not EPA had reliable data to reduce the 10X FQPA factor to 3X, in the absence of the DNT study. Therefore, the issue was remanded to EPA to further clarify the Agency's position regarding the use of a 3X factor in the absence of the DNT study.

HED notes that a DNT study with pymetrozine was subsequently submitted and evaluated (R. Mitkus, D300889, 7/13/2005). The purpose of this memorandum is to provide an assessment of human health risks associated with registered pymetrozine uses and corresponding tolerances, incorporating the results of the submitted DNT study, and concomitant updated hazard characterization. The updated human health risks are based on the most recent aggregate exposure and risk assessment conducted to support a new use on asparagus (W. Drew, D285517, 12/29/2004); however, a new dietary exposure assessment has been conducted to incorporate updated usage information (D372578, C. Swartz). HED has not attempted to further clarify the previous rationale for retaining the 3X FQPA factor to account for the lack of the DNT, since the DNT has been received and the results incorporated into the assessment. The updated hazard characterization, dose-response assessment, FQPA evaluation and endpoint selection have been provided as an attachment to this document (See Appendix A).

General Overview of the Use Patterns and Pathways of Exposure

Pymetrozine is a selective insecticide and a member of the chemical class known as pyridine azomethines, which has activity against a variety of sucking insect pests such as aphids and whiteflies. It is registered for use on a number of agricultural crops, including asparagus, head and stem Brassica, Brassica leafy greens, cotton, hops, pecans, turnips, fruiting, cucurbit and leafy vegetables, as well as tuberous and corm vegetables. The associated tolerances in raw agricultural commodities (RACs) range from 0.02 ppm (in tuberous/corm vegetables) to 6 ppm (hops, dried cones). The use patterns generally allow 1 or more applications to agricultural crops, using standard application equipment and methods. Although use on ornamental crops is permitted on registered labels, these uses are not expected to result in significant residential exposure, and there are no uses registered that would result in significant residential exposure following application, or that allow applications to be made by homeowners. Therefore, potential pathways of exposure for aggregate assessments include food and water, for which acute, chronic (non-cancer) and cancer risks have been evaluated using the updated endpoints and doses for acute and chronic dietary risk assessment, and the previously calculated cancer potency factor.

Updated Aggregate Exposure and Risk from Pymetrozine

A new dietary exposure assessment was conducted for pymetrozine based on all established commodity tolerances and an updated (12/2009) evaluation of percent crop treated (%CT) for most of the more heavily-consumed of these commodities. Although the tolerance expression includes only the parent, pymetrozine, dietary exposure and risk assessments include additional residues of toxicological concern. For the acute dietary assessment, residues included were greater than the established tolerances with the exception of asparagus; in asparagus, combined residues were less than the limit of quantitation (LOQ), which served as the basis for the tolerance of 0.04 pm, which was used in the acute analysis. For the chronic and cancer analyses, average field trial residues were used, and in addition estimates of %CT were also used. The updated dietary and aggregate assessments demonstrate that using the endpoints selected from the DNT study, risks are not of concern. The dietary exposure estimates are considered to be upper bound, and further refinements would likely result in reduced exposure and risk estimates. The dietary risk assessment (D372578) is attached as an appendix to this document (See Appendix B), and the results are shown in the table below.

Pymetrozine Aggregate Dietary (Food + Drinking Water) Exposure and Risk Estimates.

	Acute (95th Percentile)		Chronic		Cancer	
Population Subgroup	Exposure (mg/kg/day)	% aPAD*	Exposure (mg/kg/day)	% cPAD*	Exposure (mg/kg/day)	Risk
General U.S. Population	0.002831	35	0.000237	2.9	0.000151	1.8×10^{-6}
All Infants (< 1 year old)	0.003882	48	**0.000707**	**8.7**		
Children 1-2 years old	**0.004368**	**54**	0.000350	4.3		
Children 3-5 years old	0.004034	50	0.000329	4.1		
Children 6-12 years old	0.003027	37	0.000224	2.8		
Youth 13-19 years old	0.002312	28	0.000174	2.2		
Adults 20-49 years old	0.002698	33	0.000222	2.7		
Adults 50+ years old	0.002669	33	0.000235	2.9		
Females 13-49 years old	0.002625	32	0.000217	2.7		

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

Conclusions

HED has evaluated the available hazard data for pymetrozine, including the developmental neurotoxicity study. Despite the missing immunotoxicity study now required for conventional pesticides, the database is adequate to provide endpoints and doses for risk assessment which are both conservative and protective. Estimated aggregate risks remain below HED's level of concern.

Appendix A. Pymetrozine Hazard Characterization, Doses and Endpoints for Risk Assessment.

3.0 HAZARD CHARACTERIZATION/ASSESSMENT

3.1 Hazard and Dose-Response Characterization

3.1.1 Database Summary

The scientific quality of the submitted studies is high, and the toxicity profile of pymetrozine can be characterized for potential carcinogenic, mutagenic, developmental, and reproductive effects. The required developmental, reproductive, subchronic and chronic toxicity studies, including the acute and subchronic neurotoxicity studies were available for the 12/29/2004 risk assessment. However, the developmental neurotoxicity study (TXR# 0052459; D300889) has only been recently reviewed and made available for incorporation into this risk assessment. As part of the new EPA Part 158 guidelines, an immunotoxicity study in rats must be submitted to the Agency for review. This study will be required during registration review and could be required sooner as a condition of registration if any new uses of pymetrozine are proposed.

3.1.1.1 Studies available and considered (Animal, Human, General Literature)

The acceptable/guideline studies available for risk assessment include: 1) 90-day subchronic oral toxicity studies in rats, dogs, and mice; 2) 28-day dermal study in rats; 3) developmental studies in rats and rabbits, as well as a 2-generation reproduction study in rats; 4) chronic and/or carcinogenicity studies in rats, mice, and dogs; 5) neurotoxicity studies in rats (acute, subchronic, and developmental (DNT)); 6) single and repeated-dose rat metabolism studies; and 7) a complete mutagenic battery. A dermal penetration study was available to determine a dermal absorption factor for risk assessment.

3.1.1.2 Mode of Action

Pymetrozine is active against a variety of sucking insect pests such as aphids and whiteflies. It has a unique mode of action in that it is a feeding inhibitor. Pymetrozine affects the mechanism by which an aphid inserts its stylus into the plant tissue. The cellular mode of action of pymetrozine is not described, but is believed to be related to some aspect of neuroregulation or actual effect on the nerve-muscle interaction.

3.1.2 Toxicological Effects

Pymetrozine has low acute toxicity being classified as III or IV in the acute oral, dermal, inhalation and irritation studies. Pymetrozine is regarded as a slight sensitizer.

The liver was the primary target in rats with hepatocellular hypertrophy and increases in both absolute and relative liver weights occurring at a dose level of 100 ppm and higher. Other effects in rats included decreases in body weight, increases in bilirubin and evidence of leukocytosis and changes in spleen weight. Changes in kidney, testis, ovary, brain and heart weights were not accompanied by pathological changes. Cholesterol and phospholipid levels

were also increased. Liver pathology was also evident in the multi-generation reproduction study. In the dog, anemia and associated increases in bilirubin appeared to be a primary effect, although liver weight increases, intrahepatic bile duct hyperplasia, and skeletal muscle hypertrophy were also evident.

Pymetrozine is considered positive for liver tumors in both rats and mice. In accordance with the EPA *Proposed Guidelines for Carcinogen Risk Assessment* (April 10, 1996), the Cancer Assessment Review Committee (CARC) classified pymetrozine as a "likely human carcinogen" and recommended that quantification of risk be estimated by a cancer potency factor of 0.0119 $(mg/kg/day)^{-1}$ for combined liver tumors (benign hepatomas and/or carcinomas) in male and female mice and female rats. Pymetrozine is not considered to have a mutagenic or genetic toxicity concern.

In the developmental toxicity studies, maternal toxicity consisted of decreased body weight and body weight gain and an associated decrease in food consumption for both the rat and rabbit. At dose levels higher than those producing maternal toxicity, there were indications of skeletal anomalies (such as poor or absent ossification and dumbbell shaped thoracic vertebral centers) in the rat. In the rabbit, skeletal abnormalities were evident at the same dose that caused maternal toxicity; these abnormalities included an increase in additional (13^{th}) ribs, fused sternebrae, additional caudal vertebrae centers, and poor ossification. Additional effects included reduced litter size and increased postimplantation loss. In the multi-generation reproduction study, toxicity in the dams included reduced body weight and associated food consumption, liver pathology as well as liver, spleen and thymus weight effects. There was also decreased body weight gain in the pups during lactation and some delay in eye opening.

Finally, there was evidence of neurotoxicity in the acute, subchronic, and the developmental neurotoxicity studies. In the acute study, a transient decrease in the body temperature and decreased activity in the FOB and motor activity assessments were evident; stereotypy (excessive head movement and sniffing) and tiptoe gait were observed in the subchronic study; and changes in brain morphometrics were observed in all dose groups examined in the DNT. While present, the indications of neurotoxicity were not consistent between the acute, subchronic, and DNT studies.

3.1.3 Dose Response

The liver was affected in a dose-dependent and time-dependent manner in the rat, dog and mouse as indicated by increased hepatocellular hypertrophy and relative size. In the rat, liver effects were evident at lower doses after chronic administration and males appeared to be more sensitive than females. The lowest dose associated with hepatic hypertrophy was 360/370 (M/F) mg/kg/day in the subchronic rat study, 3.76/4.48 (M/F) mg/kg/day in the chronic rat study, and 13.9/16.0 (M/F) mg/kg/day in the two generation rat reproduction study. In the mouse, hepatocellular hypertrophy was observed in the 90-day range-finding study at the lowest dose tested (143 mg/kg/day) and the carcinogenicity study at the mid-dose (250 mg/kg/day). The incidences and severity of hypertrophy increased with dose but there was no indication of liver pathology in the rat or mouse. In dogs, intrahepatic bile duct proliferation, increased liver weights, hepatocyte necrosis and increased alkaline phosphatase activity were observed in the

90-day range-finding study at a dose level of 14 mg/kg/day. In the chronic feeding study in dogs, males had an increase in relative and absolute liver weights at a dose level as low as 5.33 mg/kg/day; however, pathology was only evident at the highest dose tested of 27.8 mg/kg/day.

Pymetrozine affects the red blood cells in the rat, mouse and dog, with the dog being the most sensitive species. In the rat, increases in bilirubin in both sexes and bilirubinemia in females were observed in the subchronic study at a dose level of 360 mg/kg/day. In the chronic study, increased bilirubin in males was evident at 123.4 mg/kg/day, the highest dose tested. It appears in this case that males may be more sensitive to the effects than females. Because of dose spacing, it is not possible to tell whether or not the effect is dose-dependent. The effects on blood cells in the rat are marginal, but are consistent with those seen in the dog. In the mouse, increases in relative spleen weight and splenic extramedullary hematopoiesis were observed in both sexes in the subchronic study at 429 mg/kg/day. In the carcinogenicity study, increases in extramedullary hematopoiesis and hemosiderosis above background, and bone marrow hypercellularity indicate possible effects on blood elements at 250 mg/kg/day; however, there were no supporting indications (*e.g.*, changes in red blood cell, hemoglobin, or hematocrit measures) from the hematology assessments. The effects in the mouse are also marginal, but are consistent with those seen in the dog. In the 90-day dog study, there was evidence of anemia at 54 mg/kg/day. However, the pathology data in the spleen and bone marrow do not consistently support the anemia, therefore the underlying cause of the anemia may be by another mechanism. In the chronic study, anemia was observed in females at 27.8 mg/kg/day. In the subchronic study, the decreases in red blood cell parameters appeared at an earlier time period in the females than in the males (4 weeks versus 8 weeks). Therefore, female dogs appear to be more sensitive than the males to this anemic effect.

Pymetrozine affects the lymphatic system in the rat, mouse and dog, with the dog being most sensitive. In the rat and dog, these effects generally appear in the subchronic studies but not in the chronic studies. This observation could possibly be explained by the fact that the thymus normally tends to diminish in aging animals, thereby reducing the differences between the control and treated groups in older animals. In the rat, leucocytosis and atrophy of the thymus were observed at 360 mg/kg/day in the subchronic study. Hyperplasia of the lymphatic follicles of the splenic white pulp (females) and decreased absolute and relative thymus weights (males) were observed in the reproduction study at 136.9/151.6 (M/F) mg/kg/day. No effects on the lymphatic system were observed in the chronic rat study at dose levels up to 148.3 mg/kg/day. There does not appear to be any difference in sensitivity between the sexes with respect to the effects on the lymphatic system.

In the dog, decreases in thymus weight and atrophy of the thymus were observed in both sexes in the subchronic study at 54 mg/kg/day. White pulp lymphatic hyperplasia of the spleen was observed in the chronic study, but only in 1 female at 5.33 mg/kg/day, and 1 male and 1 female at 27.8 mg/kg/day. This effect was not seen in the 90-day dog study nor does it indicate a specific impact on the immune system or anemia. In the mouse, decreased thymus weights were observed in the carcinogenicity study at 675 mg/kg/day.

There was evidence of neurotoxicity in the acute, subchronic, and developmental neurotoxicity studies in the rat. In the acute study, there was a decrease in body temperature in males and

females at all doses; a 2% decline was observed in the low dose (125 mg/kg/day), up to a 7% decrease in the high dose group (2000 mg/kg/day). In the functional observation battery (FOB) decreased activity was observed at all dose levels. Furthermore, clinical signs including tremors, decreased mobility, and abnormal hindlimb positioning were observed in the males (2000 mg/kg) and females (500 and 2000 mg/kg). In the subchronic neurotoxicity study in rats, stereotypy (males) and tiptoe gait (females) were observed at the highest dose (201 mg/kg/day). However, these effects were observed in only a few animals or occurred inconsistently. In the developmental neurotoxicity study, there were no clinical signs of neurotoxicity in the dams or offspring. However, changes in brain morphometrics of the offspring included increased thickness of the corpus callosum and dorsal cortex in the lowest dose tested. There was also an increased thickness of the inner granular and molecular layers of the pre-pyramidal fissure in the cerebellum in the high-dose rats. Neurotoxicity was not observed in any of the other studies.

3.2 Absorption, Distribution, Metabolism, Excretion (ADME)

In oral and intravenous (iv) metabolism studies, rats were dosed with radiolabeled pymetrozine. Greater than 90% of the administered dose of pymetrozine was eliminated within 7 days of exposure. Urine accounted for the greatest percentage of radioactivity; 52-73.5% after 24 hours and 56.3-80.3% after 7 days. Other significant sources of radioactivity (determined after 7 days) included expired air (0.2-0.7%), tissues (0.3-3.8%), feces (15.4-38.9%), and cage washes (0.2-0.7%). After a high dose was administered, 12 urinary and fecal metabolites were recovered, isolated and characterized. There was a relatively high level of unchanged test material in the urine at the high dose of 100 mg/kg, suggesting metabolic saturation. Three major metabolic pathways were observed: 1) oxidation of the methyl substituent at the triazine ring which was further oxidized to corresponding carboxylic acid; 2) oxidation at methylene group within the triazine ring; and 3) cleavage of the bridge between the two rings giving rise to several single ring metabolites. There was no indication that conjugated metabolites were formed. Maximum blood concentrations were attained at 15 minutes (0.3 ppm) and at 4 hours (60 ppm) following low and high oral dosing, respectively. Calculated half life times ($t_{½}$) for the depletion of radiolabel from all the tissues ranged from 1 to 2 hours at the 0.5 mg/kg dose (both labels) and from 2 to 11 hours at the 100 mg/kg dose, with the pyridine label having a relatively longer $t_{½}$ than the triazine label.

A dermal absorption study in the rat indicated dermal penetration values of up to 0.28%, not including material that adhered to the skin. However HED determined that the low amount of radioactivity used may have compromised the detectability of the actual penetration and determined that an upper bound 1% dermal absorption factor would be more appropriate. It is very unlikely that pymetrozine associated with the skin will be available systemically.

3.3 FQPA Considerations

3.3.1 Adequacy of the Toxicity Database

The toxicology database for pymetrozine is adequate for an FQPA assessment based on the available acceptable/guideline studies: (1) developmental toxicity studies in rats and rabbits; (2) a two-generation reproduction toxicity study in rats; and (3) a developmental neurotoxicity (DNT) study in rats (acceptable/non-guideline).

Study deficiencies were identified in the DNT: *i*) there was technical failure of the recording equipment for auditory startle resulting in a lack of data for 3 rats/dose on postnatal day (PND) 23, one control on PND 61, and three rats in the 500 ppm group on PND 61. HED determined that the loss of data was minor and did not significantly impact the study results; *ii*) The DNT was classified as acceptable/non-guideline because the positive control data have not been reviewed. Positive control data were submitted for tail flick response, learning and memory, motor activity, functional observational battery (FOB) and neuropathology for pymetrozine. HED is currently in the process of reviewing the positive control data for the all the submitted DNT studies, including the pymetrozine DNT study. However, until all of the control data have been reviewed, the DNT will be classified as acceptable/non-guideline.

3.3.2 Evidence of Neurotoxicity

In the acute neurotoxicity study in rats, there was a transient decrease in the body temperature and decreased activity at the low dose along with tremors, decreased mobility, and abnormal hindlimb positioning at the mid and high-dose. In the subchronic neurotoxicity study in rats, stereotypy in males and tiptoe gate (walking on toes) in females were observed at the high dose. The frequency and magnitude of these effects were low.

In the rat developmental neurotoxicity study, pup toxicity was observed below parentally toxic dose levels. Parental toxicity was based on complete litter losses, with a NOAEL of 8.1 mg/kg/day and a LOAEL of 38.7 mg/kg/day. Toxic effects including distended abdomen, slight hunched posture, difficult parturition, pale, sides pinched in, staining around nose, and subdued behavior were observed in dams at the highest dose tested, 173.1 mg/kg/day. All dams in this dose group were sacrificed prior to scheduled termination due to clinical signs of toxicity and complete litter losses. In the pups, changes in brain morphometry were observed at the low- and mid-dose; a NOAEL for the effect was not identified. Excessive toxicity in the high-dose rats precluded examination of this group.

3.3.3 Developmental Toxicity Studies

In both the rat and rabbit developmental toxicity studies, developmental toxicity was only observed in the presence of maternal toxicity. In the rat, the maternal and developmental NOAELs were 30 mg/kg/day, with LOAELs of 100 mg/kg/day based on reduced body weight gains/food consumption in the dams and increased incidence of skeletal anomalies in the fetuses. In the rabbit study, the maternal and developmental NOAELs were 10 mg/kg/day, with LOAELs of 75 mg/kg/day based on reduced body weight gains/reduced food consumption in the dams and increased incidence of skeletal anomalies in the fetuses.

In the DNT, no treatments effects on offspring body weight, body weight gain, food consumption, developmental landmarks, clinical signs, FOB, motor activity, acoustic startle response, learning and memory, or brain weights were observed. However, significant changes in brain morphometry including increased thickness of the corpus callosum (9% in PND 63 males) and dorsal cortex (10% in PND 12 females) were observed in the offspring at a LOAEL of 8.1 mg/kg/day, the lowest dose tested. At the mid-dose of 38.7 mg/kg/day, the corpus

callosum thickness increased was slightly greater in the males (15% at PND12 and 13% at PND 63) and there was an increased thickness of the inner granular (19%) and molecular layers (6%) of the pre-pyramidal fissure in the cerebellum in PND 63 males. However, at the mid-dose, the dorsal cortex thickness in females (↑ 9%) was similar to that observed at the LOAEL. It should be noted that these parameters could not be evaluated at the highest dose levels due to early sacrifice of the high dose group. A NOAEL for brain morphometric changes was not determined.

3.3.4 Reproductive Toxicity

There is no evidence of treatment related reproductive toxicity in the rat reproduction study. Offspring effects were seen at similar or higher doses than those which caused parental/systemic effects. The parental systemic NOAEL of 1.4 /1.6 mg/kg/day (M/F) was based on liver effects observed in the F0 and F1 males at the LOAEL of 13.9/16.0 mg/kg/day. The offspring systemic/developmental NOAEL of 13.9/16.0 mg/kg/day was based on decreased pup weight and delay in eye opening in both F1 and F2 litters at the LOAEL of 136.9/151.6 mg/kg/day.

Conversely, the maternal LOAEL in the DNT was 38.7 mg/kg/day based on complete litter loss, with a NOAEL of 8.1 mg/kg/day. Complete litter losses for the control, low-, mid- and high-dose groups were 2/30 (#litters lost/#litters in dose-group), 3/30, 5/59, and 4/15, respectively. Furthermore, there was a dose-dependent increase in the number of pups dying on PNDs 1-5; 48, 57, 95, and 151 deaths in the control, low-, mid- and high-dose groups, respectively. However, when whole litter losses are excluded, no treatment-related findings were observed on litter size or viability indicating a litter-effect as opposed to general systemic toxicity in the offspring.

3.3.5 Additional Information from Literature Sources

No outside literature has been used to characterize potential hazard at this time.

3.3.6 Pre-and/or Postnatal Toxicity

3.3.6.1 Determination of Susceptibility

There is no evidence (qualitative or quantitative) of increased susceptibility following *in utero* and/or pre-/post-natal exposure in adequate developmental toxicity studies in rats or rabbits, and in a two-generation reproduction study in rats. However, quantitative susceptibility was observed in the developmental neurotoxicity study in rats. The parental LOAEL was 38.7 mg/kg/day based on complete litter losses, with a NOAEL for this effect of 8.1 mg/kg/day. The offspring LOAEL was the lowest dose tested of 8.1 mg/kg/day based on changes in pup brain morphometrics on PND 12 (females) and PND 63 (males). No offspring NOAEL was established.

3.3.6.2 Degree of Concern Analysis and Residual Uncertainties for Pre- and/or Postnatal Susceptibility

The degree of concern for susceptibility is low based on the results of the prenatal developmental and reproduction studies, since the fetal and offspring effects occurred at doses similar to or higher than the doses at which maternal/parental toxicity was observed. These studies indicate a lack of qualitative and quantitative susceptibility. In addition, the effects in each of these studies were well characterized, with conservative NOAELs established for all developmental and offspring effects.

There is a concern for the quantitative susceptibility observed in the developmental neurotoxicity study, in which brain morphometric changes in pups were observed at the lowest dose tested, a dose that did not cause maternal toxicity. However, this concern is reduced because the severity of the effect on the corpus callosum and cerebellum pre-pyramidal fissure increased with dose and the marginal effects at the low-dose indicate that the 8.1 mg/kg/day LOAEL is near the threshold dose for this effect. The lack of neurotoxic effects or clinical signs of toxicity at this level also lowers the concern for functional impairment due to the changes in brain morphometry. Furthermore, changes in brain morphometry are not likely to be the result of a single acute exposure; however, HED has taken a conservative approach by assuming the effects on morphometry could be the result of either a single dose or multiple doses. With the addition of a 10X UF for the extrapolation from a LOAEL to a NOAEL, the residual uncertainty is low.

3.3.6.3 Degree of Concern Analysis and Residual Uncertainties for Immunotoxicity

The degree of concern for potential immunotoxic effects for pymetrozine is low. There are a number of apparent immunotoxic effects associated with pymetrozine including effects on the blood, thymus and spleen at high doses. However, based on a review of the toxicity database, HED has determined that the liver is the primary target organ of pymetrozine; apparent immunotoxic effects are the result of either exceedingly high doses or secondary effects.

Potential immune organ effects include atrophy of the thymus in the subchronic rat and dog studies at 360 and 54 mg/kg/day, respectively; decreased thymus weight in the chronic mouse study at 675 mg/kg/day; increased leucocytes in the subchronic rat at 360 mg/kg/day; and hyperplasia of the splenic lymphocyte follicles in the reproduction study at 136.9 mg/kg/day. Clear NOAELs were identified for these potential immunotoxic effects at higher doses than the endpoint that was selected for risk assessment, i.e., the 8.1 mg/kg/day LOAEL from the DNT study based on brain morphometric changes in the offspring. Lymphocytic infiltration in the prostate and thyroid was observed at 14 mg/kg/day in the subchronic dog study but these organs are not a primary part of the immune system and the lymphocytic infiltration is considered an immune system reaction to other toxic effects on these organs and not an immunotoxic effect.

A 10X database uncertainty factor is being applied to the DNT LOAEL to extrapolate a projected NOAEL for that study. Because that projected NOAEL (i.e., 0.81 mg/kg/day) is the lowest NOAEL in the database and is applicable to acute and chronic dietary, and short- and intermediate-term dermal and inhalation scenarios, it is being used as a Point of Departure (PoD) for each of these scenarios.

The Agency does not believe that conducting a functional immunotoxicity study will result in a lower PoD than the endpoint currently selected for overall risk assessment (i.e. the extrapolated NOAEL from the DNT study) based on *i*) potential immunotoxic responses occurred at doses greater than the endpoint selected for risk assessment, *ii*) clear NOAELs were identified for the potential immunotoxic effects, again at doses greater the endpoint selected for risk assessment; *iii*) the lymphohistocytic effects were determined not to be directly related to immunotoxicity; and *iv*) the additional 10X for the extrapolation from a LOAEL in calculating the PoD provides a more than adequate margin of safety for potential immunotoxicity (i.e., the PoD for assessing risk is more than 10X below the NOAEL for any potential immunotoxic effect seen in the database). Therefore, an additional database uncertainty factor (UF_{DB}) is not needed to account for the lack of the immunotoxicity study.

3.4 FQPA Safety Factor for Infants and Children

After evaluating the toxicological and exposure data, the pymetrozine risk assessment team recommends that the 10X FQPA SF be retained in the form of a LOAEL-to-NOAEL extrapolation factor based on the selection of the pup LOAEL for endpoint (brain morphometric changes) and dose selection, and for the observed quantitative susceptibility. For the following reasons, EPA concludes that retention of the 10X factor will be safe for infants and children:

- With the exception of the required immunotoxicity study, the database for pymetrozine is complete. An immunotoxicity study is required as a part of new data requirements in the 40 CFR Part 158 for conventional pesticide registration; however, the Agency does not believe that conducting a functional immunotoxicity study will result in a lower PoD than the endpoint currently selected for overall risk assessment because *i*) the liver is the primary target organ for pymetrozine toxicity; *ii*) clear NOAELs exist for the potential immunotoxic effects, again at doses greater the endpoint selected for risk assessment; and *iii*) the additional 10X for the extrapolation from a NOAEL provides an adequate margin of safety for potential immunotoxicity.

- While there is concern for the quantitative susceptibility observed in pups in the DNT study, the brain morphometric changes were observed in the absence of impacts on developmental landmarks, clinical signs, FOB, motor activity, acoustic startle response, learning and memory, and brain weights. The dose response of the morphological changes and the minimal effects at the LOAEL suggest that 8.1 mg/kg/day is a threshold dose for the effect. The use of the DNT LOAEL for the point of departure for the aPAD is particularly conservative for the reasons discussed in section 3.3.6.2.

- Nondietary exposure is expected to be minimal, since the only potential exposure in residential settings is associated with post-application exposure following application of pymetrozine to ornamental plants.

- The acute dietary exposure assessment for residues in food is a conservative assessment using tolerance-level residues and 100% crop treated assumptions. Chronic and cancer dietary assessments for residues in food use reliable data on anticipated residues from

crop field trials and percent crop treated information. For commodities for which usage data were not available, HED assumed 100% crop treated.

- The dietary assessment incorporated drinking water residue estimates generated by models and associated modeling parameters which are designed to provide conservative, health protective, high-end estimates of water concentrations.

- The overall exposure assessment does not underestimate potential exposure and risk associated with agricultural uses of pymetrozine.

3.5 Hazard Identification and Toxicity Endpoint Selection

3.5.1 Acute Reference Dose (aRfD) – All Populations

Study Selected: Developmental Neurotoxicity Study in Rats
MRID No.: 46170301
Dose and Endpoint for Establishing the aRfD: The dose is the developmental LOAEL of 8.1 mg/kg/day at which morphometric changes were observed in the brains of female pups on PND 12 and in male pups on PND 63. A NOAEL was not identified.

Uncertainty Factor: 1000X (10X interspecies extrapolation, 10X intraspecies variability, 10X extrapolation from the LOAEL).

$$Acute\ RfD = \frac{8.1\ mg/kg/day}{1000\ (UF)} = 0.008\ mg/kg/day$$

Comments about Study/Endpoint/Uncertainty Factors:

The developmental neurotoxicity study is appropriate for determining an acute RfD for females 13-50 for the following reasons: 1) the route of administration (oral) is appropriate for assessing dietary exposure; 2) changes in brain morphometrics in pups may have been caused by a single dose to the dams. However, since the DNT involves multiple doses, this is a conservative assumption; and 3) the observation of changes in brain morphometrics occurred in offspring and the dose selected is therefore protective of developmental effects.

Quantitative susceptibility was observed in the DNT study, since the brain morphometric changes in pups occurred at a dose which did not cause maternal toxicity. As stated above, the pymetrozine risk assessment team recommends the 10X FQPA SF be retained due to the 1) extrapolation from a LOAEL to a NOAEL for dose selection; and 2) observed quantitative susceptibility.

3.5.2 Chronic Reference Dose (cRfD)

Study Selected: Developmental Neurotoxicity Study in Rats

MRID No.: 46170301
Dose and Endpoint for Establishing the cRfD: The dose is the developmental LOAEL of 8.1 mg/kg/day at which morphometric changes were observed in the brains of female pups on PND 12 and in male pups on PND 63.

Uncertainty Factor: 1000 (10X interspecies extrapolation, 10X intraspecies variability, 10X extrapolation from the LOAEL).

$$Chronic\ RfD = \frac{8.1\ mg/kg/day}{1000\ (UF)} = 0.008\ mg/kg/day$$

Comments about Study/Endpoint/Uncertainty Factors:
The developmental neurotoxicity study is appropriate for determining a chronic RfD for the following reasons: 1) the route of administration (oral) is appropriate for assessing dietary exposure; 2); the changes in brain morphometrics may have been caused by a single dose or repeated dosing; and 3) the observation of changes in brain morphometrics occurred in offspring and therefore selection of the endpoint is protective of potential developmental effects. The chronic rat study (NOAEL 3.8 mg/kg/day; LOAEL 38.5 mg/kg/day based on decreased body weight and body weight gain and increased liver, spleen, and kidney weights) provides a more appropriate dosing duration, and the chronic NOAEL is slightly lower than the DNT LOAEL of 8.1 mg/kg/day. However, the chronic rat study did not assess potential impacts on brain development following repeated dosing, and selection of the endpoint and dose from the study might not be protective of the observed offspring effect. Furthermore, the extrapolated NOAEL is 0.81 mg/kg/day, which is more conservative than the chronic rat study NOAEL (3.8 mg/kg/day).

In the 2001 and 2004 risk assessments, the observed hepatic hypertrophy was selected as the endpoint for chronic dietary exposure and risk assessment. Hepatic hypertrophy was evident in several studies at multiple doses; see below for hypertrophy LOAELs:

- Rat Hepatic Hypertrophy effective doses
  - Subchronic 360 mg/kg/day
  - Chronic 3.76 mg/kg/day
  - Reproductive 13.9 mg/kg/day
- Dog Hepatic Hypertrophy effective doses
  - Subchronic 14 mg/kg/day
  - Chronic 5.4 mg/kg/day

However, HED has more recently adopted the policy that hepatic hypertrophy in the absence of liver pathology or changes in relevant clinical chemistry parameters is considered an adaptive effect and is not sufficient to identify an adverse effect even when liver pathology is identified at higher doses (HED Guidance Document #G2002.01, 10/21/02). Hepatocellular hypertrophy is often an adaptive and reversible effect in response to the presence of a chemical (i.e. induction of microsomal enzymes in the liver). Liver pathology or changes in clinical chemistry parameters were not seen at the doses identified above.

The current risk assessment team has selected morphometric brain changes at 8.1 mg/kg/day as the endpoint for assessing risk for all exposure durations and routes. Using a safety factor of 1000 (10X for inter-species variability, intra-species variability, and the FQPA safety factor), the new cPAD is 0.008 mg/kg/day. This cPAD is slightly higher than the earlier cPAD (0.0038); however, as explained above the earlier cPAD was based on effects that are no longer considered adverse. Use of the LOAEL from the DNT study and retention of the 10X FQPA safety factor is considered protective of any potential liver effects, including the adaptive effects, given the considerations discussed above.

3.5.3 Incidental Oral Exposure: Short-Term (1-30 days) and Intermediate-Term 1-6 Months)

There are no current residential uses that would result in incidental oral exposure, so no endpoints and doses were selected for assessing short- and intermediate-term exposure.

3.5.4 Dermal Absorption

The dermal absorption study in rats (MRID No.: 44024958) indicated dermal penetration values of up to 0.28%, excluding material that adhered to the skin. However, HED concluded that the amount of radioactivity used may have compromised the detectability of the actual penetration and determined that use of an upper-bound 1% dermal penetration factor would be more appropriate.

3.5.5 Dermal and Inhalation Exposure: Short-Term (1-30 days) and Intermediate-Term (1-6 Months)

Study Selected: Developmental Neurotoxicity Study in Rats
MRID No.: 46170301
Dose and Endpoint Selected for Risk Assessment: The dose is the developmental LOAEL of 8.1 mg/kg/day at which morphometric changes were observed in the brains of female pups on PND 12 and in male pups on PND 63.

Uncertainty Factor: 1000X (10X interspecies extrapolation, 10X intraspecies variability, 10X extrapolation from the LOAEL).

Comments about Study/Endpoint/Uncertainty Factors:

The duration of the DNT study is appropriate for short- and intermediate-term exposure and risk assessment based on similar duration and route of exposure [when used in conjunction with a 1% dermal absorption factor (DAF) (section 3.5.4)]. Although a 21-day dermal toxicity study in rats with a systemic NOAEL of 1000 mg/kg/day was available for dermal endpoint selection, the oral equivalent NOAEL of 10 mg/kg/day would not be protective of the effects observed in offspring in the DNT study. Furthermore, since the dermal study did not assess either neurotoxic or developmental toxicity parameters, use of the study for endpoint and dose selection would not be protective for these effects. The use of the DNT study for dermal risk assessment is conservative but also protective of potential offspring effects which were not measured in other studies that could be used for risk assessment purposes (e.g., the developmental rabbit study).

For inhalation exposure and risk assessment, an inhalation absorption factor of 100% (default value assuming equivalent inhalation and oral absorption) should be used for route-to-route extrapolation, since an appropriate inhalation study is not available. Therefore, the oral endpoint from the developmental neurotoxicity study is considered appropriate for the short- and intermediate-term exposure because the effects observed in the developmental neurotoxicity study could be attributable to short-term or intermediate-term exposure.

For both dermal and inhalation risk assessments, the pymetrozine risk assessment team has retained a 10X factor for the extrapolation from a LOAEL in the DNT study.

The selection of brain morphometric changes in offspring for assessing dermal and inhalation risk for occupational workers is considered to be conservative, since maternal and parental toxicity occurred at higher doses in most of the studies that would be appropriate for these exposure routes and durations. However, the selection of the developmental effect (i.e., brain morphometric changes) for risk assessments ensures adequate protection for potentially pregnant workers who may be exposed to pymetrozine when applying the pesticide to agricultural or ornamental crops, or when re-entering previously treated areas.

3.5.6 Level of Concern for Margin of Exposure

Table 5 summarizes the level of concern (LOC) for margin of exposure (MOE) for pymetrozine risk assessment. For occupational assessment for pymetrozine, MOEs below 1000 represent a risk concern for HED. The LOC is based on the standard 100X factor to account for interspecies extrapolation and intraspecies variability, and an additional 10X factor to account for the use of a LOAEL as the dose for risk assessment. Since the endpoint (effects) selected for risk assessment could be the result of *in utero* exposure, a body weight of 60 kg (for females) should be used in the occupational assessments in order to be protective of female workers.

Table 1. Summary of Levels of Concern for Risk Assessment			
Route	Short-Term (1-30 Days)	Intermediate-Term (1-6 Months)	Long-Term (> 6 Months)
Occupational (Worker) Exposure			
Dermal	1000	1000	NA
Inhalation	1000	1000	NA
Residential Exposure			
There are no proposed or registered residential uses for pymetrozine			

NA = Not Applicable

3.5.7 Recommendation for Aggregate Exposure Risk Assessments

According to FQPA (1996), when there are potential residual exposures to a pesticide, an aggregate risk assessment must consider exposures from three major routes - oral, dermal and inhalation.

Acute and chronic endpoints have been selected as appropriate for use in dietary human health risk assessments for all populations, including infants and children. There is no incidental oral exposure scenario. In addition, there are no dermal or inhalation exposure scenarios for residential human health risk assessments.

Therefore, acute and long-term aggregate risks are equivalent to acute and chronic dietary risks, respectively.

For occupational assessments, since the same endpoint was chosen for dermal and inhalation risk assessment, exposures from the two routes should be combined to determine an overall risk from exposure to pymetrozine.

3.5.8 Classification of Carcinogenic Potential

In the combined chronic toxicity/carcinogenicity study in rats there were incidents of "benign hepatoma" in females at the mid and high dose which were outside the historical control range. The dose levels selected were considered adequate to assess the carcinogenic potential of pymetrozine in rats. In mice, liver tumors were associated with the higher doses of pymetrozine, with incidents of hepatocellular "benign adenoma" observed in females. Males did not show increases in adenomas. The dose levels selected were considered adequate to assess the carcinogenic potential of pymetrozine in rats.

In accordance with the EPA *Proposed Guidelines for Carcinogen Risk Assessment* (April 10, 1996), the CARC classified Pymetrozine as a "likely human carcinogen" and recommended that quantification of risk be estimated for combined liver tumors (benign hepatomas and/or carcinomas) in male and female mice and female rats. The most potent unit risk, or slope factor, of the three would be used for further calculations by the Agency. In this case, the most potent slope factor, or cancer potency factor, is that for male mouse liver benign hepatoma and/or carcinoma combined tumor rates at 0.0119 $(mg/kg/day)^{-1}$ in human equivalents (memorandum from L. Brunsman to J. Doherty, dated 3/9/2000). While there were limited mode-of-action data

available for pymetrozine, the data were considered insufficient to affect the classification of carcinogenicity.

3.5.9 Summary of Toxicological Doses and Endpoints for Pymetrozine for Use in Human Risk Assessments.

Table 2.a. Toxicological Doses and Endpoints for Pymetrozine for Use in Dietary and Non-Occupational Human Health Risk Assessments.

Exposure/ Scenario	Point of Departure	Uncertainty/ FQPA Safety Factors	Level of Concern for Risk Assessment	Study and Toxicological Effects
Acute Dietary (All Populations)	LOAEL = 8.1 mg/kg/day	UF_A = 10X UF_H = 10X FQPA SF/ UF_{LOAEL} = 10X	Acute RfD = 8.1 mg/kg/day aPAD = 0.008 mg/kg/day	**Developmental Neurotoxicity (Rat)** LOAEL = 8.1 mg/kg/day, based on morphometric changes in the brains of female pups on PND 12 and male pups on PND 63.
Chronic Dietary (All Populations)	LOAEL = 8.1 mg/kg/day	UF_A = 10X UF_H = 10X FQPA SF/ UF_{LOAEL} = 10X	Chronic RfD = 8.1 mg/kg/day cPAD = 0.008 mg/kg/day	**Developmental Neurotoxicity (Rat)** LOAEL = 8.1 mg/kg/day, based on morphometric changes in the brains of female pups on PND 12 and male pups on PND 63.
Cancer (oral, dermal, inhalation)	Classification: "likely human carcinogen". A cancer potency factor of 0.0119 $(mg/kg/day)^{-1}$ was calculated for pymetrozine based on male mouse liver benign hepatoma and/or carcinoma combined tumors.			

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 (interspecies). UF_H = potential variation in sensitivity among members of the human population (intraspecies). 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.b. Summary of Toxicological Doses and Endpoints for Pymetrozine 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- (1-30 days) and Intermediate-Term (1-6 months)	LOAEL = 8.1 mg/kg/day DAF = 1%	UF_A = 10X UF_H = 10X UF_{LOAEL} = 10X	Occupational LOC for MOE = 1000	**Developmental Neurotoxicity (Rat)** LOAEL = 8.1 mg/kg/day, based on morphometric changes in the brains of female pups on PND 12 and male pups on PND 63
Inhalation Short- (1-30 days) and Intermediate-Term (1-6 months)	LOAEL = 8.1 mg/kg/day IAF=100%	UF_A = 10X UF_H = 10X UF_{LOAEL} = 10X	Occupational LOC for MOE = 1000	**Developmental Neurotoxicity (Rat)** LOAEL = 8.1 mg/kg/day, based on morphometric changes in the brains of female pups on PND 12 and male pups on PND 63
Cancer (oral, dermal, inhalation)	Classification: "likely human carcinogen". A cancer potency factor of 0.0119 $(mg/kg/day)^{-1}$ was calculated for pymetrozine based on male mouse liver benign hepatoma and/or carcinoma combined tumors.			

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 (interspecies). UF_H = potential variation in sensitivity among members of the human population (intraspecies). 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.

3.6. Endocrine Disruption

As required under FFDCA section 408(p), EPA has developed the Endocrine Disruptor Screening Program (EDSP) to determine whether certain substances (including pesticide active and other ingredients) may have an effect in humans or wildlife similar to an effect produced by a "naturally occurring estrogen, or other such endocrine effects as the Administrator may designate." The EDSP employs a two-tiered approach to making the statutorily required determinations. Tier 1 consists of a battery of 11 screening assays to identify the potential of a chemical substance to interact with the estrogen, androgen, or thyroid (E, A, or T) hormonal systems. Chemicals that go through Tier 1 screening and are found to have the potential to interact with E, A, or T hormonal systems will proceed to the next stage of the EDSP where EPA will determine which, if any, of the Tier 2 tests are necessary based on the available data. Tier 2 testing is designed to identify any adverse endocrine related effects caused by the substance, and establish a dose-response relationship between the dose and the E, A, or T effect.

Between October 2009 and February 2010, EPA is issuing test orders/data call-ins for the first group of 67 chemicals, which contains 58 pesticide active ingredients and 9 inert ingredients. This list of chemicals was selected based on the potential for human exposure through pathways such as food and water, residential activity, and certain post-application agricultural scenarios. This list should not be construed as a list of known or likely endocrine disruptors.

Pymetrozine is not among the group of 58 pesticide active ingredients on the initial list to be screened under the EDSP. Under FFDCA sec. 408(p) the Agency must screen all pesticide chemicals. Accordingly, EPA anticipates issuing future EDSP test orders/data call-ins for all pesticide active ingredients.

For further information on the status of the EDSP, the policies and procedures, the list of 67 chemicals, the test guidelines and the Tier 1 screening battery, please visit our website: http://www.epa.gov/endo/.

11.0 Data Needs and Recommendations

Based upon its assessment of the proposed pymetrozine label, HED recommends the following:

- Immunotoxicology Study in Rats (**870.7800**)

A.1 Toxicology Data Requirements

The requirements (40 CFR 158.340) for pymetrozine residential and occupational use are in Table 1. Use of the new guideline numbers does not imply that the new (1998) guideline protocols were used.

Test		Technical	
		Required	Satisfied
870.1100	Acute Oral Toxicity	yes	yes
870.1200	Acute Dermal Toxicity	yes	yes
870.1300	Acute Inhalation Toxicity	yes	yes
870.2400	Primary Eye Irritation	yes	yes
870.2500	Primary Dermal Irritation	yes	yes
870.2600	Dermal Sensitization	yes	yes
870.3100	Oral Subchronic (rodent)	yes	yes
870.3150	Oral Subchronic (nonrodent)	yes	yes
870.3200	21/28-Day Dermal	no	yes
870.3250	90-Day Dermal	yes	no[1]
870.3465	90-Day Inhalation	no	---
870.3700a	Developmental Toxicity (rodent)	yes	yes
870.3700b	Developmental Toxicity (nonrodent)	yes	yes
870.3800	Reproduction	yes	yes
870.4100a	Chronic Toxicity (rodent)	yes	yes
870.4100b	Chronic Toxicity (nonrodent)	no	yes
870.4200a	Oncogenicity (rat)	yes	yes
870.4200b	Oncogenicity (mouse)	yes	yes
870.4300	Chronic/Oncogenicity	yes	yes
870.5100	Mutagenicity—Gene Mutation - bacterial	yes	yes
870.5300	Mutagenicity—Gene Mutation - mammalian	yes	yes
870.5375	Mutagenicity—Structural Chromosomal Aberrations	yes	yes
870.5395	Mutagenicity—Mammalian Erythrocyte Micronucleus.	no	yes
870.5550	Mutagenicity—Unscheduled DNA Synthesis	no	yes
870.5915	Mutagenicity—*In Vivo* Sister Chromatid Exchange	no	--
870.6100a	Acute Delayed Neurotox. (hen)	no	---
870.6100b	90-Day Neurotoxicity (hen)	no	---
870.6200a	Acute Neurotox. Screening Battery (rat)	yes	yes
870.6200b	90 Day Neurotox. Screening Battery (rat)	yes	yes
870.6300	Develop. Neuro	yes	yes
870.7485	General Metabolism	yes	yes
870.7600	Dermal Penetration	no	yes
870.7800	Immunotoxicity	yes	no

[1] Requirement fulfilled by 21/28 day study.

A.2 Pymetrozine Hazard Profile

Table 1. Acute Toxicity of Pymetrozine Technical

Guideline Number	Study Type	MRID #	Results	Toxicity Category
81-1	Acute Oral (rat)	44024926	Oral LD_{50}: Males: 5693 mg/kg Females: 5955 mg/kg Combined: 5820 mg/kg	IV
81-2	Acute Dermal (rat)	44024928	Dermal LD_{50}: Males: > 2.0 g/kg Females: > 2.0 g/kg	III
81-3	Acute Inhalation (rat)	44024930	Inhalation LC_{50}: Males: >1.8 mg/L Females: > 1.8 mg/L Combined: > 1.8 mg/L	IV
81-4	Primary Eye Irritation	44024932	Is a slight ocular irritant. Primary Irritation Score (PIS): 12.8 at 1 hour; 1.0 at 72 hours.	III
81-5	Primary Dermal Irritation	44024934	Primary Irritation Index (PII): Is not a dermal irritant.	IV
81-6	Dermal Sensitization	44024936	Is a slight dermal sensitizer with intradermal challenge.	N/A
81-8	Acute Neurotoxicity (rat)	44411317	NOAEL (both sexes) < 125 mg/kg (LDT) LOAEL (both sexes) = 125 mg/kg	N/A

Table 2. Toxicity Profile of Pymetrozine Technical

Study Type	MRID No.	Results
870.3100 Subchronic Feeding (rats)	44024939 (1992) Acceptable/Guideline 0, 50, 500, 5000 ppm (0/0, 3.4/3.6, 32.5/33.9, 360/370 mg/kg/day [M/F])	LOAEL = 360/370 mg/kg/day based primarily on decreased body weight and liver effects (increased weight and centrilobular hypertrophy in males). Other effects included leukocytosis, bilirubinuria (females) and decreased urine volume (males), increased relative liver and spleen weights, calcification of kidneys (males), and atrophy of the thymus in both sexes. NOAEL = 32.5/33.9 mg/kg/day
870.3100 Subchronic Feeding (Mouse - Dose range-finding study)	44024938 (1992) Acceptable/Nonguideline 0, 1000, 3000, 7000 ppm (0, 143, 429, 1002 mg/kg/day)	LOAEL (males & females) = 143 mg/kg/day (LDT) based on increased liver weight and increased focal cell necrosis in hepatic parenchyma NOAEL (males & females) = Not established
870.3151 Subchronic Feeding (Beagle dogs)	44572201 (1992) Acceptable/Guideline 0, 100, 500, 2500 ppm (0, 3.1, 14, 54 mg/kg/day)	LOAEL = 14 mg/kg/day based on liver pathology (bile duct proliferation in both sexes and hepatocyte necrosis in females), skeletal muscle atrophy, and lymphocytic infiltration in several organs. NOAEL = 3.12 mg/kg/day
870.3200 28-Day Dermal Toxicity (Sprague-Dawley rats)	44024942 (1993) Acceptable/Guideline0, 10, 100, 1000 mg/kg/day (6 hrs/day, 5 days/week for 4 weeks)	Systemic/Dermal Irritation LOAEL > 1000 mg/kg/day Systemic/Dermal Irritation NOAEL = 1000 mg/kg/day
870.4100 Chronic Feeding (beagle dog)	44024943 (1994) Acceptable/Guideline 0, 20, 200, 1000 ppm (0, 0.57, 5.33, 27.8 mg/kg/day)	LOAEL = 27.8 mg/kg/day based primarily on myopathy and anemia. Additional effects included Liver effects included inflammatory cell infiltration in the liver (males), cholesterol, phospholipids, hemosiderosis, decreased testis weight and increased liver weight. NOAEL = 5.33 mg/kg/day. An equivocal increase in liver weight at 5.33 mg/kg/day did not show related pathology or dose response and was considered adaptive and not toxicological.

870.4200 Carcinogenicity (mouse)	44024944 (1995) Acceptable/Guideline 0, 10, 100, 2000, 5000 ppm (0, 1.2, 12, 250, 675 mg/kg/day)	LOAEL = 250 mg/kg/day based on liver weight and hepatocyte hypertrophy, hemosiderosis and extramedullary hematopoiesis NOAEL = 12 mg/kg/day At ≥ 250 mg/kg/day, increased incidences of benign liver hepatomas and/or carcinomas combined in both sexes.
83-3a: Developmental Toxicity (Sprague-Dawley rat)	44024948 (1992) Acceptable/Guideline 0, 30, 100, 300 mg/kg	Maternal LOAEL = 100 mg/kg/day based on reduced body weight gain and food consumption Maternal NOAEL = 30 mg/kg/day Developmental LOAEL = 300 mg/kg/day based on increased skeletal anomalies including delayed ossification of digits and dumbbell shaped thoracic vertebral centers Developmental NOAEL = 100 mg/kg/day
870.3700 Developmental Toxicity (Russian rabbits)	44024949 (1992) Acceptable/Guideline 0, 10, 75, 125 mg/kg	Maternal LOAEL = 75 mg/kg/day based on decreased body weight and body weight gain Maternal NOAEL = 10 mg/kg/day Developmental LOAEL = 75 mg/kg/day based on skeletal anomalies including increased incidences of 13th ribs, fused sternebrae, and delayed ossification of digits Developmental NOAEL = 10 mg/kg/day
870.3800 Reproductive Toxicity (Sprague-Dawley rat)	44024950 (1993) Acceptable/Guideline 0, 20, 200, 2000 ppm (0/0, 1.4/1.6, 13.9/16.0, 136.9/151.6 mg/kg/day [M/F])	Parental /Systemic LOAEL = 13.9/16.0 mg/kg/day based on increased liver weight and hepatocellular hypertrophy Parental/Systemic NOAEL = 1.4/1.6 mg/kg/day Offspring LOAEL = 136.9/151.6 mg/kg/day based on decreased pup weight and delay in eye opening on both F1 and F2 litters Offspring NOAEL = 13.9/16.0 mg/kg/day Reproductive LOAEL ≥ 136.9/151.6 mg/kg/day Reproductive NOAEL > 136.9/151.6 mg/kg/day
870.4300 Combined Chronic Feeding and Carcinogenicity (Sprague-Dawley rat)	44024951 (1995) Acceptable/Guideline 0, 10, 100, 1000, 3000 ppm (0/0, 0.38/0.45, 3.76/4.48, 38.5/46.3, 123.4/148.3 mg/kg/day [M/F])	LOAEL = 38.5/46.3 mg/kg/day based on hepatocellular hypertrophy in males. NOAEL = 3.76/4.48 mg/kg/day Increased incidence of benign liver hepatomas and/or carcinomas combined at 1000 and 3000 ppm in females
870.5100 Gene Mutation - *Salmonella* & E. Coli	44024952 (1991) Acceptable/Guideline 312.5 to 5000 µg/plate	Non-mutagenic (±) activation in *Salmonella* and *E.* coli.

870.5300 Gene Mutation - HGPRT with V79 cells	44024954 (1991) Acceptable/Guideline 5.21 to 333.3 µg/ml	Non-mutagenic up to the solubility limit (±) activation.
870.5375 *In vitro* cytogenetics assay in CHO cells	44024953 (1991) Acceptable/Guideline2.58 to 330 µg/ml	Not clastogenic up to the solubility limit of the test substance.
870.5395 Micronucleus Assay in Mice	44024955 (1991) Acceptable/Guideline 0, 1000, 2000, 4000 mg/kg	No clastogenic response at any dose or sacrifice time.
870.5550 Unscheduled DNA Synthesis in Primary Rat Hepatocytes	44024956 (1991) Acceptable/Guideline 2.78 to 300 µg/ml	No evidence of induced UDS.
870.6200 Acute Neurotoxicity (Sprague-Dawley rats)	44411317 (1997) Acceptable/Guideline 0, 125, 500, 2000 mg/kg	LOAEL = 125 mg/kg based on decreases in body temperature, FOB changes and decreased motor activity (males) related to decreased activity NOAEL < 125 mg/kg
870.6200 Subchronic neurotoxicity (Sprague-Dawley rats)	44411318 (1997) Acceptable/Guideline 0, 500, 1000, 3000 ppm (0/0, 35/41, 68/81, 201/224 mg/kg/day [M/F])	LOAEL = 201 mg/kg/day based on decreased weight and stereotypy (excessive head movement and sniffing) in males and tiptoe gait in females NOAEL = 68 mg/kg/day
870.6300 Developmental Neurotoxicity (Wistar-derived rat)	46170301 (2003) Acceptable/Nonguideline 0, 100, 500, 2500 ppm (0/0, 8.1/16.8, 38.7/82.6, 173.1/NA mg/kg/day [gestation/lactation])	Maternal LOAEL = 38.7 mg/kg/day based on complete litter losses Maternal NOAEL = 8.1 mg/kg/day Offspring LOAEL = 8.1 mg/kg/day based on morphometric changes in the brains of female pups on PND 12 and male pups on PND 63. Offspring NOAEL < 8.1 mg/kg/day

870.7485 Metabolism and Pharmacokinetics (Sprague-Dawley rat)	44024957 (1993) 44517720	Absorption and excretion studies were conducted after a single low dose iv injection (0.5 mg/kg); single low (0.5 mg/kg) and high (100 mg/kg) oral doses; 14 daily low (0.5 mg/kg) or high (100 mg/kg) oral doses followed by a single low (0.5 mg/kg) oral dose; and after a single high oral dose with the chemical labeled at different site. Both the oral and iv doses had similar urine values at 24 hours. 7 days post-dosing: recovered radioactivity in urine (56.3-80.3%), expired air (0.2-1.4%), tissues (0.3-3.8%), feces (15.4-38.9%), and cage washes (0.2-0.7%). Both sexes excreted more via the kidneys after a high dose (M/F: 72.5%/78.3%) than after a low dose (M/F: 56.3%/ 62.1%). Twelve urinary and fecal metabolites were recovered after a high dose and were isolated and characterized. There was a relatively high level of unchanged test material in the urine, which suggests metabolic saturation at the high dose of 100 mg/kg. Three major metabolic pathways: oxidation of methyl substituent at triazine ring, which is further oxidized to corresponding carboxylic acid, oxidation at methylene group within the triazine ring, and cleavage of the bridge between the two rings to give rise to several single ring metabolites. No indication that conjugated metabolites formed. Maximum blood concentrations attained at 15 minutes (0.3 ppm) and at 4 hours (60 ppm) following low and high oral dosing, respectively. Calculated half life times ($t_{½}$) for the depletion of radiolabel from all the tissues ranged from 1 to 2 hours at 0.5 mg/kg dose (both labels) and from 2 to 11 hours at the 100 mg/kg dose, with the pyridine label having a relatively longer $t_{½}$ than the triazine label. **Details: see summaries of toxicology studies.**
870.7600 Dermal absorption (rat)	44024958 (1996) Acceptable/Guideline0, 0.007, 0.040, 0.375 mg/cm^2 (CMC)	After 10 hours of dermal application, the percent of dose absorbed was 0.01%, 0.01% and <0.005% for the low-, mid- and high-dose groups, respectively.

A.3 Data Call-In Studies

Guideline Number: 870.7800
Study Title: Immunotoxicity

Rationale for Requiring the Data

The immunotoxicity study is a new data requirement under 40 CFR Part 158 as a part of the data requirements for registration of a pesticide (food and non-food uses).

The Immunotoxicity Test Guideline (OPPTS 870.7800) prescribes functional immunotoxicity testing and is designed to evaluate the potential of a repeated chemical exposure to produce adverse effects (i.e., suppression) on the immune system. Immunosuppression is a deficit in the ability of the immune system to respond to a challenge of bacterial or viral infections such as tuberculosis (TB), Severe Acquired Respiratory Syndrome (SARS), or neoplasia. Because the immune system is highly complex, studies not specifically conducted to assess immunotoxic endpoints are inadequate to characterize a pesticide's potential immunotoxicity. While data from hematology, lymphoid organ weights, and histopathology in routine chronic or subchronic toxicity studies may offer useful information on potential immunotoxic effects, these endpoints alone are insufficient to predict immunotoxicity.

Practical Utility of the Data

How will the data be used?
Immunotoxicity studies provide critical scientific information needed to characterize potential hazard to the human population on the immune system from pesticide exposure. Since epidemiologic data on the effects of chemical exposures on immune parameters are limited and are inadequate to characterize a pesticide's potential immunotoxicity in humans, animal studies are used as the most sensitive endpoint for risk assessment. These animal studies can be used to select endpoints and doses for use in risk assessment of all exposure scenarios and are considered a primary data source for reliable reference dose calculation. For example, animal studies have demonstrated that immunotoxicity in rodents is one of the more sensitive manifestations of TCDD (2,3,7,8-tetrachlorodibenzo-p-dioxin) among developmental, reproductive, and endocrinologic toxicities. Additionally, the EPA has established an oral reference dose (RfD) for tributyltin oxide (TBTO) based on observed immunotoxicity in animal studies (IRIS, 1997).

How could the data impact the Agency's future decision-making?
If the immunotoxicity study shows that the test material poses either a greater or a diminished risk than that given in the interim decision's conclusion, the risk assessments for the test material may need to be revised to reflect the magnitude of potential risk derived from the new data.

If the Agency does not have these data, a 10X database uncertainty factor may be applied for conducting a risk assessment from the available studies.

Appendix B. Pymetrozine Acute, Chronic and Cancer Dietary Risk Assessments.

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

OFFICE OF PREVENTION, PESTICIDES AND TOXIC SUBSTANCES

MEMORANDUM

Date: April 2, 2010

SUBJECT: Pymetrozine – Acute, Chronic and Cancer Combined Dietary (Food + Drinking Water) Exposure and Risk Assessments.

PC Code: 101103
Decision No.: NA
Petition No.: NA
Risk Assess Type: Single Chemical Aggregate
TXR No.: NA
MRID No.: NA

DP Barcode: D372578
Registration No.: NA
Regulatory Action: NA
Case No.: NA
CAS No.: 123312-89-0
40 CFR: 40 CFR §180.556

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Executive Summary

Acute, chronic and cancer combined dietary (food + drinking water) exposure and risk assessments were conducted for the insecticide pymetrozine using the Dietary Exposure Evaluation Model DEEM-FCID™, Version 2.03 which uses food consumption data from the U.S. Department of Agriculture's (USDA's) Continuing Surveys of Food Intakes by Individuals (CSFII) from 1994-1996 and 1998. The analyses were performed to support HED's response to the Natural Resources Defense Council (NRDC) objections to pymetrozine tolerances established in 2001. The HED response includes an updated hazard characterization and aggregate risk assessment (D371299); since the most recent dietary exposure assessment included percent crop treated (%CT, or PCT) data from 2001, the current dietary assessment was undertaken to incorporate the 2009 usage (PCT) estimates generated by OPP's Biological and Economic Analysis Division (BEAD) as well as revised endpoints and doses for acute and chronic dietary risk assessment.

The acute dietary exposure analysis is based on the assumption that all foods with pymetrozine tolerances bear maximum pymetrozine residues of concern, which include the parent and a number of plant metabolites. In addition, HED assumed 100 %CT for all commodities included in the acute analysis. Finally, it was assumed that all drinking water has a constant concentration of pymetrozine at 0.0163 ppm, which is the highest applicable concentration from conservative surface- and ground-water models. Even with these assumptions, the acute dietary (food + water) risk estimates are below HED's level of concern of 100% aPAD. The most highly exposed population subgroup was children 1-2 years old, at 54% aPAD. Acute risks for the general US population (35% aPAD) and all other population subgroups were lower.

The chronic and cancer dietary exposure analyses are slightly more refined than the acute assessment in that average residue values from supervised crop field trials were used rather than maximum residues. In addition, the chronic and cancer analyses incorporated PCT estimates for most of the more heavily-consumed commodities, including potatoes, peppers, and tomatoes; however, 100 %CT was assumed for numerous commodities for which usage data were not available. The chronic and cancer assessments also include modeled residues in surface- and ground-water sources of drinking water. The chronic assessment used an annual average value (0.0101 ppm), whereas the cancer assessment used the average of the annual averages (0.006 ppm).

Chronic dietary risk estimates are below HED's level of concern of 100% cPAD. The most highly exposed population subgroup was all infants, at 9% cPAD. Chronic risks for the general US population (3% cPAD) and all other population subgroups were lower. The cancer risk estimate for the general US population is 2×10^{-6}, and approximately 83% of the exposure is from potential residues in drinking water. Generally, HED considers cancer risks in the range of 1×10^{-6} to be negligible. Considering the precision with which cancer hazard can be estimated and the conservativeness of the low-dose linear extrapolation, cancer risk should generally not be assumed to exceed the benchmark level of concern of 1×10^{-6} until the calculated risk exceeds approximately 3×10^{-6}. This is particularly the case where some conservatism is maintained in the exposure assessment. Drinking water monitoring data for pymetrozine are not available at this time, and conservative assumptions were used in generating the modeled drinking water

estimates. Further, limited PDP monitoring data for pymetrozine on foods show that residues are low or not detected.

I. Introduction

Dietary risk assessment incorporates both exposure and toxicity of a given pesticide. For acute and chronic assessments, the risk is expressed as a percentage of a maximum acceptable dose (i.e., the dose which HED has concluded will result in no unreasonable adverse health effects). This dose is referred to as the population adjusted dose (PAD). The PAD is equivalent to the point of departure (POD, NOAEL, LOAEL, e.g.) divided by the required uncertainty or safety factors.

For acute and non-cancer chronic exposures, HED is concerned when estimated dietary risk exceeds 100% of the PAD. Generally, HED considers cancer risks in the range of 1×10^{-6} to be negligible. Considering the precision with which cancer hazard can be estimated and the conservativeness of the low-dose linear extrapolation, cancer risk should generally not be assumed to exceed the benchmark level of concern of 1×10^{-6} until the calculated risk exceeds approximately 3×10^{-6}. This is particularly the case where some conservatism is maintained in the exposure assessment. References which discuss the acute and chronic risk assessments in more detail are available on the EPA/pesticides web site: "Available Information on Assessing Exposure from Pesticides, A User's Guide," 21-JUN-2000, web link: http://www.epa.gov/fedrgstr/EPA-PEST/2000/July/Day-12/6061.pdf; or see SOP 99.6 (20-AUG-1999).

The most recent dietary risk assessment for pymetrozine was conducted using the LifeLine Model (M. Doherty, 12/29/04, D310560) in support of a proposed use on asparagus.

II. Residue Information

No new residue information has been received for pymetrozine. The residue information described in the 2004 dietary exposure and risk assessment has been repeated herein, with minor changes to reflect updated/current policy and wording:

Tolerances for residues of pymetrozine have been established for a number of commodities (40 CFR §180.556) and range from 0.02 ppm in/on pecans to 6.0 ppm in/on dried hop cones. Although the tolerance expression reflects residues of pymetrozine *per se*, the residues of concern for risk assessment include parent pymetrozine as well as the following: the plant metabolites GS-23199, CGA-215525, CGA-249257, and CGA-294849; and the ruminant metabolite CGA-313124. The metabolite GS-23199 serves as a marker compound for CGA-215525, CGA-249257, and CGA-294849. As a result, the residue values used in the dietary analyses (acute, chronic, and cancer) include both parent and metabolites of potential risk concern. Residues of GS-23199 were reported in the available field trial data, and ratios based on metabolism studies were used to estimate residue levels for the remaining metabolites of concern (see D276195, D. Dotson, 11/19/2001). The residue inputs for food commodities have not changed since the 2004 dietary assessment, and are provided in Appendix 1 along with the processing factors and both 2004 and 2009 PCT estimates. For acute analysis, maximum

residues of parent plus metabolites were used; for chronic and cancer analyses, average residues of parent plus metabolites were used. For asparagus, tolerance-level residues and 100% crop treated were assumed for acute, chronic, and cancer assessments. The percent crop treated estimates provided by BEAD are presented in Appendix 2.

III. Drinking Water Data

Since there has been no change in the use pattern, the estimated drinking water concentrations (EDWCs) used in the previous dietary risk assessment were used for the current assessment, and were provided by the Environmental Fate and Effects Division (EFED) in the following memorandum: "EFED Water Assessment/Environmental Risk Assessment for Pymetrozine New Use: Asparagus" (D283937, 10/5/2004, J. Wolf and L. Shanaman). The EDWCs shown in Table 1 were generated using the linked Pesticide Root Zone Model/Exposure Analysis Modeling System (PRZM-EXAMS) models, and were incorporated directly into the dietary assessment in the DEEM-FCID™ food categories "water, direct, all sources" and "water, indirect, all sources." As noted in the table, the drinking water estimates included a Percent Cropped Area (PCA) factor. The EFED memorandum states that a PCA factor is not available for asparagus, so the default of 87% was used, and this was considered to be high based on the growing areas typically used for asparagus. A ground water EDWC of 0.038 ppb was generated using the Screening Concentration in Ground Water (SCI-GROW) model, but since it was lower than the values predicted for surface water, only the surface water estimates were incorporated into the dietary model.

Table 1. Pymetrozine Residues in Surface Water (Aerial or Ground Spray Application to Asparagus).

Drinking Water (Percent Cropped Area applied)	EDWC (ppb)	
	Parent	Parent + CGA-359009
(Method of spray application)	Aerial/Ground	Aerial/Ground
Surface Water - Peak (Acute)	9.0/8.4	**16.3**/15.7
Surface Water - Annual Average (Chronic)	4.2/3.5	**10.1**/9.2
Surface Water - Average of Annual Averages (Cancer)	2.5/1.8	**6.0**/5.0

NOTE: **Bold** values were used in the dietary exposure analyses.

The models used to estimate drinking water concentrations, along with their descriptions, are available at the EPA internet site: http://www.epa.gov/oppefed1/models/water/.

IV. DEEM-FCID™ Program and Consumption Information

Pymetrozine acute, chronic and cancer dietary exposure assessments were conducted using the Dietary Exposure Evaluation Model software with the Food Commodity Intake Database DEEM-FCID™, Version 2.03 which incorporates consumption data from USDA's Continuing Surveys of Food Intakes by Individuals (CSFII), 1994-1996 and 1998. The 1994-96, 98 data are based on the reported consumption of more than 20,000 individuals over two non-consecutive survey days. Foods "as consumed" (e.g., apple pie) are linked to EPA-defined food commodities (e.g., apples, peeled fruit - cooked; fresh or N/S; baked; or wheat flour - cooked; fresh or N/S, baked) using publicly available recipe translation files developed jointly by USDA/ARS and

EPA. For chronic exposure assessment, consumption data are averaged for the entire U.S. population and within population subgroups, but for acute exposure assessment are retained as individual consumption events. Based on analysis of the 1994-96, 98 CSFII consumption data, which took into account dietary patterns and survey respondents, HED concluded that it is most appropriate to report risk for the following population subgroups: the general U.S. population, all infants (<1 year old), children 1-2, children 3-5, children 6-12, youth 13-19, adults 20-49, females 13-49, and adults 50+ years old.

For chronic and cancer dietary exposure assessment, an estimate of the residue level in each food or food-form (e.g., orange or orange juice) on the food commodity residue list is multiplied by the average daily consumption estimate for that food/food form to produce a residue intake estimate. The resulting residue intake estimate for each food/food form is summed with the residue intake estimates for all other food/food forms on the commodity residue list to arrive at the total average estimated exposure. Exposure is expressed in mg/kg body weight/day and as a percent of the cPAD. This procedure is performed for each population subgroup.

For acute exposure assessments, individual one-day food consumption data are used on an individual-by-individual basis. The reported consumption amounts of each food item can be multiplied by a residue point estimate and summed to obtain a total daily pesticide exposure for a deterministic exposure assessment, or "matched" in multiple random pairings with residue values and then summed in a probabilistic assessment. The resulting distribution of exposures is expressed as a percentage of the aPAD on both a user (i.e., only those who reported eating relevant commodities/food forms) and a per-capita (i.e., those who reported eating the relevant commodities as well as those who did not) basis. In accordance with HED policy, per capita exposure and risk are reported for all tiers of analysis. However, for less refined assessments, any significant differences in user vs. per capita exposure and risk are specifically identified and noted in the risk assessment.

V. Toxicological Information

The hazard characterization and endpoint selection for pymetrozine have been updated to incorporate the results of the developmental neurotoxicity study received and evaluated in 2004. The pymetrozine database is largely complete, missing only an immunotoxicity study now required based on the updated Part 158 Data Requirements (12/2007). Refer to the updated risk assessment, D371299 for a complete description of the updated endpoints and doses for pymetrozine. Both acute and chronic dietary endpoints and doses have changed; however, the cancer potency factor of 0.0119 $(mg/kg/day)^{-1}$ has not changed.

The endpoints for use in pymetrozine dietary risk assessments are summarized in Table 2, below.

Table 2. Pymetrozine Toxicological Doses and Endpoints for Dietary Exposure and Risk Assessments.				
Exposure/ Scenario	Point of Departure	Uncertainty/FQPA Safety Factors	Level of Concern for Risk Assessment	Study and Toxicological Effects
Acute Dietary (All populations including infants and children)	LOAEL = 8.1 mg/kg/day	UF_A= 10x UF_H= 10x UF_L= 10x SF_{FQPA}= 1x	aRfD= 0.0081 mg/kg/day aPAD= 0.008 mg/kg/day	Developmental Neurotoxicity (Rat) LOAEL = 8.1 mg/kg/day, based on morphometric changes in the brains of female pups on PND 12 and male pups on PND 63. [NOAEL not identified]
Chronic Dietary (All populations including infants and children)	LOAEL = 8.1 mg/kg/day	UF_A= 10x UF_H= 10x UF_L= 10x SF_{FQPA}= 1x	cRfD= 0.0081 mg/kg/day cPAD= 0.0081 mg/kg/day	Developmental Neurotoxicity (Rat) LOAEL = 8.1 mg/kg/day, based on morphometric changes in the brains of female pups on PND 12 and male pups on PND 63. [NOAEL not identified]
Cancer	Classification: "likely human carcinogen." A cancer potency factor of 0.0119 $(mg/kg/day)^{-1}$ was calculated for pymetrozine based on male mouse liver benign hepatoma and/or carcinoma combined tumors.			

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 (interspecies). UF_H = potential variation in sensitivity among members of the human population (intraspecies). UF_L = uncertainty factor for extrapolation from a LOAEL to a NOAEL. FQPA SF = FQPA Safety Factor. PAD = population adjusted dose (a = acute, c = chronic). RfD = reference dose.

VI. Results

As stated above, for acute and chronic assessments, HED is concerned when dietary risk exceeds 100% of the PAD. For cancer risk assessment, HED is generally concerned when risk exceeds the range of one in a million, or 1×10^{-6}, taking into account the extent of refinement used in the analysis. The DEEM-FCID™ analyses estimate the dietary exposure of the U.S. population and various population subgroups. The results reported in Table 3 are for the general U.S. Population, all infants (<1 year old), children 1-2, children 3-5, children 6-12, youth 13-19, females 13-49, adults 20-49, and adults 50+ years.

Table 3. Summary of Combined Dietary (Food + Drinking Water) Exposure and Risk Estimates for Pymetrozine.						
	Acute (95th Percentile)		Chronic		Cancer	
Population Subgroup	Exposure (mg/kg/day)	% aPAD*	Exposure (mg/kg/day)	% cPAD*	Exposure (mg/kg/day)	Risk
General U.S. Population	0.002831	35	0.000237	2.9	0.000151	1.8×10^{-6}
All Infants (< 1 year old)	0.003882	48	**0.000707**	**8.7**		
Children 1-2 years old	**0.004368**	**54**	0.000350	4.3		
Children 3-5 years old	0.004034	50	0.000329	4.1		
Children 6-12 years old	0.003027	37	0.000224	2.8		
Youth 13-19 years old	0.002312	28	0.000174	2.2		
Adults 20-49 years old	0.002698	33	0.000222	2.7		
Adults 50+ years old	0.002669	33	0.000235	2.9		
Females 13-49 years old	0.002625	32	0.000217	2.7		

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

VII. Characterization of Inputs/Outputs

The acute dietary risk assessment is an upper-bound conservative estimate of potential exposure and risk, since all commodities were assumed to be treated, and all potential residues of concern have been incorporated into the residue estimates (i.e., maximum residue values were used). Although average residues in all commodities were used in the chronic and cancer assessments, these were based on field trial values, and therefore still reflect conservative estimates of dietary exposure. Limited monitoring data for pymetrozine are available from USDA's Pesticide Data Program (PDP). Based on the low number of detections, and the residues which were significantly below the tolerance levels, the current assessment is likely to be conservative. However, PDP data could not be used quantitatively because only pymetrozine *per se* was measured. A tabular summary of the PDP data is presented in Appendix 6.

The PDP monitoring data did not include potential residues in raw and finished drinking water. Furthermore, there are no other monitoring data available that would provide characterization of the modeled drinking water estimates.

The updated estimates of percent crop treated provided by BEAD are generally lower than those used in 2004, with some exceptions such as lettuce, for which the estimate doubled. However, as in 2004, usage data are not available for all commodities with tolerances, and therefore 100 %CT was assumed for most of the commodities in the analysis.

Acute and chronic non-cancer risks are not of concern for the general US population or any population subgroups. Acute risks were 54% of the aPAD for children 1-2 years old, the most highly exposed sub-population. For chronic non-cancer, the most highly exposed sub-population was all infants, at approximately 9 % cPAD. All other sub-populations had lower exposure and risk.

The cancer risk estimate is approximately 2×10^{-6}. Generally, HED considers cancer risks in the range of 1×10^{-6} to be negligible. Considering the precision with which cancer hazard can be estimated and the conservativeness of the low-dose linear extrapolation, cancer risk should generally not be assumed to exceed the benchmark level of concern of 1×10^{-6} until the calculated risk exceeds approximately 3×10^{-6}. This is particularly the case where some conservatism is maintained in the exposure assessment. For pymetrozine, there is considerable conservatism in the exposure assessment due to the use of upper-bound drinking water residue estimates generated from the environmental models and the use of field trial residues in the assessment. A commodity contribution analysis (see Appendix 4) indicates that 83% of the cancer risk is due to exposure from potential residues in drinking water. The assessment is inherently conservative in that all drinking water consumed is assumed to have residues of pymetrozine. Future assessments should incorporate potential refinements to estimates of drinking water concentrations, especially if monitoring data become available.

VIII. Conclusions

Although there have been changes in the endpoints for acute and chronic dietary risk assessment since 2004, HED continues to conclude that dietary exposure and risk for pymetrozine are below

HED's level of concern. Cancer risk remains essentially unchanged since the 2004 assessment, and is largely driven by exposure through potential residues in drinking water. HED considers the calculated cancer risk of 2×10^{-6} to be an overestimate and within the range of a 1 in 1 million risk and thus negligible.

IX. List of Appendices

Appendix 1. Residue, Processing and Usage Factors Used in the Pymetrozine Assessment.
Appendix 2. Acute Dietary Assessment.
Appendix 3. Chronic Non-Cancer Dietary Assessment.
Appendix 4. Chronic Cancer Dietary Assessment and Commodity Contribution Analysis.
Appendix 5. BEAD Usage Report, 11/19/2009 (DP Barcode No. D371624).
Appendix 6. Summary of USDA's Pesticide Data Program Monitoring Data for Pymetrozine.

Appendix 1 – Residue, Processing and Usage Factors Used in the Pymetrozine Assessment.

Commodity	Residue Estimates, ppm			Factors		
	Acute	Chronic	Cancer	Processing	Use (2004)	Use (2009)
Amaranth, leafy	0.726	0.21921	0.21921	1.00	1.00	1.00
Arrowroot, flour	0.046	0.0046	0.0046	1.00	1.00	1.00
Arrowroot, flour- babyfood	0.046	0.0046	0.0046	1.00	1.00	1.00
Artichoke, Jerusalem	0.046	0.0046	0.0046	1.00	1.00	1.00
Arugula	0.726	0.18537	0.18537	1.00	1.00	1.00
Asparagus	0.04	0.04	0.04	1.00	1.00	1.00
Balsam pear	0.13	0.066	0.06181	1.00	1.00	1.00
Broccoli	0.6278	0.05314	0.05314	1.00	0.25	0.025
Broccoli- babyfood	0.6278	0.05314	0.05314	1.00	0.25	0.025
Broccoli raab	0.358	0.26369	0.26369	1.00	1.00	1.00
Broccoli, Chinese	0.6278	0.05314	0.05314	1.00	0.25	0.025
Brussels sprouts	0.6278	0.07906	0.07906	1.00	1.00	1.00
Cabbage	0.6278	0.07906	0.07906	1.00	0.12	0.05
Cabbage, Chinese, bok choy	0.358	0.26369	0.26369	1.00	1.00	1.00
Cabbage, Chinese, mustard	0.6278	0.05314	0.05314	1.00	0.12	0.05
Cabbage, Chinese, napa	0.6278	0.05314	0.05314	1.00	0.12	0.05
Cantaloupe	0.13	0.066	0.066	1.00	0.25	0.05
Cardoon	0.726	0.06362	0.06362	1.00	1.00	1.00
Casaba	0.13	0.066	0.066	1.00	1.00	1.00
Cassava	0.046	0.0046	0.0046	1.00	1.00	1.00
Cassava- babyfood	0.046	0.0046	0.0046	1.00	1.00	1.00
Cauliflower	0.6278	0.05314	0.05314	1.00	1.00	0.05
Celery	0.726	0.06362	0.06362	1.00	0.25	0.05
Celery- babyfood	0.726	0.06362	0.06362	1.00	0.25	0.05
Celery, juice	0.726	0.06362	0.06362	1.00	0.25	0.05
Celtuce	0.726	0.06362	0.06362	1.00	1.00	1.00
Chayote, fruit	0.13	0.066	0.066	1.00	1.00	1.00
Chinese waxgourd	0.13	0.066	0.066	1.00	1.00	1.00
Chrysanthemum, garland	0.726	0.21921	0.21921	1.00	1.00	1.00
Collards	0.358	0.26369	0.26369	1.00	1.00	1.00
Cottonseed, oil	0.3936	0.084	0.084	1.00	0.06	1.00
Cottonseed, oil - babyfood	0.3936	0.084	0.084	1.00	0.06	1.00
Cress, garden	0.726	0.21921	0.21921	1.00	1.00	1.00
Cress, upland	0.726	0.21921	0.21921	1.00	1.00	1.00
Cucumber	0.13	0.06181	0.06181	1.00	0.10	0.01
Dandelion, leaves	0.726	0.21921	0.21921	1.00	1.00	1.00

Commodity	Residue Estimates, ppm			Factors		
	Acute	Chronic	Cancer	Processing	Use (2004)	Use (2009)
Dasheen, corm	0.046	0.0046	0.0046	1.00	1.00	1.00
Eggplant	0.23	0.052333	0.052333	1.00	1.00	1.00
Endive	0.726	0.21921	0.21921	1.00	1.00	1.00
Fennel, Florence	0.726	0.06362	0.06362	1.00	1.00	1.00
Ginger	0.046	0.0046	0.0046	1.00	1.00	1.00
Ginger - babyfood	0.046	0.0046	0.0046	1.00	1.00	1.00
Ginger, dried	0.046	0.0046	0.0046	1.00	1.00	1.00
Honeydew melon	0.13	0.066	0.066	1.00	1.00	1.00
Hop	6.18	2.784	2.784	1.00	1.00	0.20
Kale	0.358	0.26369	0.26369	1.00	1.00	1.00
Kohlrabi	0.6278	0.07906	0.07906	1.00	1.00	1.00
Lettuce, head	0.726	0.062	0.062	1.00	0.25	0.05
Lettuce, leaf	0.726	0.18537	0.18537	1.00	0.25	0.05
Mustard greens	0.358	0.26369	0.26369	1.00	1.00	1.00
Okra	0.23	0.052333	0.052333	1.00	1.00	1.00
Parsley, leaves	0.726	0.21921	0.21921	1.00	1.00	1.00
Pecan	0.056	0.046	0.046	1.00	1.00	0.01
Pepper, bell	0.23	0.052333	0.052333	1.00	0.08	0.05
Pepper, bell- babyfood	0.23	0.052333	0.052333	1.00	0.08	0.05
Pepper, bell, dried	0.23	0.052333	0.052333	1.00	0.08	0.05
Pepper, bell, dried- babyfood	0.23	0.052333	0.052333	1.00	0.08	0.05
Pepper, non-bell	0.23	0.052333	0.052333	1.00	0.08	0.05
Pepper, non-bell, - babyfood	0.23	0.052333	0.052333	1.00	0.08	0.05
Pepper, non-bell, dried	0.23	0.052333	0.052333	1.00	0.08	0.05
Potato, chips	0.046	0.0046	0.0046	1.00	0.20	0.05
Potato, dry (granules/ flakes)- babyfood	0.046	0.0046	0.0046	6.50	0.20	0.05
Potato, dry (granules/ flakes)	0.046	0.0046	0.0046	6.50	0.20	0.05
Potato, flour	0.046	0.0046	0.0046	6.50	0.20	0.05
Potato, flour - babyfood	0.046	0.0046	0.0046	6.50	0.20	0.05
Potato, tuber, w/o peel	0.046	0.0046	0.0046	1.00	0.20	0.05
Potato, tuber, w/o peel- babyfood	0.046	0.0046	0.0046	1.00	0.20	0.05
Potato, tuber, w/peel	0.046	0.0046	0.0046	1.00	0.20	0.05
Potato, tuber, w/peel- babyfood	0.046	0.0046	0.0046	1.00	0.20	0.05
Pumpkin	0.13	0.0601	0.0601	1.00	0.10	0.01
Pumpkin, seed	0.13	0.0601	0.0601	1.00	0.10	0.01
Radicchio	0.726	0.21921	0.21921	1.00	1.00	1.00
Rape greens	0.358	0.26369	0.26369	1.00	1.00	1.00
Rhubarb	0.726	0.06362	0.06362	1.00	1.00	1.00

Commodity	Residue Estimates, ppm			Factors		
	Acute	Chronic	Cancer	Processing	Use (2004)	Use (2009)
Spinach	0.726	0.21921	0.21921	1.00	0.16	0.025
Spinach- babyfood	0.726	0.21921	0.21921	1.00	0.16	0.025
Squash, summer	0.13	0.0601	0.0601	1.00	0.08	0.025
Squash, summer- babyfood	0.13	0.0601	0.0601	1.00	0.08	0.025
Squash, winter	0.13	0.0601	0.0601	1.00	0.08	0.025
Squash, winter- babyfood	0.13	0.0601	0.0601	1.00	0.08	0.025
Sweet potato	0.046	0.0046	0.0046	1.00	1.00	1.00
Sweet potato- babyfood	0.046	0.0046	0.0046	1.00	1.00	1.00
Swiss chard	0.726	0.06362	0.06362	1.00	1.00	1.00
Tanier, corm	0.046	0.0046	0.0046	1.00	1.00	1.00
Tomatillo	0.23	0.052333	0.052333	1.00	1.00	1.00
Tomato	0.23	0.056125	0.056125	1.00	0.12	0.07
Tomato- babyfood	0.23	0.056125	0.056125	1.00	0.12	0.07
Tomato, dried	0.23	0.056125	0.056125	14.30	0.12	0.07
Tomato, dried - babyfood	0.23	0.056125	0.056125	14.30	0.12	0.07
Tomato, juice	0.102	0.04984	0.04984	1.00	0.12	0.07
Tomato, paste	0.225	0.17284	0.17284	1.00	0.12	0.07
Tomato, paste- babyfood	0.225	0.17284	0.17284	1.00	0.12	0.07
Tomato, puree	0.102	0.04984	0.04984	1.00	0.12	0.07
Tomato, puree- babyfood	0.102	0.04984	0.04984	1.00	0.12	0.07
Turmeric	0.046	0.0046	0.0046	1.00	1.00	1.00
Turnip, tops	0.358	0.26369	0.26369	1.00	1.00	1.00
Watermelon	0.13	0.066	0.066	1.00	0.20	0.01
Watermelon, juice	0.13	0.066	0.066	1.00	0.20	0.01
Yam bean	0.046	0.0046	0.0046	1.00	1.00	1.00
Yam, true	0.046	0.0046	0.0046	1.00	1.00	1.00
Drinking Water	0.0163	0.0101	0.006	N/A	N/A	NA

Appendix 2 – Acute Dietary Assessment

Acute Input File:

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U.S. Environmental Protection Agency                                    Ver. 2.02
DEEM-FCID Acute analysis for PYMETROZINE 101103
Residue file name: C:\Documents and Settings\cswart02.AA\My
Documents\RAB2chemicals\Pymetrozine\2009Deem_NRDC\Acute Input File.R98
Analysis Date 01-12-2010            Residue file dated: 01-12-2010/11:31:44/8
Reference dose: aRfD = 0.0081 mg/kg bw/day  NOEL = 8.1 mg/kg bw/day
Comment: For NRDC response.  New %CTused for Chronic/Cancer
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EPA Code	Crop Grp	Food Name	Def Res (ppm)	Adj.Factors #1	#2	Comment
04010050	4A	Amaranth, leafy	0.726000	1.000	1.000	
01030150	1CD	Arrowroot, flour	0.046000	1.000	1.000	
01030151	1CD	Arrowroot, flour-babyfood	0.046000	1.000	1.000	
01030170	1CD	Artichoke, Jerusalem	0.046000	1.000	1.000	
04010180	4A	Arugula	0.726000	1.000	1.000	
95000190	O	Asparagus	0.040000	1.000	1.000	
09020210	9B	Balsam pear	0.130000	1.000	1.000	
05010610	5A	Broccoli	0.627800	1.000	1.000	
05010611	5A	Broccoli-babyfood	0.627800	1.000	1.000	
05010620	5A	Broccoli, Chinese	0.627800	1.000	1.000	
05020630	5B	Broccoli raab	0.358000	1.000	1.000	
05010640	5A	Brussels sprouts	0.627800	1.000	1.000	
05010690	5A	Cabbage	0.627800	1.000	1.000	
05020700	5B	Cabbage, Chinese, bok choy	0.358000	1.000	1.000	
05010710	5A	Cabbage, Chinese, napa	0.627800	1.000	1.000	
05010720	5A	Cabbage, Chinese, mustard	0.627800	1.000	1.000	
09010750	9A	Cantaloupe	0.130000	1.000	1.000	
04020760	4B	Cardoon	0.726000	1.000	1.000	
09010800	9A	Casaba	0.130000	1.000	1.000	
01030820	1CD	Cassava	0.046000	1.000	1.000	
01030821	1CD	Cassava-babyfood	0.046000	1.000	1.000	
05010830	5A	Cauliflower	0.627800	1.000	1.000	
04020850	4B	Celery	0.726000	1.000	1.000	
04020851	4B	Celery-babyfood	0.726000	1.000	1.000	
04020860	4B	Celery, juice	0.726000	1.000	1.000	
04020870	4B	Celtuce	0.726000	1.000	1.000	
09020880	9B	Chayote, fruit	0.130000	1.000	1.000	
09021020	9B	Chinese waxgourd	0.130000	1.000	1.000	
04011040	4A	Chrysanthemum, garland	0.726000	1.000	1.000	
05021170	5B	Collards	0.358000	1.000	1.000	
95001280	O	Cottonseed, oil	0.393600	1.000	1.000	
95001281	O	Cottonseed, oil-babyfood	0.393600	1.000	1.000	
04011330	4A	Cress, garden	0.726000	1.000	1.000	
04011340	4A	Cress, upland	0.726000	1.000	1.000	
09021350	9B	Cucumber	0.130000	1.000	1.000	
04011380	4A	Dandelion, leaves	0.726000	1.000	1.000	
01031390	1CD	Dasheen, corm	0.046000	1.000	1.000	
08001480	8	Eggplant	0.230000	1.000	1.000	
04011500	4A	Endive	0.726000	1.000	1.000	
04021520	4B	Fennel, Florence	0.726000	1.000	1.000	
01031660	1CD	Ginger	0.046000	1.000	1.000	
01031661	1CD	Ginger-babyfood	0.046000	1.000	1.000	
01031670	1CD	Ginger, dried	0.046000	1.000	1.000	
09011870	9A	Honeydew melon	0.130000	1.000	1.000	
95001880	O	Hop	6.180000	1.000	1.000	
05021940	5B	Kale	0.358000	1.000	1.000	
05011960	5A	Kohlrabi	0.627800	1.000	1.000	
04012040	4A	Lettuce, head	0.726000	1.000	1.000	
04012050	4A	Lettuce, leaf	0.726000	1.000	1.000	
05022290	5B	Mustard greens	0.358000	1.000	1.000	
08002340	8	Okra	0.230000	1.000	1.000	
04012480	4A	Parsley, leaves	0.726000	1.000	1.000	
19012490	19A	Parsley, dried leaves	0.726000	1.000	1.000	
19012491	19A	Parsley, dried leaves-babyfood	0.726000	1.000	1.000	

14002690	14	Pecan	0.056000	1.000	1.000
08002700	8	Pepper, bell	0.230000	1.000	1.000
08002701	8	Pepper, bell-babyfood	0.230000	1.000	1.000
08002710	8	Pepper, bell, dried	0.230000	1.000	1.000
08002711	8	Pepper, bell, dried-babyfood	0.230000	1.000	1.000
08002720	8	Pepper, nonbell	0.230000	1.000	1.000
08002721	8	Pepper, nonbell-babyfood	0.230000	1.000	1.000
08002730	8	Pepper, nonbell, dried	0.230000	1.000	1.000
01032960	1C	Potato, chips	0.046000	1.000	1.000
01032970	1C	Potato, dry (granules/ flakes)	0.046000	6.500	1.000
01032971	1C	Potato, dry (granules/ flakes)-b	0.046000	6.500	1.000
01032980	1C	Potato, flour	0.046000	6.500	1.000
01032981	1C	Potato, flour-babyfood	0.046000	6.500	1.000
01032990	1C	Potato, tuber, w/peel	0.046000	1.000	1.000
01032991	1C	Potato, tuber, w/peel-babyfood	0.046000	1.000	1.000
01033000	1C	Potato, tuber, w/o peel	0.046000	1.000	1.000
01033001	1C	Potato, tuber, w/o peel-babyfood	0.046000	1.000	1.000
09023080	9B	Pumpkin	0.130000	1.000	1.000
09023090	9B	Pumpkin, seed	0.130000	1.000	1.000
04013130	4A	Radicchio	0.726000	1.000	1.000
05023180	5B	Rape greens	0.358000	1.000	1.000
04023220	4B	Rhubarb	0.726000	1.000	1.000
04013550	4A	Spinach	0.726000	1.000	1.000
04013551	4A	Spinach-babyfood	0.726000	1.000	1.000
09023560	9B	Squash, summer	0.130000	1.000	1.000
09023561	9B	Squash, summer-babyfood	0.130000	1.000	1.000
09023570	9B	Squash, winter	0.130000	1.000	1.000
09023571	9B	Squash, winter-babyfood	0.130000	1.000	1.000
01033660	1CD	Sweet potato	0.046000	1.000	1.000
01033661	1CD	Sweet potato-babyfood	0.046000	1.000	1.000
04023670	4B	Swiss chard	0.726000	1.000	1.000
01033710	1CD	Tanier, corm	0.046000	1.000	1.000
08003740	8	Tomatillo	0.230000	1.000	1.000
08003750	8	Tomato	0.230000	1.000	1.000
08003751	8	Tomato-babyfood	0.230000	1.000	1.000
08003760	8	Tomato, paste	0.225000	1.000	1.000
08003761	8	Tomato, paste-babyfood	0.225000	1.000	1.000
08003770	8	Tomato, puree	0.102000	1.000	1.000
08003771	8	Tomato, puree-babyfood	0.102000	1.000	1.000
08003780	8	Tomato, dried	0.230000	14.300	1.000
08003781	8	Tomato, dried-babyfood	0.230000	14.300	1.000
08003790	8	Tomato, juice	0.102000	1.000	1.000
01033870	1CD	Turmeric	0.046000	1.000	1.000
05023890	5B	Turnip, greens	0.358000	1.000	1.000
86010000	O	Water, direct, all sources	0.016300	1.000	1.000
86020000	O	Water, indirect, all sources	0.016300	1.000	1.000
09013990	9A	Watermelon	0.130000	1.000	1.000
09014000	9A	Watermelon, juice	0.130000	1.000	1.000
01034060	1CD	Yam, true	0.046000	1.000	1.000
01034070	1CD	Yam bean	0.046000	1.000	1.000

Acute Results:

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U.S. Environmental Protection Agency                                    Ver. 2.02
DEEM-FCID ACUTE Analysis for PYMETROZINE 101103                    (1994-98 data)
Residue file: Acute Input File.R98                Adjustment factor #2 NOT used.
Analysis Date: 01-12-2010/11:56:58    Residue file dated: 01-12-2010/11:31:44/8
NOEL (Acute) =    8.100000 mg/kg body-wt/day
Daily totals for food and foodform consumption used.
Run Comment: "For NRDC response.  New %CTused for Chronic/Cancer"
================================================================================

Summary calculations (per capita):
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	95th Percentile			99th Percentile			99.9th Percentile	
	Exposure	% aRfD	MOE	Exposure	% aRfD	MOE	Exposure	% aRfD	MOE
U.S. Population:	**0.002831**	**34.95**	2861	0.004753	58.69	1704	0.008607	106.26	941
All infants:	**0.003882**	**47.92**	2086	0.008560	105.67	946	0.014529	179.37	557
Children 1-2 yrs:	**0.004368**	**53.93**	1854	0.008373	103.37	967	0.014855	183.40	545
Children 3-5 yrs:	**0.004034**	**49.80**	2007	0.007410	91.48	1093	0.012133	149.79	667
Children 6-12 yrs:	**0.003027**	**37.37**	2675	0.005079	62.71	1594	0.010271	126.80	788
Youth 13-19 yrs:	**0.002312**	**28.54**	3503	0.003756	46.37	2156	0.005989	73.94	1352
Adults 20-49 yrs:	**0.002698**	**33.31**	3002	0.004439	54.81	1824	0.007132	88.05	1135
Adults 50+ yrs:	**0.002669**	**32.96**	3034	0.004208	51.95	1925	0.006788	83.80	1193
Females 13-49 yrs:	**0.002625**	**32.41**	3085	0.004267	52.68	1898	0.007651	94.45	1058

Appendix 3 – Chronic Non-Cancer Dietary Assessment

Chronic Non-Cancer Input File:

U.S. Environmental Protection Agency Ver. 2.00
DEEM-FCID Chronic analysis for PYMETROZINE 101103 1994-98 data
Residue file: C:\Documents and Settings\cswart02.AA\My Documents\RAB2chemicals\Pymetrozine\2009Deem_NRDC\Chronic Input File.R98
Adjust. #2 used
Analysis Date 01-12-2010 Residue file dated: 01-12-2010/15:35:06/8
Reference dose (RfD) = 0.0081 mg/kg bw/day
Comment:For NRDC response. New %CTused for Chronic/Cancer

Food Crop EPA Code	Grp	Food Name	Residue (ppm)	Adj.Factors #1	#2	Comment
04010050	4A	Amaranth, leafy	0.219210	1.000	1.000	
01030150	1CD	Arrowroot, flour	0.004600	1.000	1.000	
01030151	1CD	Arrowroot, flour-babyfood	0.004600	1.000	1.000	
01030170	1CD	Artichoke, Jerusalem	0.004600	1.000	1.000	
04010180	4A	Arugula	0.185370	1.000	1.000	
95000190	O	Asparagus	0.040000	1.000	1.000	
09020210	9B	Balsam pear	0.066000	1.000	1.000	
05010610	5A	Broccoli	0.053140	1.000	0.025	
05010611	5A	Broccoli-babyfood	0.053140	1.000	0.025	
05010620	5A	Broccoli, Chinese	0.053140	1.000	0.025	
05020630	5B	Broccoli raab	0.263690	1.000	1.000	
05010640	5A	Brussels sprouts	0.079060	1.000	1.000	
05010690	5A	Cabbage	0.079060	1.000	0.050	
05020700	5B	Cabbage, Chinese, bok choy	0.263690	1.000	1.000	
05010710	5A	Cabbage, Chinese, napa	0.053140	1.000	0.050	
05010720	5A	Cabbage, Chinese, mustard	0.053140	1.000	0.050	
09010750	9A	Cantaloupe	0.066000	1.000	0.050	
04020760	4B	Cardoon	0.063620	1.000	1.000	
09010800	9A	Casaba	0.066000	1.000	1.000	
01030820	1CD	Cassava	0.004600	1.000	1.000	
01030821	1CD	Cassava-babyfood	0.004600	1.000	1.000	
05010830	5A	Cauliflower	0.053140	1.000	0.050	
04020850	4B	Celery	0.063620	1.000	0.050	
04020851	4B	Celery-babyfood	0.063620	1.000	0.050	
04020860	4B	Celery, juice	0.063620	1.000	0.050	
04020870	4B	Celtuce	0.063620	1.000	1.000	
09020880	9B	Chayote, fruit	0.066000	1.000	1.000	
09021020	9B	Chinese waxgourd	0.066000	1.000	1.000	
04011040	4A	Chrysanthemum, garland	0.219210	1.000	1.000	
05021170	5B	Collards	0.263690	1.000	1.000	
95001280	O	Cottonseed, oil	0.084000	1.000	1.000	
95001281	O	Cottonseed, oil-babyfood	0.084000	1.000	1.000	
04011330	4A	Cress, garden	0.219210	1.000	1.000	
04011340	4A	Cress, upland	0.219210	1.000	1.000	
09021350	9B	Cucumber	0.061810	1.000	0.010	
04011380	4A	Dandelion, leaves	0.219210	1.000	1.000	
01031390	1CD	Dasheen, corm	0.004600	1.000	1.000	
08001480	8	Eggplant	0.052333	1.000	1.000	
04011500	4A	Endive	0.219210	1.000	1.000	
04021520	4B	Fennel, Florence	0.063620	1.000	1.000	
01031660	1CD	Ginger	0.004600	1.000	1.000	
01031661	1CD	Ginger-babyfood	0.004600	1.000	1.000	
01031670	1CD	Ginger, dried	0.004600	1.000	1.000	
09011870	9A	Honeydew melon	0.066000	1.000	1.000	
95001880	O	Hop	2.784000	1.000	0.200	
05021940	5B	Kale	0.263690	1.000	1.000	
05011960	5A	Kohlrabi	0.079060	1.000	1.000	
04012040	4A	Lettuce, head	0.062000	1.000	0.050	
04012050	4A	Lettuce, leaf	0.185370	1.000	0.050	
05022290	5B	Mustard greens	0.263690	1.000	1.000	
08002340	8	Okra	0.052333	1.000	1.000	
04012480	4A	Parsley, leaves	0.219210	1.000	1.000	

19012490	19A	Parsley, dried leaves	0.219210	1.000	1.000
19012491	19A	Parsley, dried leaves-babyfood	0.219210	1.000	1.000
14002690	14	Pecan	0.046000	1.000	0.010
08002700	8	Pepper, bell	0.052333	1.000	0.050
08002701	8	Pepper, bell-babyfood	0.052333	1.000	0.050
08002710	8	Pepper, bell, dried	0.052333	1.000	0.050
08002711	8	Pepper, bell, dried-babyfood	0.052333	1.000	0.050
08002720	8	Pepper, nonbell	0.052333	1.000	0.050
08002721	8	Pepper, nonbell-babyfood	0.052333	1.000	0.050
08002730	8	Pepper, nonbell, dried	0.052333	1.000	0.050
01032960	1C	Potato, chips	0.004600	1.000	0.050
01032970	1C	Potato, dry (granules/ flakes)	0.004600	6.500	0.050
01032971	1C	Potato, dry (granules/ flakes)-b	0.004600	6.500	0.050
01032980	1C	Potato, flour	0.004600	6.500	0.050
01032981	1C	Potato, flour-babyfood	0.004600	6.500	0.050
01032990	1C	Potato, tuber, w/peel	0.004600	1.000	0.050
01032991	1C	Potato, tuber, w/peel-babyfood	0.004600	1.000	0.050
01033000	1C	Potato, tuber, w/o peel	0.004600	1.000	0.050
01033001	1C	Potato, tuber, w/o peel-babyfood	0.004600	1.000	0.050
09023080	9B	Pumpkin	0.060100	1.000	0.010
09023090	9B	Pumpkin, seed	0.060100	1.000	0.010
04013130	4A	Radicchio	0.219210	1.000	1.000
05023180	5B	Rape greens	0.263690	1.000	1.000
04023220	4B	Rhubarb	0.063620	1.000	1.000
04013550	4A	Spinach	0.219210	1.000	0.025
04013551	4A	Spinach-babyfood	0.219210	1.000	0.025
09023560	9B	Squash, summer	0.060100	1.000	0.025
09023561	9B	Squash, summer-babyfood	0.060100	1.000	0.025
09023570	9B	Squash, winter	0.060100	1.000	0.025
09023571	9B	Squash, winter-babyfood	0.060100	1.000	0.025
01033660	1CD	Sweet potato	0.004600	1.000	1.000
01033661	1CD	Sweet potato-babyfood	0.004600	1.000	1.000
04023670	4B	Swiss chard	0.063620	1.000	1.000
01033710	1CD	Tanier, corm	0.004600	1.000	1.000
08003740	8	Tomatillo	0.052333	1.000	1.000
08003750	8	Tomato	0.056125	1.000	0.070
08003751	8	Tomato-babyfood	0.056125	1.000	0.070
08003760	8	Tomato, paste	0.172840	1.000	0.070
08003761	8	Tomato, paste-babyfood	0.172840	1.000	0.070
08003770	8	Tomato, puree	0.049840	1.000	0.070
08003771	8	Tomato, puree-babyfood	0.049840	1.000	0.070
08003780	8	Tomato, dried	0.056125	14.300	0.070
08003781	8	Tomato, dried-babyfood	0.056125	14.300	0.070
08003790	8	Tomato, juice	0.049840	1.000	0.070
01033870	1CD	Turmeric	0.004600	1.000	1.000
05023890	5B	Turnip, greens	0.263690	1.000	1.000
86010000	O	Water, direct, all sources	0.010100	1.000	1.000
86020000	O	Water, indirect, all sources	0.010100	1.000	1.000
09013990	9A	Watermelon	0.066000	1.000	0.010
09014000	9A	Watermelon, juice	0.066000	1.000	0.010
01034060	1CD	Yam, true	0.004600	1.000	1.000
01034070	1CD	Yam bean	0.004600	1.000	1.000

Chronic Non-Cancer Results:

U.S. Environmental Protection Agency Ver. 2.00
DEEM-FCID Chronic analysis for PYMETROZINE 101103 (1994-98 data)
Residue file name: C:\Documents and Settings\cswart02.AA\My Documents\RAB2chemicals\Pymetrozine\2009Deem_NRDC\Chronic Input File.R98
Adjustment factor #2 used.
Analysis Date 01-12-2010/15:36:27 Residue file dated: 01-12-2010/15:35:06/8
Reference dose (RfD, Chronic) = .0081 mg/kg bw/day
COMMENT 1: For NRDC response. New %CTused for Chronic/Cancer

Total exposure by population subgroup

Population Subgroup	Total Exposure mg/kg body wt/day	Percent of Rfd
U.S. Population (total)	0.000237	2.9%
U.S. Population (spring season)	0.000235	2.9%
U.S. Population (summer season)	0.000255	3.2%
U.S. Population (autumn season)	0.000230	2.8%
U.S. Population (winter season)	0.000227	2.8%
Northeast region	0.000217	2.7%
Midwest region	0.000237	2.9%
Southern region	0.000228	2.8%
Western region	0.000269	3.3%
Hispanics	0.000258	3.2%
Non-hispanic whites	0.000227	2.8%
Non-hispanic blacks	0.000250	3.1%
Non-hisp/non-white/non-black	0.000309	3.8%
All infants (< 1 year)	0.000707	8.7%
Nursing infants	0.000263	3.3%
Non-nursing infants	0.000876	10.8%
Children 1-6 yrs	0.000330	4.1%
Children 7-12 yrs	0.000212	2.6%
Females 13-19 (not preg or nursing)	0.000167	2.1%
Females 20+ (not preg or nursing)	0.000235	2.9%
Females 13-50 yrs	0.000225	2.8%
Females 13+ (preg/not nursing)	0.000217	2.7%
Females 13+ (nursing)	0.000313	3.9%
Males 13-19 yrs	0.000181	2.2%
Males 20+ yrs	0.000218	2.7%
Seniors 55+	0.000236	2.9%
Children 1-2 yrs	0.000350	4.3%
Children 3-5 yrs	0.000329	4.1%
Children 6-12 yrs	0.000224	2.8%
Youth 13-19 yrs	0.000174	2.2%
Adults 20-49 yrs	0.000222	2.7%
Adults 50+ yrs	0.000235	2.9%
Females 13-49 yrs	0.000217	2.7%

Appendix 4 – Chronic Cancer Dietary Assessment

Chronic Cancer Input File:

```
U.S. Environmental Protection Agency                                    Ver. 2.00
DEEM-FCID Chronic analysis for PYMETROZINE 101103                     1994-98 data
Residue file: C:\Documents and Settings\cswart02.AA\My
Documents\RAB2chemicals\Pymetrozine\2009Deem_NRDC\Cancer Input File.R98
                                                                  Adjust. #2 used
Analysis Date 01-12-2010            Residue file dated: 01-12-2010/15:34:37/8
Q* = 0.0119
Comment:For NRDC response.  New %CTused for Chronic/Cancer
```

Food Crop EPA Code	Grp	Food Name	Residue (ppm)	Adj.Factors #1	#2	Comment
04010050	4A	Amaranth, leafy	0.219210	1.000	1.000	
01030150	1CD	Arrowroot, flour	0.004600	1.000	1.000	
01030151	1CD	Arrowroot, flour-babyfood	0.004600	1.000	1.000	
01030170	1CD	Artichoke, Jerusalem	0.004600	1.000	1.000	
04010180	4A	Arugula	0.185370	1.000	1.000	
95000190	O	Asparagus	0.040000	1.000	1.000	
09020210	9B	Balsam pear	0.061810	1.000	1.000	
05010610	5A	Broccoli	0.053140	1.000	0.025	
05010611	5A	Broccoli-babyfood	0.053140	1.000	0.025	
05010620	5A	Broccoli, Chinese	0.053140	1.000	0.025	
05020630	5B	Broccoli raab	0.263690	1.000	1.000	
05010640	5A	Brussels sprouts	0.079060	1.000	1.000	
05010690	5A	Cabbage	0.079060	1.000	0.050	
05020700	5B	Cabbage, Chinese, bok choy	0.263690	1.000	1.000	
05010710	5A	Cabbage, Chinese, napa	0.053140	1.000	0.050	
05010720	5A	Cabbage, Chinese, mustard	0.053140	1.000	0.050	
09010750	9A	Cantaloupe	0.066000	1.000	0.050	
04020760	4B	Cardoon	0.063620	1.000	1.000	
09010800	9A	Casaba	0.066000	1.000	1.000	
01030820	1CD	Cassava	0.004600	1.000	1.000	
01030821	1CD	Cassava-babyfood	0.004600	1.000	1.000	
05010830	5A	Cauliflower	0.053140	1.000	0.050	
04020850	4B	Celery	0.063620	1.000	0.050	
04020851	4B	Celery-babyfood	0.063620	1.000	0.050	
04020860	4B	Celery, juice	0.063620	1.000	0.050	
04020870	4B	Celtuce	0.063620	1.000	1.000	
09020880	9B	Chayote, fruit	0.066000	1.000	1.000	
09021020	9B	Chinese waxgourd	0.066000	1.000	1.000	
04011040	4A	Chrysanthemum, garland	0.219210	1.000	1.000	
05021170	5B	Collards	0.263690	1.000	1.000	
95001280	O	Cottonseed, oil	0.084000	1.000	1.000	
95001281	O	Cottonseed, oil-babyfood	0.084000	1.000	1.000	
04011330	4A	Cress, garden	0.219210	1.000	1.000	
04011340	4A	Cress, upland	0.219210	1.000	1.000	
09021350	9B	Cucumber	0.061810	1.000	0.010	
04011380	4A	Dandelion, leaves	0.219210	1.000	1.000	
01031390	1CD	Dasheen, corm	0.004600	1.000	1.000	
08001480	8	Eggplant	0.052333	1.000	1.000	
04011500	4A	Endive	0.219210	1.000	1.000	
04021520	4B	Fennel, Florence	0.063620	1.000	1.000	
01031660	1CD	Ginger	0.004600	1.000	1.000	
01031661	1CD	Ginger-babyfood	0.004600	1.000	1.000	
01031670	1CD	Ginger, dried	0.004600	1.000	1.000	
09011870	9A	Honeydew melon	0.066000	1.000	1.000	
95001880	O	Hop	2.784000	1.000	0.200	
05021940	5B	Kale	0.263690	1.000	1.000	
05011960	5A	Kohlrabi	0.079060	1.000	1.000	
04012040	4A	Lettuce, head	0.062000	1.000	0.050	
04012050	4A	Lettuce, leaf	0.185370	1.000	0.050	
05022290	5B	Mustard greens	0.263690	1.000	1.000	
08002340	8	Okra	0.052333	1.000	1.000	
04012480	4A	Parsley, leaves	0.219210	1.000	1.000	

19012490	19A	Parsley, dried leaves	0.219210	1.000	1.000
19012491	19A	Parsley, dried leaves-babyfood	0.219210	1.000	1.000
14002690	14	Pecan	0.046000	1.000	0.010
08002700	8	Pepper, bell	0.052333	1.000	0.050
08002701	8	Pepper, bell-babyfood	0.052333	1.000	0.050
08002710	8	Pepper, bell, dried	0.052333	1.000	0.050
08002711	8	Pepper, bell, dried-babyfood	0.052333	1.000	0.050
08002720	8	Pepper, nonbell	0.052333	1.000	0.050
08002721	8	Pepper, nonbell-babyfood	0.052333	1.000	0.050
08002730	8	Pepper, nonbell, dried	0.052333	1.000	0.050
01032960	1C	Potato, chips	0.004600	1.000	0.050
01032970	1C	Potato, dry (granules/ flakes)	0.004600	6.500	0.050
01032971	1C	Potato, dry (granules/ flakes)-b	0.004600	6.500	0.050
01032980	1C	Potato, flour	0.004600	6.500	0.050
01032981	1C	Potato, flour-babyfood	0.004600	6.500	0.050
01032990	1C	Potato, tuber, w/peel	0.004600	1.000	0.050
01032991	1C	Potato, tuber, w/peel-babyfood	0.004600	1.000	0.050
01033000	1C	Potato, tuber, w/o peel	0.004600	1.000	0.050
01033001	1C	Potato, tuber, w/o peel-babyfood	0.004600	1.000	0.050
09023080	9B	Pumpkin	0.060100	1.000	0.010
09023090	9B	Pumpkin, seed	0.060100	1.000	0.010
04013130	4A	Radicchio	0.219210	1.000	1.000
05023180	5B	Rape greens	0.263690	1.000	1.000
04023220	4B	Rhubarb	0.063620	1.000	1.000
04013550	4A	Spinach	0.219210	1.000	0.025
04013551	4A	Spinach-babyfood	0.219210	1.000	0.025
09023560	9B	Squash, summer	0.060100	1.000	0.025
09023561	9B	Squash, summer-babyfood	0.060100	1.000	0.025
09023570	9B	Squash, winter	0.060100	1.000	0.025
09023571	9B	Squash, winter-babyfood	0.060100	1.000	0.025
01033660	1CD	Sweet potato	0.004600	1.000	1.000
01033661	1CD	Sweet potato-babyfood	0.004600	1.000	1.000
04023670	4B	Swiss chard	0.063620	1.000	1.000
01033710	1CD	Tanier, corm	0.004600	1.000	1.000
08003740	8	Tomatillo	0.052333	1.000	1.000
08003750	8	Tomato	0.056125	1.000	0.070
08003751	8	Tomato-babyfood	0.056125	1.000	0.070
08003760	8	Tomato, paste	0.172840	1.000	0.070
08003761	8	Tomato, paste-babyfood	0.172840	1.000	0.070
08003770	8	Tomato, puree	0.049840	1.000	0.070
08003771	8	Tomato, puree-babyfood	0.049840	1.000	0.070
08003780	8	Tomato, dried	0.056125	14.300	0.070
08003781	8	Tomato, dried-babyfood	0.056125	14.300	0.070
08003790	8	Tomato, juice	0.049840	1.000	0.070
01033870	1CD	Turmeric	0.004600	1.000	1.000
05023890	5B	Turnip, greens	0.263690	1.000	1.000
86010000	O	Water, direct, all sources	0.006000	1.000	1.000
86020000	O	Water, indirect, all sources	0.006000	1.000	1.000
09013990	9A	Watermelon	0.066000	1.000	0.010
09014000	9A	Watermelon, juice	0.066000	1.000	0.010
01034060	1CD	Yam, true	0.004600	1.000	1.000
01034070	1CD	Yam bean	0.004600	1.000	1.000

Chronic Cancer Results:

```
U.S. Environmental Protection Agency                                    Ver. 2.00
DEEM-FCID Chronic analysis for PYMETROZINE 101103                    (1994-98 data)
Residue file name: C:\Documents and Settings\cswart02.AA\My
Documents\RAB2chemicals\Pymetrozine\2009Deem_NRDC\Cancer Input File.R98
                                                      Adjustment factor #2 used.
Analysis Date 01-12-2010/15:37:27     Residue file dated: 01-12-2010/15:34:37/8
Q* = 0.0119
COMMENT 1: For NRDC response.  New %CTused for Chronic/Cancer
================================================================================
                    Total exposure by population subgroup
--------------------------------------------------------------------------------

                                                 Total Exposure
                                          ----------------------------------
          Population                          mg/kg          Lifetime risk
           Subgroup                        body wt/day        (Q*= .0119)
-----------------------------------   -------------      -------------
U.S. Population (total)                     0.000151          1.79E-06
```

Cancer Commodity Contribution Analysis:

```
U.S. Environmental Protection Agency                                    Ver. 2.00
DEEM-FCID Chronic analysis for PYMETROZINE 101103                    (1994-98 data)
Residue file name: C:\Documents and Settings\cswart02.AA\My
Documents\RAB2chemicals\Pymetrozine\2009Deem_NRDC\Cancer Input File.R98
                                                      Adjustment factor #2 used.
Analysis Date 01-12-2010/15:37:59     Residue file dated: 01-12-2010/15:34:37/8
Q* = 0.0119
COMMENT 1: For NRDC response.  New %CTused for Chronic/Cancer
================================================================================
                 Critical Commodity Contribution Analysis for
                           U.S. Population (total)

                 Total Exposure =.0001506 mg/kg bw/day

             Crop groups with total exposure contribution > 10%
               Foods/Foodforms with exposure contribution > 10%
--------------------------------------------------------------------------------

Crop group                                 -----------Exposure analysis----------
   Food                                       mg/kg    | % of Total| Lifetime Risk
      Foodform                             body wt/day|  Exposure  |(Q*= .0119)
-----------------------------------------   -----------|-----------|--------------

Crop Group = (O)  Other
   Water, direct, all sources (86010000):
        FoodForm N/S                          0.0000728    48.34%        8.66E-07
   Water, indirect, all sources (86020000):
        FoodForm N/S                          0.0000537    35.63%        6.39E-07
-----------------------------------------   -----------|-----------|--------------
  Total for crop group                        0.0001330    88.30%        1.58E-06

Total for crop groups listed above:           0.0001330    88.30%        1.58E-06
--------------------------------------------------------------------------------
```

Appendix 5 – BEADs Usage Report Dated 11/19/09.

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

NOV 19 2009

OFFICE OF
PREVENTION, PESTICIDES AND
TOXIC SUBSTANCES

MEMORANDUM

SUBJECT: Usage Report Package in Support of Registration Review for the Insecticide Pymetrozine (101103)

FROM: Arthur H. Grube, Senior Economist
Economic Analysis Branch
Biological and Economic Analysis Division (7503P)

THROUGH: Stephen M. Jarboe, Acting Branch Chief
Science Information & Analysis Branch
Biological & Economic Analysis Division (7503P)

TO: Christina B. Swartz, Branch Chief
Registration Action Branch 2
Health Effects Division (7509P)

This memorandum transmits the Usage report for Pymetrozine. The data included in this memorandum were reviewed by Jihad A. Alsadek, Economist. This report can be written in various formats (MS Word, Excel, Adobe Acrobat). It is advisable to open or save each report to view or print from the appropriate program.

For questions, comments and other usage or label use information requests, please contact me at (703) 308-8095. Other requests for information may be addressed to **OPP Usage and Label Use Team**, our group e-mail address in Lotus Notes.

The **Usage** report electronically-transmitted through Lotus Notes links includes:
Screening Level Usage Analysis (SLUA)

Pymetrozine (101103)
Screening Level Usage Analysis (SLUA)
Date: November 6, 2009

What is a Screening Level Usage Analysis (SLUA)?

- Available estimates of pesticide usage data for a particular active ingredient that is used on **agricultural** crops in the United States.
- Pesticide usage data obtained from various sources. The data are then merged, averaged, and rounded so that the presented information is not proprietary, business confidential, or trade secret.

What does it contain?

- Pesticide usage data for a **single** active ingredient only.
- Agricultural use sites (crops) that the pesticide is *reported* to be used on.
- Available pesticide usage information from U.S. states that produce 80% or more of a crop, in most cases, or less than 80%, in rare cases, depending on the scope of the survey and available resources.
- Annual percent of crop treated **(average & maximum)** for each agricultural crop.
- Average annual pounds of the pesticide applied for each agricultural crop (i.e., for the states surveyed, not for the entire United States).

What assumptions can I make about the reported data?

- **Average pounds of active ingredient applied** - Values are calculated by merging pesticide usage data sources together; averaging across all observations, then rounding. ***Note:*** *If the estimated value is less than 500, then that value is labeled <500. Estimated values between 500 & <1,000,000 are rounded to 1 significant digit. Estimated values of 1,000,000 or greater are rounded to 2 significant digits.)*
- **Average percent of crop treated** - Values are calculated by merging data sources together; averaging by year, averaging across all years, & rounding to the nearest multiple of 5. ***Note:*** *If the estimated value is less than 2.5, then the value is labeled <2.5. If the estimated value is less than 1, then the value is labeled <1.*
- **Maximum percent of crop treated** - Value is the single maximum value reported across all data sources, across all years, & rounded up to the nearest multiple of 5. ***Note:*** *If the estimated value is less than 2.5, then the value is labeled <2.5.*

What are the data sources used?

- **USDA-NASS** (United States Department of Agriculture's National Agricultural Statistics Service) – pesticide usage data from 2001 to 2007.
- **Private pesticide market research** – pesticide usage data from 2001 to 2007.
- **NPUD 2002** (National Pesticide Use Database) pesticide usage data from the CropLife America Foundation are used ***only*** if data are not available from the other sources.
- **California Department of Pesticide Regulation (DPR) Pesticide Use Reporting (PUR)** data for 2000 to 2005 when 95% or more of a crop is grown California.

What are the limitations to the data?

- Additional registered uses may exist but are not included because the available surveys do not report usage (e.g., small acreage crops).
- Lack of reported usage data for the pesticide on a crop **does not imply** zero usage.
- Usage data on a particular site may be noted in data sources, but **not quantified**. In these instances, the site would not be reported in the SLUA.
- Non-agricultural use sites (e.g., turf, post-harvest, mosquito control, etc.) are not reported in the SLUA. A separate request must be made to receive these estimates.
- Some sites show some use, even though they are not on the label. This usage could be due to various factors, including, but not limited to Section 18 requests, existing stocks of the chemical, data collection errors, and experimental use permits (EUPs).

November 6 2009
Screening Level Estimates of Agricultural Uses of Pymetrozine (101103)
Sorted Alphabetically

	Crop	Lbs. A.I.	Percent Crop Ttd. Avg.	Max.
1	Broccoli	<500	<2.5	5
2	Cabbage	<500	5	5
3	Cantaloupes +	<500	5	10
4	Cauliflower	<500	5	5
5	Celery	<500	5	15
6	Cherries +	<500	<1	<2.5
7	Cucumbers	<500	<1	<2.5
8	Hops (NPUD '02)	1,000	20	N/C
9	Lettuce	1,000	5	15
10	Pecans	1,000	<1	<2.5
11	Peppers	<500	5	25
12	Potatoes	5,000	5	10
13	Pumpkins	<500	<1	<2.5
14	Seed Crops(NPUD '02) +	<500	10	N/C
15	Spinach	<500	<2.5	5
16	Squash	<500	<2.5	10
17	Tobacco	1,000	<2.5	<2.5
18	Tomatoes	1,000	7	20
19	Watermelons	<500	<1	<2.5

All numbers rounded.

<500 Less than 500 pounds of active ingredient
<2.5 Less than 2.5 percent of crop treated
<1 Less than 1 percent of crop treated
N/C Not Calculated
\+ Crops not known to be listed on active end use product registrations or as Section 18 emergency exemptions when this report was run

SLUA data sources include:
USDA-NASS (United States Department of Agriculture's National Agricultural Statistics Service)
Private Pesticide Market Research
NPUD 2002 (National Pesticide Use Database) of the CropLife America Foundation
California DPR (Department of Pesticide Regulation)

These results reflect amalgamated data developed by the Agency and are releasable to the public.

Appendix 6. Summary of USDA's Pesticide Data Program Monitoring Data for Pymetrozine.

Year	Commodity	# Analyzed	# Detects	% Detects	Min Conc.	Max Conc.	Avg Conc.	LOD Range (ppm)	Tolerance
2002	Sweet Bell Peppers	186	0					0.0102 - 0.0102	0.2
2003	Sweet Bell Peppers	725	0					0.009 - 0.0102	0.2
2003	Sweet Potatoes	436	0					0.013 - 0.013	0.02
2004	Cauliflower	124	0					0.0045 - 0.0045	0.5
2004	Lettuce	483	2	0.4	0.0075	0.015	0.01	0.0045 - 0.009	0.6
2004	Sweet Bell Peppers	370	2	0.5	0.015	0.031	0.02	0.009 - 0.009	0.2
2004	Sweet Potatoes	392	0					0.087 - 0.087	0.02
2005	Cauliflower	648	0					0.0045 - 0.0045	0.02
2005	Lettuce	469	1	0.2	0.033	0.033	0.03	0.0045 - 0.0045	0.6
2005	Soybean grain	306	0					3 - 3 (ppb)	N/A
2006	Broccoli	169	0					0.0045 - 0.0045	0.5
2006	Cauliflower	558	0					0.0045 - 0.0045	0.5
2006	Potatoes, Frozen	22	0					0.003 - 0.003	0.02
2006	Spinach	366	10	2.7	0.0075	0.046	0.02	0.0045 - 0.0045	0.6
2007	Broccoli	736	0					0.0045 - 0.0045	0.5
2007	Celery	495	1	0.2	0.0075	0.0075	0.01	0.0045 - 0.0045	0.6

13544

R181956

Chemical Name: 1,2,4-Triazin-3(2H)-one, 4,5-dihydro-6-methyl-4-{(3-pyridinylmethylene)amino}-, (E)-

PC Code: 101103
HED File Code: 14000 Risk Reviews
Memo Date: 4/2/2010
File ID: 00000000
Accession #: 000-00-0134

HED Records Reference Center
4/22/2010