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

OFFICE OF
PREVENTION, PESTICIDES AND
TOXIC SUBSTANCES

May 7, 1998

MEMORANDUM

SUBJECT: The HED Chapter of the Reregistration Eligibility Decision Document (RED) for Azinphos methyl; PC CODE 058001, List A Case No. 0235. DP Barcode: D233730.

FROM: Catherine Eiden, Chemist
Risk Characterization and Analysis Branch
Health Effects Division (7509C)

THRU: Steve Knizner, Branch Senior Scientist
Risk Characterization and Analysis Branch
Health Effects Division (7509C)

TO: Tom Moriarity, Special Review Manager
Special Review Branch
Special Review and Reregistration Division (7508W)

Please find attached the Human Health Assessment for the Azinphos methyl Reregistration Eligibility Decision Document (RED) Case No. 0235. This chapter includes the Toxicology chapter from Tim McMahon (ATTACHMENT I), the Product and Residue Chemistry chapter from Felicia Fort (ATTACHMENT II), the Occupational/Residential Exposure Assessment from Jack Arthur (ATTACHMENT III), and the Dietary Risk Analysis from Brian Steinwand (ATTACHMENT IV).

Required Data:

<u>Residue Chemistry</u>

Residue field trial data are required for cauliflower, walnuts, and cotton gin byproducts.

Labeling Requirements:

Labels bearing uses on grapes should be revised to clarify specific use rates that correspond to

the PHIs listed. The labels bearing use directions for filberts and pecans should specify a 45-day PHI; the reference to shuck-split for pecans should be deleted from the labels. The FlC labels should be revised to specify a maximum seasonal rate for cotton. (See Table A - Food/Feed Use Patterns Subject to Reregistration).

Attachments
cc: N. McCarroll, F. Fort, J. Arthur, B. Steinwand (DRES), C. Eiden, S. Knizner,
RCAB File, List B File, Subject File
RDI: CAE 05/08/98, SAK 05/08/98
CM#2: Room 718O: 305-7887: 7509C

I. EXECUTIVE SUMMARY

The Health Effects Division (HED) has evaluated the azinphos methyl data base and determined that the data are adequate to support reregistration. The toxicological data base is adequate to support reregistration. Residue chemistry requirements are substantially complete pending residue field trial data for cauliflower, walnuts and cotton gin byproducts. Occupational post-application exposure studies are being conducted by the registrant. Additional data requirements are dependent on the outcome of these studies.

Azinphos methyl is an organophosphate pesticide. The toxicology data base provides overwhelming evidence confirming that azinphos methyl has anticholinesterase activity in various species including dogs, rabbits, rats, mice and hens. In acute toxicity studies, azinphos methyl exhibits low to high toxicity depending on the route of administration and the species used. It is acutely toxic at relatively low oral or dermal doses when tested in rats, but was found to be less toxic in rabbits exposed dermally because it is detoxified in the rabbit's skin. Toxic signs observed in animals treated acutely with azinphos methyl are consistent with cholinesterase inhibition and are typical of the acute toxic signs induced by other organophosphate chemicals. They include: tremors, convulsions salivation, and dyspnea (labored breathing). Inhibition of plasma, erythrocyte and brain cholinesterase (ChE) activity is directly dose-related and occurs by all routes of exposure and following exposure for various durations. There is no indication of an increased sensitivity of the offspring of rats or rabbits after pre-natal and/or postnatal exposure to azinphos methyl. In all studies examined, maternal or parental no observed effect levels (NOELs) are lower or equivalent to the offspring NOELs. Azinphos methyl has been classified in **"Group E"** (i.e., the chemical is characterized as **"Not Likely"** to be carcinogenic in humans via relevant routes of exposure) because there is no evidence that azinphos methyl altered the spontaneous tumor profile in rats or mice. Based on metabolism studies in rats, azinphos methyl is degraded and/or eliminated within 72 hours postdosing and does not accumulate in tissues. The metabolism of azinphos methyl in rats proceeds largely through the action of glutathione-S-transferase and mixed function oxidases. There were no major sex- or dose-related differences in the disposition or metabolism of azinphos methyl.

Five exposure and risk assessments were conducted for azinphos methyl: acute dietary, chronic dietary, non-dietary short- and intermediate-term dermal, and non-dietary inhalation (for any time period). The acute and chronic dietary assessments capture exposure estimates for the general public. The latter three assessments are for occupational exposures. The five different assessments were conducted separately based on different hazard (toxicological) endpoints.

For the acute dietary exposure and risk assessment, the toxic endpoint selected was the lowest observed effect level (LOEL) based on plasma, erythrocyte, and brain cholinesterase inhibition from an acute neurotoxicity study in rats (1.0 mg/kg/day). The LOEL was selected because the no observed effect level (NOEL) was not established in the study. The uncertainty factor used in this assessment was 300 and resulted in an acute RfD of 0.003 mg/kg/day. For the chronic

dietary exposure and risk assessment, the toxic endpoint selected was the NOEL of 0.149 mg/kg/day based on erythrocyte cholinesterase inhibition at a LOEL of 0.688 mg/kg/day from a 1-year chronic toxicity study in dogs (0.149 mg/kg/day). The uncertainty factor used in this assessment was 100 and resulted in a chronic RfD of 0.0015 mg/kg/day. For the short- and intermediate-term dermal exposure and risk assessments, the toxic endpoints selected were based on erythrocyte cholinesterase inhibition from a dermal absorption toxicity rats (NOEL = mg/kg/day and LOEL = 5.6 mg/kg/day) and the aforementioned 1-year chronic feeding study in dogs, respectively. A dermal absorption factor of 41.7% was applied to the NOEL selected for the intermediate-term assessment, resulting in an equivalent dermal dose of 0.36 mg/kg/day. For inhalation exposure (any time period), the endpoint selected was a NOEL (0.0012 mg/L) based on inhibition of plasma and erythrocyte cholinesterase at a LOEL of 0.0047 mg/L from a 90-day inhalation toxicity study. An uncertainty factor of 100 was used for all of the occupational exposure assessments.

The main route of exposure to azinphos methyl for the general public (non-occupational exposures) is through food. Acute dietary risk estimates associated with the consumption of azinphos methyl residues representing the high-end of exposure in food (tolerance level residues without the use of percent crop-treated information) exceed HED's level of concern for all populations. The highest risk estimates are for infants and children. According to the consumption data currently used in this assessment (USDA '77-'78), apples, peaches, pears, tomatoes, and milk are among the ten most highly consumed commodities by children and infants. The tolerances for the four fruit commodities are 2 ppm; for milk, the tolerance is 0.04 ppm (40 CFR 180.154). These five commodities are likely to be driving the risk for these most highly exposed subpopulations, as well as, much of the risk for the other subpopulations. Because acute dietary risk estimates from exposure to azinphos methyl in food alone exceed HED's level of concern, any exposure through drinking water would only contribute more to an already unacceptable risk estimate from food, and result in an unacceptable aggregate acute dietary risk estimate. Probabilistic acute dietary exposure and risk assessments were reviewed and deemed inadequate for regulatory purposes because monitoring data from composited samples were used to establish the distribution of azinphos methyl residues in the diet, and the consumption data used in this analysis were not provided for review.

Aggregate chronic dietary risk estimates associated with the consumption of azinphos methyl residues in food and water do not exceed HED's level of concern. Although monitoring data on azinphos methyl residues in drinking water were not available for this assessment, conservative estimates of exposure to azinphos methyl in drinking water (tier 1) indicate that relative to exposure in food, residues in drinking water would not contribute significantly to chronic aggregate risk. Because azinphos methyl does not have any registered residential uses, exposure to the chemical through this route was not considered in the aggregate risk assessment.

Occupational exposure to azinphos methyl residues can occur for pesticide handlers, mixers, loaders, applicators, and post-application workers during harvesting activities. For occupational exposures of a short duration (1 to 7 days), there are only 3 exposure scenarios for which risk

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estimates did not exceed HED's level of concern after maximum mitigation measures have been applied. For exposures of an intermediate duration (7 days to several months), there are only 2 exposure scenarios for which risk estimates did not exceed HED's level of concern after maximum mitigation measures have been applied. Long-term occupational exposures are not expected to occur for the registered uses of azinphos methyl. For post-application exposure, only two uses resulted in risk estimates that do not exceed HED's level of concern. Azinphos methyl ranked sixth among 28 pesticides selected on the basis of a high incidence of pesticide poisonings, relatively high toxicity, and high usage. Azinphos methyl ranked fifth on percentage of occupational poisoning cases requiring hospitalization. In cases where use of azinphos methyl is considered the primary cause of fieldworker poinsoning, the incidences of poisoning are directly related to the amount of azinphos methyl applied.

Risk Characterization

Dietary Risk (Food):

The risk estimate for acute dietary exposure greatly exceeds HED's levels of concern for existing and proposed uses. Presently, tolerance level residues on registered commodities result in margins of exposure (MOEs) ranging from 3 for children (1-6 years old) and infants (<1 year) to 17 for males 13+ years of age. The acute dietary risk estimate expressed as a MOE for the general U.S. population is 7. An acceptable MOE for exposure to this chemical relative to the acute dietary toxicity endpoint is > 300. The acute dietary exposure analysis estimates the distribution of single-day exposures for the overall U.S. population and certain subgroups. The analysis evaluates individual food consumption as reported by respondents in the USDA 1977-78 Nationwide Food Consumption Survey (NFCS) and accumulates exposure to the chemical for each commodity. Each analysis assumes uniform distribution of azinphos methyl in the commodity supply. This analysis is highly conservative in that it assumes tolerance level residues and 100% crop-treated for all commodities with azinphos methyl tolerances. The LOEL used to calculate the acute dietary risk (1 mg/kg/day) is based on the results of an acute neurotoxicity study. A LOEL was used because a NOEL was not established in the acute neurotoxicity study.

An acute dietary analysis using probabilistic (Monte Carlo) techniques was submitted to the Agency, reviewed and found to be inadequate. Because the analysis is inadequate, based on the use of inappropriate residue data, and because the consumption data used in the analysis were not provided and therefore not available for review, the analysis cannot be used for regulatory purposes. Even if the residue data that were used had been considered appropriate, and the consumption data had been provided for review, all MOEs calculated based on the analysis were well below the acceptable MOE of 300.

The risk estimate for chronic dietary exposure from the registered uses of azinphos methyl, does not exceed HED's level of concern. The chronic dietary exposure analysis estimates that existing uses result in an anticipated residue concentration (ARC) which represents 13% of the

RfD for the U.S. general population. The subgroup with the highest exposure, Non-Nursing Infants (<1 year old), occupies 54% of the RfD, and the subgroup Children (1-6 years old) occupies 33% of the RfD. This highly refined analysis used percent crop-treated data and anticipated residues based on field trials and FDA monitoring data.

Dietary Risk (Drinking Water):

Currently, HED uses drinking water levels of concern (DWLOCs) as a surrogate to capture risk associated with exposure to pesticides in drinking water. A DWLOC is the concentration of a pesticide in drinking water that would be acceptable as an upper limit in light of total aggregate exposure to that pesticide from food, water, and residential uses (if any). A DWLOC may vary with drinking water consumption patterns and body weights for specific subpopulations.

Because the acute exposure to residues of azinphos methyl from food alone exceeds HED's level of concern, no exposure to azinphos methyl in drinking water is acceptable. Effectively, until the exposure to azinphos methyl from food is reduced, the DWLOC for acute exposure to azinphos methyl in drinking water is zero.

Conservative model estimates of the average concentration of azinphos methyl in ground water indicate that **chronic exposure** through drinking water will be minimal. Estimated average concentrations in ground water (0.325 ppb) do not exceed drinking water levels of concern (DWLOCs) for chronic exposure for the general U.S. population, females (13+), children (1-6 years old), and infants, non-nursing (<1 year). The DWLOCs for chronic exposure for these subpopulations are: 45, 39, 10, and 7 ppb, respectively. Based on the concentration estimates of azinphos methyl in ground water used in this analysis, it appears that the chronic exposure from azinphos methyl in the diet and in drinking water from registered uses of azinphos methyl, is not of concern. An estimate of the average concentration of azinphos methyl in surface water for comparison against the above DWLOC values was not available at the time of this writing; however, based on its physical-chemical properties, residues of azinphos methyl are not expected to persist in either ground- or surface-water-sourced drinking water and are therefore, not expected to significantly impact the chronic aggregate risk assessment.

Non-Occupational (Residential) Risk:

There are no registered residential uses of azinphos methyl. HED does not expect any residential exposure scenarios to exist for registered uses of azinphos methyl. Therefore, no exposure or risk calculations for residential uses are warranted.

Occupational Risk:

Mixer/ Loader/Applicator Exposure - **When inhalation and dermal risks are aggregated, 11 out of 14 major occupational exposure scenarios produce unacceptable MOEs (i.e., <100). Risks remain unacceptable despite additional protective clothing/equipment for all**

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scenarios. The use of engineering controls results in acceptable risk estimates for 3 out of 14 mixer/loader/applicator exposure scenarios: (1c) mixing/loading liquids for airblast application, (6) applying sprays with an airblast sprayer (1 lb. ai/acre), (10) flagging liquid sprays for aerial application (0.75 lb. ai/acre).

No chemical specific exposure data were available for the exposure assessments for mixer/loader/applicators. Short-term and intermediate-term dermal and inhalation exposure assessments were made using Pesticide Handlers Exposure Database (PHED) Version 1.1 surrogate data. **HED has concerns regarding occupational exposures and risks** for a number of exposure scenarios during application for **pesticide handlers**. The estimated risks consider baseline protection (long pants and a long-sleeved shirt, no gloves, and an open cab or tractor), additional personal protective equipment (PPE, which includes a double layer of clothing and gloves), and engineering controls (closed application and mixing systems, and water soluble packets).

For **dermal short-term and intermediate-term** exposures using baseline protection, risk estimates expressed as MOEs are less than 100 for all of the 14 major applicator/handler scenarios. Risk estimates remain unacceptable despite the use of additional PPE; all MOEs are less than 100 for all 14 of the major scenarios. Using engineering controls, short-term MOEs are greater than 100 for 3 out of 10 major scenarios for which engineering controls were applicable; but, only two of these have acceptable MOEs for intermediate-term exposures. **This still leaves 11 occupational exposure scenarios for which MOEs are less than 100 and exceed HED's level of concern despite maximum mitigation measures.** These 3 scenarios are the same as those listed above as having acceptable MOEs after aggregating dermal and inhalation risk estimates.

For **inhalation exposures (any time period)** using baseline protection, risk estimates expressed as MOEs are greater than 100 for 9 out of 14 major applicator/handler scenarios. Risk estimates improved using additional PPE; MOEs are greater than 100 for 10 out of 14 major scenarios. Using engineering controls results in MOEs that are greater than 100 for 13 of the major scenarios for which engineering controls were applicable. **However, this leaves 1 occupational exposure scenario for which the MOE is less than 100 and exceeds HED's level of concern despite maximum mitigation measures.** That is scenario (8) mixing/loading applying liquids with a high pressure handwand as in green house uses at 1000 gallons.

Post-Applicator Exposure - **HED has serious concern for reentry workers because of post-application exposure and risk estimates associated with all uses of azinphos methyl (except its use in the WP50 formulation on cotton and tomatoes at 1.5 lbs ai/acre). Risks expressed as MOEs associated with harvesting and tending activities for all other analyzed crops were well below 100.**

Mitigation measures and labeling requirements to address these concerns have been deferred pending a meeting/decision with SRRD on handler and post-application risk

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mitigation.

Chemical-specific studies are available for estimating post-application worker exposure. Post-applicator risk estimates from the use of azinphos methyl WP50 formulation on **tomatoes and cotton** at the maximum labelled rate (1.5 lbs. a.i./A) result in acceptable MOEs (i.e., >100) at existing 2-day and 1-day restricted entry intervals (REIs), respectively. Post-applicator risks for uses of the 2S formulation of azinphos methyl on **potatoes** at the actual maximum application rate of 0.75 lbs. a.i./A and at the existing 2-day REI are unacceptable. Similarly, uses of the WP50 formulation on potatoes at 0.75 lbs. a.i./A, also result in unacceptable MOEs at the existing 2-day REI. For both use patterns, an 8-day REI is required to achieve acceptable MOEs. Based on **apple** data, post-applicator risks for orchard crops were calculated for harvesting, propping, and thinning activities. MOEs calculated for propper activities are unacceptable, i.e., less than 100, for all application rates > 1.0 lbs. a.i./A. MOEs are unacceptable for all harvesting and thinning activities regardless of the application rates and REIs. MOE calculations are unacceptable for all post-applicator risks for **citrus, grape, and berry** uses of azinphos methyl at all labelled use rates and existing REIs.

Sensitivity to Infants and Children:

The application of an additional uncertainty factor to ensure the protection of infants and children from exposure to azinphos methyl, as required by FQPA, will be determined by the FQPA Safety Factor Assessment Review Committee.

The Hazard Identification Assessment Review Committee (HIARC), **based solely on the hazard assessment, recommends** to the FQPA Safety Committee, that the additional **10x** factor **should be removed** because:

(i) Developmental toxicity studies showed no increased sensitivity in fetuses as compared to maternal animals following *in utero* exposure in rats and rabbits.

(ii) Both a one- and a two-generation reproductive toxicity study in rats showed no increased susceptibility in pups when compared to adults.

(iii) There was no evidence of abnormalities in the development of the fetal nervous system in the pre/postnatal studies. Neither brain weight nor histopathology (nonperfused) of the nervous system was affected in the subchronic and chronic toxicity studies.

(iv) The toxicology data base is complete and there are no data gaps. There is no evidence to require a developmental neurotoxicity study.

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Aggregate Exposure/Risk:

Acute Aggregate Risk:
The aggregate acute dietary risk includes exposures to azinphos methyl residues in food and water. However, HED notes that exposure to azinphos methyl residues in food alone exceed HED's levels of concern for acute dietary risk. At this point in time and until the exposure to azinphos methyl in the diet is reduced or a more refined acceptable risk assessment is provided, any additional exposure to azinphos methyl through drinking water would only cause acute risk estimates to further exceed HED's level of concern. In effect, the drinking water level of concern (DWLOC) for acute effects of azinphos methyl is zero and a conservative estimate (tier 1) of the concentration of azinphos methyl in ground water is 0.325 ppb. This is in excess of the DWLOC (zero) for acute aggregate exposure to azinphos methyl.

Chronic Aggregate Risk:
The chronic aggregate risk assessment for azinphos methyl will include risk estimates associated with dietary exposure through food and water, only, because azinphos methyl has no registered residential uses. Anticipated residues and percent crop-treated data for commodities with published tolerances result in an exposure to azinphos methyl through food which represents 13% of the RfD for the U.S. general population. The most highly exposed subgroup, Non-Nursing Infants (<1 year old), occupies 54% of the RfD and Children (1-6 years old) occupies 33% of the RfD.

HED has calculated drinking water levels of concern (DWLOCs) for chronic exposure to azinphos methyl in drinking water for the following four subpopulations: the general U.S. population/Hispanics (45 ppb), females, 13-19 (39 ppb), children, 1 to 6 years old (10 ppb), and non-nursing infants, <1 year old (7 ppb). These subpopulations were selected because they contain the individuals believed to be those most highly exposed subpopulations representing males, females, children, and infants, respectively. A conservative estimate (tier 1) of average concentrations of azinphos methyl in ground water is 0.325 ppb. The estimated average concentration of azinphos methyl in ground water is less than HED's levels of concern. Concentration estimates of azinphos methyl in surface water were not available for comparison against DWLOC values.

Therefore, based on the ground water estimate only, HED concludes with reasonable certainty that residues of azinphos methyl in drinking water (when considered along with exposure from food) would not result in an unacceptable chronic aggregate human health risk estimate at this time. HED bases this determination on a comparison of estimated concentrations of azinphos methyl in ground water to back-calculated "levels of concern" for azinphos methyl in drinking water. The estimate of azinphos methyl in ground water is derived from a water quality model that uses conservative assumptions (health-protective) regarding the pesticide transport from the point of application to ground water. Because HED considers the aggregate risk resulting from multiple exposure pathways associated with a pesticide's uses, levels of concern in drinking water may vary as those uses change. If new uses are added in the future, HED will reassess the

potential impacts of azinphos methyl on drinking water as a part of the aggregate risk assessment process.

Once concentration estimates of azinphos methyl in surface water become available, they should be compared to the aforementioned DWLOC values to determine if the estimates exceed the DWLOC values.

In conclusion, according to the exposure and risk assessments described here, currently registered uses of azinphos methyl result in dietary risk estimates for acute exposures through food alone that exceed HED's level of concern. Any additional acute exposure through drinking water would worsen an already unacceptable risk estimate. Dietary risk estimates for chronic exposures through food and water do not exceed HED's level of concern. Occupational risk estimates associated with application, mixing, loading and reentry activities exceed HED's of concern for a majority of exposure scenarios. Documented incident data on reported cases of azinphos methyl poisonings bolster the results of these occupational exposure and risk estimates.

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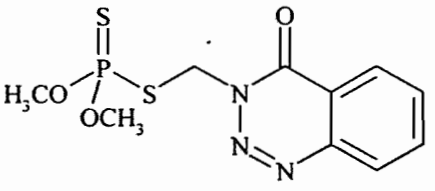
II. SCIENCE ASSESSMENT

A. PHYSICAL AND CHEMICAL PROPERTIES ASSESSMENT

1. Description of Chemical

Azinphos methyl [O,O-dimethyl-S-((4-oxo-1,2,3-benzotriazin-3(4H)-yl)methyl)phosphorodithioate] is an insecticide used for control of pests on various fruits, melons, nuts, vegetables, field crops, ornamentals, and shade trees.



Empirical Formula: $C_{10}H_{12}N_3O_3PS_2$
Molecular Weight: 317.1
CAS Registry No.: 86-50-0
Shaughnessy No.: 058001

2. Identification of Active Ingredients

Pure azinphos methyl is a colorless to white odorless crystalline solid with a melting point of 72-74° C. Technical azinphos methyl is a cream to yellow-brown granular solid with a melting point of 67-70° C. Azinphos methyl is readily soluble in most organic solvents (acetone, toluene, chloroform, acetonitrile, benzene, xylene, carbon tetrachloride, and chlorobenzene), slightly soluble in methanol, ethanol, and 1-propanol, and nearly insoluble in water (28 ppm at 20° C). Azinphos methyl is subject to hydrolysis and decomposes with gas evolution at elevated temperatures.

3. Manufacturing Use Products

A search of the Reference Files System (REFS) conducted 12/10/96 identified five azinphos methyl manufacturing-use products (MPs) registered under Shaughnessy No. 058001. The registered azinphos methyl MPs are listed in Table 1; only these products are subject to a reregistration eligibility decision.

Table 1. Registered azinphos methyl manufacturing-use products.

Formulation	EPA Reg. No.	Registrant
94% T	10163-95	Gowan Company
85% T	11678-4	Makhteshim Chemical Works, Ltd.
85% FI	11678-53	
85% T [1]	3125-108	Bayer Corporation [2]
85% FI	3125-425	

[1] REFS currently identifies this product as a formulation intermediate; however, it has been correctly identified in previous Agency reviews as a technical product.

[2] Formerly Mobay Corporation.

4. Regulatory Background

The Azinphos methyl Reregistration Standard dated 4/4/86 and Guidance Document dated 9/11/86 required additional generic and product-specific product chemistry data for the registered MPs. In response, updated data were submitted for the Makhteshim and Bayer 85% Ts. The Azinphos methyl Reregistration Standard Update dated 1/8/91 (update) reviewed submitted data and summarized the product chemistry database. The update required additional data concerning GLNs 62-1, 62-2, 62-3, and 63-13 (OPPTS 830.1700, 830.1750, 830.1800, and 830.6313) for the Makhteshim 85% T (EPA Reg. No. 11678-4); and additional data concerning GLNs 62-1 and 62-2 (OPPTS 830.1700 and 830.1750) for the Bayer 85% T (EPA Reg. No. 3125-108). These data with the exception of data for 830.6313 were submitted and reviewed (MRIDs 41873601, 41521401, 44121301, 44121302, and 44121303). All product chemistry data were required for the Gowan 94% T (EPA Reg. No. 10163-95).

The Makhteshim and Bayer 85% FIs (EPA Reg. Nos. 3125-425 and 11678-53) were not registered until after the Update was issued, and data pertaining to reregistration have not been submitted for these products. HED has determined, based on comparison of the CSFs, that the composition of the Makhteshim 85% FI is identical to the composition of the Makhteshim 85% T; thus, the product should be identified as a technical product, and data requirements for the 85% FI will be fulfilled by data submitted for the 85% T. Examination of the CSF for the Bayer 85% FI suggests that this product should be identified as a technical product.

The current status of the product chemistry data requirements for the azinphos methyl products is presented in the data summary tables attached in Appendix I. Refer to these tables for a listing of the outstanding product chemistry data requirements.

5. Conclusions

All pertinent data requirements are not satisfied for the azinphos methyl MPs. Additional data

are required for the Makhteshim 85% T and 85% FI (OPPTS 830.1750, 830.6313, and 830.7050) and for the Bayer 85% T (OPPTS 830.1750 and 830.7050). All product chemistry data remain outstanding for the Gowan 94% T and the Bayer 85% FI. Provided that the registrants submit the data required in the attached data summary tables for the 94% T, 85% Ts, and 85% FIs, and either certify that the suppliers of beginning materials and the manufacturing processes for the azinphos methyl MPs have not changed since the last comprehensive product chemistry review or submit complete updated product chemistry data packages, HED has no objections to the reregistration of azinphos methyl with respect to product chemistry data requirements.

B. HUMAN HEALTH RISK ASSESSMENT

1. Hazard Identification

On September 16, 1993, the Health Effect's Division's RfD/Peer Review Committee established a Reference Dose of 0.00149 mg/kg/day based on a NOEL of 0.149 mg/kg/day established in a chronic toxicity study in dogs and an Uncertainty Factor of 100 for inter-species extrapolation and intra-species variation (*Memorandum:* G. Ghali, HED to L. Rossi, RD, Dated 12/07/93).

On February 27, 1997, the Health Effects Division's Toxicology Endpoint Selection (TES) Committee selected the doses and endpoints for acute dietary as well as occupational and residential exposure risk assessments. The TES Committee did not address the FQPA requirement because of the pending Agency's assessment of organophosphates and their neurotoxic potential (TES Document, 2/27/97).

On December 10, 1997, the Health Effects Division's Hazard Identification Assessment Review Committee (HIARC) met to re-evaluate the Uncertainty Factors and MOEs for dietary as well as non-dietary risk assessments. This re-evaluation was necessary to ensure consistency with the other organophosphate chemicals that were recently reviewed by the HIARC to address the enhanced sensitivity of infants and children as required by the FQPA. At the meeting, the Committee evaluated the toxicology data base and determined that a reexamination of the subchronic neurotoxicity study in rats, the neuropathology findings from the chronic feeding/carcinogenicity study in rats and the neuropathology data from the one-year dog study should be performed. In addition, a search of the open literature was recommended. These actions were requested to determine whether a developmental neurotoxicity study with azinphos methyl is needed.

On March 19, 1998, the Health Effects Division's Hazard Identification Assessment Review committee evaluated the toxicology data base of azinphos methyl to re-assess the Reference Dose and determine the Uncertainty Factor and/or Margins of Exposure for dietary and non-dietary exposure risk assessments. The Committee also addressed the potential sensitivity of infants and children as required by the Food Quality Protection Act (FQPA) of 1996. The application of the FQPA safety factor for the protection of infants and children as required by FQPA, will be determined by the HED FQPA (10X) Committee.

The conclusions of the March 19, 1998 HIARC meeting, which included a determination of the Uncertainty Factors and/or the Margins of Exposure for exposure scenarios (acute and chronic dietary as well as occupational/residential risk assessments), recommendations made for aggregate exposure risk assessments and the determination of the potential susceptibility to infants and children, are presented in the April 20, 1998 report of the HIARC. The 4/20/98 HIARC report supersedes previous RfD and TES Committee reports. All toxicity endpoints used in this document for the risk characterization are from the 4/20/98 HIARC report.

a. Toxicology Database

The toxicological data base on Azinphos-methyl is adequate to support reregistration eligibility. A profile of the toxicological database is given in table 2.

Table 2. Toxicology Profile

Guideline	Study Type	MRID#	Required	Satisfied
81-1	Acute oral (rats)	00155002	yes	yes
81-2	Acute dermal (rabbit)	40280102	yes	yes
81-3	Acute inhalation (rats)	40280103	yes	yes
81-4	Primary eye irritation (rabbit)	43337501	yes	yes
81-5	Primary dermal irritation (rabbit)	43337101	yes	yes
81-6	Dermal sensitization (guinea pig)	41064401	yes	yes
81-8	Acute neurotoxicity (rats)	43360301	yes	yes
82-2	21-day dermal (rabbit)	00145715	yes	yes
82-4	Subchronic inhalation (rats)	00155011	no	yes
82-7	Subchronic oral (rats)	43826601	yes	yes
82-7	Subchronic oral (dogs)	00156424	yes	yes
83-1(b)	Chronic oral - 1 year (dogs)	41804801	yes	yes
83-1(b)	Chronic oral - 2 years (dogs)	41804801	yes	yes
83-1(a) & 83-2(a)	Chronic/carcinogenicity oral - 2 years (rats)	41119901	yes	yes
83-2(b)	Carcinogenicity - 2 years (mice)	00147895	yes	yes
83-3(a)	Developmental- oral teratology (rats)	40464801	yes	yes
83-3(b)	Developmental - oral teratology (rabbit)	40713901 & 41240001	yes	yes
83-4	Reproductive - 2 generation (rats)	40332601	yes	yes

Table 2. Toxicology Profile				
Guideline	Study Type	MRID#	Required	Satisfied
83-4	Reproductive - 1 generation (rats)	41916801	no	suuplemental
84-2	Mutagenicity	40280107 40301301 40367811 00155017	yes	yes
85-1	Metabolism	40836501	yes	yes
85-3	Dermal absorption	42452701		yes

b. Acute Toxicity/Skin Sensitization

The table below summarizes the results, endpoints, and toxicity categories for the acute toxicity studies.

Acute Toxicity of Azinphos methyl				
Guideline No.	Study Type	MRID #(S).	Results	Toxicity Category
81-1	Acute Oral (Rat)	00155002	LD_{50} =4.6 mg/kg♂ 4.4 mg/kg♀	I
81-2	Acute Dermal (Rabbit)	40280102	LD_{50} = >2000 mg/kg	III
81-2	Acute Dermal (Rat)	00155003	LD_{50} =200-250 mg/kg♂ 155 mg/kg♀	I
81-3	Acute Inhalation (Rat)	40280103	LC_{50} = >0.21mg/L	II
81-4	Primary Eye Irritation (Rabbit)	43337501	No ocular effects at 48 hrs.	III
81-5	Primary Skin Irritation (Rabbit)	43337101	Non-irritating	IV
81-6	Dermal Sensitization (Guinea Pig)	41064401	Sensitizer	N/A

c. Subchronic Toxicity

i. <u>21- Day Dermal Toxicity in Rabbits (82-2)</u>

In a 21-day dermal toxicity study in rabbits, the following effects were observed: decreased body

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weight gain (40-70%) in females; decreased (10%) red cell count in males; decreased (24-38%) erythrocyte cholinesterase activity in both sexes on day 10 and 15 of treatment; increased spleen and kidney weight in males; increased incidence of inflammatory changes in kidneys of males (severity not stated) at the 20 mg/kg/day dose. **These endpoints from this study (MRID #00145715) were selected to be used for short-term and intermediate-term dermal occupational risk assessments**. Male and female New Zealand White rabbits (6/sex/dose) received repeated dermal applications of azinphos-methyl technical (94.1% a.i.), at doses of 0, 2, or 20 mg/kg, 6 hours/day, 5 days/week, for a total of 15 applications over a three week period. . Measurement of plasma and brain cholinesterase at the 2 and 20 mg/kg/day dose levels showed no effect of treatment in this study. Based on the results of this study, **the Systemic NOEL in both sexes was 2 mg/kg/day and the LOEL was 20 mg/kg/day,** based on decreased erythrocyte cholinesterase activity; increased spleen and kidney weights [males]; and decreased body weight gain [females]). The Dermal NOEL was ≥ 20 mg/kg (highest dose tested; a LOEL was not determined).

ii. Subchronic Neurotoxicity (82-5)

In a subchronic neurotoxicity study in Fischer 344 rats (18/sex/group) (MRID 43826601; Doc. No. 011898), 96.4% azinphos methyl was administered at dietary levels of 15, 45, or 120 ppm in males (0.91, 2.81, or 7.87 mg/kg/day) and at 15, 45, or 90 ppm in females (1.05, 3.23, or 6.99 mg/kg/day). **An extrapolated (benchmark) systemic NOEL was calculated to be 5 ppm (approx. 0.3 mg/kg/day).** In addition, plasma and brain cholinesterase inhibition were also observed at the mid- and high-dose, and treatment-related cholinergic signs of toxicity (increased reactivity, uncoordinated gait, and/or tremors) were noted at these dose levels. At the high-dose (90/120 ppm in M/F), decreased motor activity, locomotor activity, and forelimb grip strength were also observed. The neuropathology findings were equivocal, but suggested treatment related effects in the brain (axonal swelling of minimum severity in males) and spinal cord (nerve fiber degeneration of the cauda equina and the cervical and/or thoracic cord in both sexes) at the high dose (120 ppm; 7.87/6.99 mg/kg/day in M/F). In females, it was suggested that cervical spinal cord findings were correlated to decreased forelimb grip strength noted at all dose levels. Since the histopathology tables were not included in the DER, the Committee recommended that the incidence and severity of the equivocal neuropathological findings be reassessed.

iii. Subchronic Oral Toxicity in Rats (82-7)

As part of a response to a Data Call-In Notice of June 16, 1993, the registrant submitted a subchronic neurotoxicity study conducted with the technical grade (92.2%) of azinphos methyl in male and female Fischer 344 rats. In this study (MRID 43826601), groups of 18 male and 18 female rats were administered the technical grade of azinphos-methyl in the diet for 13 weeks at nominal doses of 0, 15, 45, or 120 ppm for males (0, 0.91, 2.81, and 7.87 mg/kg/day mean intake) and 0, 15, 45, or 90 ppm for females (0, 1.05, 3.23, and 6.99 mg/kg/day mean intake). Twelve rats per sex per dose were used for neurobehavioral evaluation, with half used for

neuropathology. The remaining six per sex per dose were used for cholinesterase determination. A statistically significant (>20%) inhibition of red cell cholinesterase was observed at all dose levels tested in this study, as was a statistically significant inhibition (>20%) of plasma and brain cholinesterase at the mid and high dose. Decreased forelimb grip strength, motor activity, and locomotor activity were observed in both sexes at the high dose, but did not correlate definitively with any pathology of the nervous system. Based on the data in this study, the **systemic LOEL = 15 ppm** (~ 1.0 mg/kg/day) for male and female rats, based on a statistically significant (>20%) inhibition of red cell cholinesterase. The **systemic NOEL was < 15 ppm and estimated to be 5 ppm (0.3 mg/kg/day)** for male and female rats, based on extrapolation of cholinesterase inhibition data. Although significant signs of cholinergic toxicity were observed in this study, there was no definitive evidence of a neurotoxic effect for azinphos-methyl in this study (MRID # 43826601).

iv. Subchronic Oral Toxicity in Dogs (82-7)

In a 19-week toxicity study in dogs, dietary levels of 0, 20, 50, 100, 200, or 400 ppm were administered to 1 dog/sex/dose. Cholinesterase inhibition (whole blood) was observed at all dose levels and was dose related (35% at 20 ppm to 80% at 400 ppm). These reductions in cholinesterase activity are considered statistically significant. **The LOEL was 20ppm (lowest dose tested; a NOEL was not determined).** (MRID # 00156424).

v. Subchronic Inhalation in Rats (82-4)

The endpoint from this study (MRID 00155011) was selected to be used for short-term and intermediate-term inhalation occupational risk assessments. In a subchronic inhalation toxicity study, male and female Wistar rats were exposed to azinphos-methyl aerosol at concentrations of 0.195, 1.24, or 4.72 mg/m^3 (equivalent to 0.0002, 0.0012, or 0.0047 mg/L, respectively) for 90 days, 6 hr/day, 5 days/week. Plasma and red blood cell cholinesterase inhibition (30-40%) were observed in males and females at 0.0047 mg/L. **The NOEL was determined to be 0.0012 mg/L, and the LOEL was determined to be 0.0047 mg/L.**

d. Chronic Toxicity and Carcinogenicity

i. Oral Toxicity Study in Dogs - One Year (83-1(b))

The endpoint from this study (MRID # 41804801) was selected to be used for determining the chronic RfD and for chronic occupational risk assessments. In a 52-week toxicity study, azinphos-methyl technical (91.9%) was administered to male and female beagle dogs (4/sex/group) at dose levels of 0, 5, 25, or 125 ppm (0.149, 0.688, or 3.844 mg/kg for males; 0.157, 0.775, or 4.333 mg/kg for females). Both sexes of dogs at 125 ppm dose level exhibited decreases in plasma cholinesterase (52-58%) erythrocyte cholinesterase (66-92%), and brain cholinesterase (20-27%) beginning at week 4 of treatment and continuing until week 52. At the 125 ppm dose level, cytochrome P-450 N- and O-demethylase activity was increased 39% in

male dogs. Serum albumin and A/G (adenine to guanine) ratio was reduced by 13% and 20% respectively in male dogs after 13 weeks of exposure. Mucoid diarrhea and occasional emesis were also observed at this dose level in male and female dogs. At the 25 ppm dose level, erythrocyte cholinesterase activity was decreased by 27-40% below control in male dogs, and by 35-43% in female dogs. Increased incidence of mucoid diarrhea was also observed. The **NOEL was 0.149 mg/kg/day for males and 0.157 mg/kg/day for females**, and the **LOEL was 0.688 mg/kg/day for males and 0.775 mg/kg/day for females**, based on the above noted significant decreases in erythrocyte cholinesterase activity in both sexes as well as increased incidence of diarrhea in males.

ii. Oral Toxicity in Dogs - Two Years (83-1(b))

In a two-year toxicity study in dogs, four groups of male and female Cocker Spaniel dogs (4/sex/dose) received azinphos-methyl technical (purity not stated) in the diet at 0, 5, 20, or 50 ppm. After 36 weeks on test diets, the 20 ppm and 50 ppm dose groups were given 50 ppm and 100 ppm respectively, based on the lack of toxic symptoms in these dose groups. After 57 weeks on test diets, the 100 ppm dose group was increased to 150 ppm and again to 300 ppm after 84 weeks on test diets. Plasma and erythrocyte cholinesterase activity were measured weekly 5 weeks prior to treatment and then weekly starting at 4 weeks after start of treatment. After the dose was increased to 300 ppm, clinical signs of toxicity (fine muscle tremors of the hind limb, lethargy, weakness) were observed, as were decreased food consumption and body weight. Inhibition of plasma cholinesterase activity ranged 25 to 50% over the 50 to 300 ppm dosing range. Inhibition of erythrocyte cholinesterase ranged from 35 to 80% over the 20 to 100 ppm dosing range. Cholinesterase inhibition generally increased with increasing dose. These reductions in cholinesterase activity are considered significant. **Based on the time weighted average, the NOEL was 5 ppm (0.125 mg/kg/day) and the LOEL was 39.2 ppm (0.98 mg/kg/day), based on inhibition of erythrocyte cholinesterase.** (MRID # 41804801).

iii. Oral Toxicity in Rats - Two Years (83-1(a)/83-2(a))

In a combined chronic toxicity and carcinogenicity study in Wistar rats, technical azinphos-methyl (87.2% a.i.) was administered in the diet at dose levels of 0, 5, 15, or 45 ppm (0.25, 0.75, or 2.33 mg/kg/day in males; 0.31, 0.96, or 3.11 mg/kg/day in females) for 104 weeks. There were no treatment-related effects on mortality, hematology, clinical chemistry, gross pathology, or histopathology. For chronic toxicity, **the NOEL was 0.25 mg/kg/day in males and 0.31 mg/kg/day in females, and the LOEL was 0.75 mg/kg/day in males and 0.96 mg/kg/day in females,** based on decreases in plasma cholinesterase (females), erythrocyte cholinesterase (both sexes), and brain cholinesterase (females). Over the period of treatment at 45 ppm, plasma cholinesterase was decreased by 38-49% in males and 54-67% in females and erythrocyte cholinesterase was decreased by 20-37% in males and by 23-31% in females. Also at this dose, at 12 months, brain cholinesterase was decreased 50% in female rats, and was also decreased 32-55% in males and females at study termination. Relative weight of the liver in females was increased 9% at the 45 ppm dose level. At 15 ppm, plasma cholinesterase was

decreased by 19-35% in females, erythrocyte cholinesterase was decreased by 10-22% in males and 12-20% in females, and brain cholinesterase by 21% in females over the 24 month test period. At 5 ppm, erythrocyte cholinesterase was decreased by 12% in male rats at study termination. A 20% decrease in cholinesterase activity is considered significant. The high dose of 45 ppm was determined to be adequate for carcinogenicity testing based on the clear evidence of compound toxicity (i.e., inhibition of cholinesterase). **There was however, no evidence of carcinogenicity from treatment with azinphos-methyl in this study**. (MRID # 41119901).

iv. Oral Toxicity in Mice - Two Years (83-2(b))

A two-year carcinogenicity study was conducted in male and female CD-1 mice in which 50 mice/sex/dose were administered technical azinphos methyl (88.6%) in the diet at dose levels of 0, 5, 20, or 80/40 ppm (0.79, 3.49, or 11.33 mg/kg/day in males; 0.98, 4.12, or 14.30 mg/kg/day in females) for 104 weeks. There were no significant treatment-related effects on body weight, body weight gain, food consumption, hematology, organ weights, macroscopic pathology, or microscopic pathology at the 40 pm dose level and below. However, at the 40 ppm dose level, plasma cholinesterase in males was decreased 34-52% and in females was decreased 23-33% vs the control. Erythrocyte cholinesterase was decreased 19-50% in males and 23-54% in females. Brain cholinesterase (measured only at 24 months) was decreased to 37% of control in males and to 33% of control in females. At the 20 ppm dose level, plasma cholinesterase in males was decreased 69-83% of control and decreased 50-77% of control in females. Erythrocyte cholinesterase was decreased 43-66% of control in males and 45-51% of control in females. Brain cholinesterase was decreased to 84% of control in males and 74% of control in females. At the 5 ppm dose level, erythrocyte cholinesterase was decreased 84-95% of control in males and 78-93% of control in females. Plasma cholinesterase was largely unaffected except in females at 12 months, where inhibition at 84% of the control was observed. **The NOEL was less than (<) 0.79 mg/kg/day in males and <0.98 mg/kg/day in females and the LOEL was 0.79 mg/kg/day in males and 0.98 mg/kg/day in females, based on decreased erythrocyte cholinesterase activity in males and females. There was no evidence of carcinogenicity from treatment with azinphos-methyl in this study** (MRID # 00147895).

e. Developmental Toxicity

i. Oral Teratology Study in Rats (83-3(a))

In a developmental toxicity (teratology) study, rats of the Crl:CDBR strain from Charles River received either 0, 0.5, 1.0, or 2.0 mg/kg/day azinphos-methyl technical (87.7% a.i.) by oral gavage on gestation days 6 through 15 inclusive (33 dams/dose). There were no reported treatment effects on maternal mortality, body weight, food consumption, or cesarean section observations at any dose level tested. No malformations of either the viscera or skeleton were reported for the fetuses of any group at any dose level tested. At the 1.0 mg/kg/day dose level, maternal brain cholinesterase activity was significantly reduced by 8% compared to control, but no corresponding decrease in fetal brain cholinesterase was observed. **For maternal toxicity,**

the NOEL was 0.5 mg/kg/day and the LOEL was 1.0 mg/kg/day, based on decreased maternal brain cholinesterase activity. For developmental toxicity, the NOEL was 2.0 mg/kg/day, the highest dose tested; a LOEL was not established (MRID # 40464801).

ii. Oral Teratology Study in Rabbits (83-3(b))

A developmental toxicity study was conducted in American Dutch rabbits, which received either 0, 1.0, 2.5, or 6 mg/kg/day azinphos methyl technical (87.7%) by oral gavage on gestation days 6 through 18 inclusive. At the 6.0 mg/kg/day dose level, two to four maternal rabbits exhibited tremors and/or ataxia during the study. There were no compound related effects on body weight, food consumption, or gross pathology in maternal rabbits at any dose level tested. On gestation day 19, activity of plasma and erythrocyte cholinesterase was decreased by 13% and 20.5% respectively at the 2.5 mg/kg/day dose level, and by 22.4 and 50.1% at the 6.0 mg/kg/day dose level, respectively. A statistically significant increase in pre-implantation loss and a numerical increase in post-implantation loss was observed at the 6.0 mg/kg/day dose level, with a significant decrease in live fetuses/does at the 6.0 mg/kg/day dose level. **For maternal toxicity, the NOEL was 1.0 mg/kg/day and the LOEL was 2.5 mg/kg/day, based on decreased plasma and erythrocyte cholinesterase activity. For developmental toxicity, the NOEL was 2.5 mg/kg/day and the LOEL was 6.0 mg/kg/day, based on the increased pre- and post-implantation loss observed at this dose**. (MRID # 40713901 and 41240001).

f. Reproductive Toxicity

i. 2-Generation Reproductive Toxicity Study in Rats (83-4)

In a two-generation reproduction study in Wistar rats (MRID 40332601; Doc No. 06533), azinphos methyl (87.2%) was administered at dietary concentrations of 0, 5, 15, or 45 ppm (equivalent to 0.25, 0.75, or 2.25 mg/kg/day). **The systemic parental NOEL was 15 ppm** (0.75 mg/kg/day), based upon mortality of dams, decreased body weight for P males and F1 males and females, and clinical signs of toxicity, including poor condition and convulsions, at the systemic LOEL of 45 ppm (2.25 mg/kg/day). **The reproductive (offspring) NOEL and LOEL were 5 and 15 ppm (0.25 and 0.75 mg/kg/day), respectively.** The LOEL was based on a reduction in pup viability and lactation indices (death of the offspring between the time periods of postnatal days 0-5 and 5-28) and decreased mean total litter weights at weaning on postnatal Day 28. No cholinesterase measurements were taken for either parental animals or pups.

ii. 1-Generation Reproductive Study in Rats (83-4)

In a supplementary one-generation toxicity study in Wistar rats (MRID# 41916801), 92% azinphos methyl was administered at dietary concentrations of 0, 5, 15, or 45 ppm (equivalent to 0.43, 1.30, or 3.73 mg/kg/day for males and 0.55, 1.54, or 4.87 mg/kg/day for females). **The maternal systemic NOEL was <5 ppm** (0.55 mg/kg/day), based upon plasma and

erythrocyte cholinesterase inhibition on day 5 of lactation at 5 ppm, the lowest dose tested. Further characterization of maternal cholinesterase inhibition revealed that plasma, RBC, and brain ChE were significantly decreased in females at 45 ppm at all timepoints tested (end of premating, gestation Day 11, lactation Day 5 and lactation Day 28). At 15 ppm, plasma and RBC (not brain) ChE were significantly inhibited at the same timepoints. For males at the end of mating, plasma ChE was significantly decreased at 15 and 45 ppm, while RBC ChE was significantly decreased at 5, 15, and 45 ppm; brain ChE was not decreased at any dietary level. **The reproductive (offspring) NOEL and LOEL were 5 and 15 ppm** (0.55 and 1.54 mg/kg/day), respectively. The LOEL was based on a reduction in the pup viability index (death of the offspring during postnatal days 0-5) and decreased pup weights at postnatal Days 14 and 21. Pup brain weight and cholinesterase activity were assessed in pups at postnatal Days 5 and 28. At 45 ppm, significant reductions in brain cholinesterase activity was noted in pups at each interval (Days 5 and 28), and a significant reduction in brain weight was observed on postnatal Day 5, but not Day 28.

g. Mutagenicity (84-2)

In an Ames Salmonella assay, azinphos-methyl technical (100% a.i.)was tested for the ability to cause gene mutations in *Salmonella typhimurium* strains TA1535, TA1537, TA1538, TA98, and TA100 in the absence and presence of metabolic activation (Aroclor 1254 induced rat liver S-9). Azinphos-methyl technical at concentrations of 0, 2, 10, 40, 80, or 160 μg/plate in the absence and presence of metabolic activation showed no evidence of mutagenicity in this study (MRID# 40280107).

In another Ames Salmonella assay, azinphos-methyl (88.8% a.i.) was tested for mutagenic activity in *Salmonella typhimurium* strains TA1535, TA1537, TA1538, TA100, and TA98 with and without metabolic activation at concentrations of 0, 33, 100, 333, 1000, 2000, 3333, or 4000 μg/plate. There was no evidence for mutagenicity at any concentration tested in the absence or presence of metabolic activation (MRID # 40301301).

In an *in vitro* cytogenetics assay using human lymphocytes, azinphos-methyl (91.9% a.i.) was tested under non-activated conditions at concentrations of 0, 1, 10, or 100 μg/ml and under S-9 activated conditions at concentrations of 0, 5, 50, or 500 μg/ml. Under non-activated conditions, azinphos-methyl was found to be non-clastogenic at all concentrations tested. Under activated conditions, azinphos-methyl was found to be clastogenic at 500 μg/ml (MRID # 40367811).

The registrant submitted a primary rat hepatocyte unscheduled DNA synthesis assay (MRID 00155017). In that study, azinphos methyl (91.1%) was found to be negative up to the highest dose tested (50.3 ug/ml).

h. Metabolism (85-1)

The metabolism of [^{14}C]azinphos-methyl was examined in male and female Sprague-Dawley rats

following oral administration of single doses of 0.125 or 2.5 mg/kg, or after a repeated oral dose of unlabeled test material at 0.125 mg/kg for 14 days followed by a single radiolabelled dose. Within 72 hours post-dose, between 92-109% of the administered radioactivity was excreted across all dose groups. Between 63-79% of the administered radioactivity was eliminated in urine, and between 20-27% in feces. Highest residual concentrations of radioactivity were observed in blood (0.013-00.319 μg/g tissue), kidney (0.008-0.257 μg/g tissue), liver (0.005-0.121 μg/g tissue), lung (0.008-0.172 μg/g tissue), and brain (0.004-0.126 μg/g tissue). Approximately 75% of the administered radioactivity was identified. The cysteinyl methyl benzazimide sulfone (13-20% of the dose) and the methyl-sulfonylmethylbenzazimide (14-20% of the dose) were identified as the major urinary metabolites. In feces, the methylsulfonylmethylbenzazimide, cyteinylmethylbenzazimide sulfoxide, desmethyl isoazinphos-methyl, azinphos-methyl oxygen analog, and methylthiomethylbenzazimide were identified, but did not comprise greater than 5% of the administered dose. No azinphos-methyl or glucuronic or sulfate conjugates were found in urine or feces. In vitro studies of azinphos-methyl metabolism supported the in vivo studies suggesting that metabolism of azinphos-methyl in rats proceeds largely through the actions of glutathione-S-transferase and mixed function oxidase. There were no major sex- or dose-related differences in disposition and metabolism of azinphos-methyl in this study (MRID # 40836501).

i. Neurotoxicity

i. Acute Delayed Neurotoxicity (81-7)

In an acute delayed neurotoxicity study in hens (MRID 40883101; Doc. No. 007132), 85% azinphos methyl was administered at 330 mg/kg in corn oil. A second dose was given by gavage at study day 21. Mortality was extensive (18/30 hens died within 3-4 days of the initial dose and one additional hen died following the second dose), and clinical signs of neurotoxicity were observed (grade 5 ataxia, prostration, hypoactivity, liquid feces). According to the DER, no gross or microscopic evidence of neuropathology (nonperfused tissues) was observed. NTE was not apparently measured. The RfD/Peer Review Committee confirmed the opinion that neuropathological observations of degeneration digestion chamber of sciatic nerves and perivascular cuffing of the brain in the treated animals were not treatment-related.

ii. Acute Neurotoxicity Study in Rats (81-8)

The endpoint from this study (MRID 43360301) was selected to be used for determining the acute RfD for the acute dietary risk assessment. In an acute neurotoxicity study in Fischer 344 rats (18/sex/group), 92.2% azinphos methyl was administered in 0.5% methylcellulose and 0.4% Tween 80 in deionized water by a single gavage dose of 2, 6, or 12 mg/kg for males and 1, 3, or 6 mg/kg/ for females, in a volume of 5 ml/kg. Significant cholinesterase inhibition (plasma and erythrocyte) was observed at the lowest dose tested (2 mg/kg for males and 1 mg/kg for females); brain cholinesterase inhibition and increased incidences of neurobehavioral effects were observed in males and females at 6 and 3 mg/kg

and above. The neurobehavioral signs included gait incoordination, repetitive chewing, muscle fasciculations, tremors, hypoactivity, no reaction to touch, abnormal righting reflex, decreased body temperature, decreased forelimb and/or hind limb grip strength, and decreased motor and locomotor activities. A high incidence of mortality (5/18 males and 15/18 females) was observed at 12/6 mg/kg (M/F). Brain weights and neuropathology findings were reported to be similar between control and treated animals. **The NOEL for neurotoxicity was not determined; the LOEL was determined to be 1 mg/kg/day.**

iii. Subchronic Neurotoxcity (82-5)

In a subchronic neurotoxicity study, groups of Fischer 344 rats (18/sex/dose) received azinphos methyl (92.2%) in the diet at dose levels of 15, 45, 90 (males and females) or 120 ppm (males) for 13 weeks. These dose levels were equivalent to 0.91, 2.81 or 7.87 mg/kg/day for males and 1.05, 3.23 or 6.99 mg/kg/day for females. Treatment-related effects included: decreases in body weight and body weight gain (both sexes at the high-dose); cholinergic signs including increased reactivity, uncoordinated gait and tremors (both sexes at mid and/or high doses); significant inhibition of plasma and brain (both sexes mid and high doses) and RBC (all doses) cholinesterase activity; decreased forelimb grip strength, motor activity and locomotor activity (both sexes high dose); and a possible increase in histopathological lesions in the spinal cord, brain, optic nerve (both sexes at high dose) (MRID No. 43826601).

The neuropathology findings were equivocal, but suggested treatment-related effects in the brain (axonal swelling of minimum severity in males) and spinal cord (nerve fiber degeneration of the cauda quina and the cervical and/or thoracic cord in both sexes) at the high dose (120 ppm; 7.87/6.99 mg/kg/day in M/F). In females, the DER noted a possible correlation between the incidence of cervical spinal cord lesions at the high dose and decreased forelimb grip strength at all dose levels. Since the histopathology tables were not included in the DER, the RfD/Peer Review Committee recommended that the incidence and severity of the equivocal neuropathological findings be reassessed. Based on a reevaluation of the neuropathology data by the Hazard Identification Assessment Review Committee (HIARC) (see Memo dated March 19, 1998), it was concluded that neither the incidence nor the severity of the neuropathological lesions noted in high-dose males and females could be attributed to treatment with azinphos methyl. The findings were not statistically significant, of minimal severity and occurred sporadically.

iv. Developmental Neurotoxicity

At the RfD Peer Review Committee meeting on September 16, 1993, it was recommended that a developmental neurotoxicity study in rats be conducted with azinphos methyl because it is a potent cholinesterase inhibitor. In retrospect, the following additional information was considered by the HIARC:

(i). Evidence that support requiring a developmental neurotoxicity study:

- SAR concern: Azinphos methyl is an organophosphate.

- Administration to various species (rat, mouse, dog) results in cholinesterase inhibition in the plasma, erythrocytes and/or brain. Systemic evidence of cholinergic effects occurs regularly in the data. Guideline neurotoxicity studies have been submitted and demonstrate neurobehavioral effects.

- In a one-generation reproduction study in rats, dietary administration of azinphos methyl (HDT) to parental animals resulted in a significant decrease in pup brain weight on postnatal Day 5 but not Day 28.

(ii). Evidence that do not support requiring a developmental neurotoxicity study:

- With the exception cited above of decreased pup brain weight in the one-generation reproduction study, no effects on brain weight or histopathology of the brain or peripheral system (without perfusion) were observed in any of the guideline subchronic or chronic studies in which these parameters were measured.

- No evidence of abnormalities in the development of the fetal nervous system were observed in the prenatal developmental toxicity studies in either rats or rabbits at maternally toxic oral doses up to 2.0 or 6.0 mg/kg/day, respectively.

- A search of the open literature from 1969 to the present revealed no evidence of neuropathology in treated animals. No studies were found in the open literature regarding potential adverse effects associated with humans accidentally or occupationally exposed to azinphos methyl.

- Azinphos methyl did not cause delayed neurotoxicity in hens following acute exposure.

Based on the weight-of-the-evidence, the HIARC determined that a developmental neurotoxicity study is **not required**.

v. <u>General Neurotoxicity Observations</u>

In addition to the clinical signs of neurotoxicity which were observed in the neurotoxicity studies in rats, the following additional clinical observations that are indicative of neurotoxicity were seen: occasional emesis and mucoid diarrhea at 125 ppm (0.688 mg/kg/day) in the 1-year dog study, convulsions at 2.25 mg/kg/day in the two-generation reproduction study in rats, and tremors at 6 mg/kg/day in the prenatal developmental toxicity study in rabbits. Similarly, ChE

inhibition (plasma, RBC, and brain) was observed at low dose levels in all subchronic and chronic studies in which this parameter was measured.

In contrast, there was no indication of decreased brain weight or histopathology of the brain or peripheral nervous system, following processing of tissues without perfusion, in any of the guideline subchronic or chronic studies. The Committee, however, noted that numerous neurological tissues were apparently not assessed in the chronic dog study (MRID No. 41804801) and that histopathology tables were not provided in the DER of the chronic rat study (MRID No. 41119901).

However, a reexamination of the neuropathology data presented in the one-year dog study (see Memo dated March 19, 1998) indicated that no lesion were found in the brain, spinal cord, eyes, optic nerve or sciatic nerve. Samples of the above tissues were processed and examined microscopically for all animals in all study groups.

Similarly, a reevaluation of the neuropathology data from the chronic rat study (see Memo dated March 19, 1998) revealed that neither the peripheral nerve nor the spinal cord were examined histologically. Although this study is currently classified as Acceptable, it does not fully satisfy the guideline requirements for a chronic feeding/ carcinogenicity study (83-1) in rats. However, it was not chosen as a critical study for the toxicity endpoint selection. In addition, reassessment of the brain weight data in this study, indicated that significantly increased relative brain weights in males of the mid-(15 ppm) and high-(45 ppm) dose groups at 12 months and in high-dose males at 24 months were accompanied by significant body weight reductions. However, absolute brain weights for these groups showed nonsignificant less than or equal to 3% increases. It was concluded, therefore, that the apparent increase in relative brain weights was an artifact resulting from decreased body weight.

The reevaluation of the data related to neurological findings indicates that while azinphos methyl is a potent cholinesterase inhibitor, there is no evidence in the submitted studies or the open literature that demonstrate an association between exposure to the test chemical and histopathological effects on the nervous system of either the rat or the dog.

j. Hazard Characterization

Azinphos methyl is an organophosphate pesticide. The toxicology data base provides overwhelming evidence confirming that azinphos methyl has anticholinesterase activity in various species including dogs, rabbits, rats, mice and hens. In acute toxicity studies, azinphos methyl exhibits low to high toxicity depending on the route of administration and the species used. It is acutely toxic at relatively low oral or dermal doses when tested in rats but found to have low toxicity in rabbits exposed dermally. This finding supports the earlier arguments regarding the suitability of conducting rabbit dermal studies on organophosphates (see Short-Term Dermal Risk Assessment). The data from the only available acute inhalation study suggest that azinphos methyl is moderately toxic via this route. It is only slightly irritating to the eye and

non-irritating to the skin but did produce dermal sensitization in guinea pigs. Other toxic signs observed in animals treated acutely with azinphos methyl are consistent with cholinesterase inhibition and are typical of the acute toxic signs induced by the organophosphate class of chemicals. They included: tremors, convulsions salivation, and dyspnea (labored breathing). Dose-related inhibition of plasma, erythrocyte and brain cholinesterase (ChE) activity occurs by all routes of exposure and following exposure for various durations. Although frank neurobehavioral observations have been noted in acute and subchronic studies, there is no evidence of histopathological effects on the central nervous system. Similarly, azinphos methyl did not cause delayed neurotoxicity in hens and there was no evidence of neuropathology in chronic studies. There is also no indication of an increased sensitivity of the offspring of rats or rabbits after pre-natal and/or postnatal exposure to azinphos methyl. In all studies examined, maternal or parental NOELs are lower or equivalent to the offspring NOELs. **Based on these considerations, the weight-of-the-evidence evaluation of the data base does not indicate the need for evaluation of functional development and, thus, there does not appear to be a need to conduct a developmental neurotoxicity study.** Azinphos methyl has been classified in **"Group E"** (i.e., the chemical is characterized as **"Not Likely"** to be carcinogenic in humans via relevant routes of exposure) because there is no evidence that azinphos methyl altered the spontaneous tumor profile in rats or mice. In both studies, the highest dose tested was considered adequate for carcinogenicity testing based on cholinesterase inhibition. Similarly, there is no mutagenicity concerns.

Based on metabolism studies in rats, azinphos methyl is degraded and/or eliminated within 72 hours postdosing and does not accumulate in tissues. The metabolism of azinphos methyl in rats proceeds largely through the action of glutathione-S-transferase and mixed function oxidases. There were no major sex- or dose-related differences in the disposition or metabolism of azinphos methyl.

2. Dose Response Assessment

a. FQPA Issues: Uncertainty/Safety Factor/Special Sensitivity

Under the Food Quality Protection Act (FQPA), P.L. 104-170, which was promulgated in 1996 as an amendment to the Federal Insecticide, Fungicide, and Rodenticide Act (FIFRA) and the Federal Food, Drug and Cosmetic Act (FFDCA), the Agency was directed to "ensure that there is a reasonable certainty that no harm will result to infants and children" from aggregate exposure to a pesticide chemical residue. The law further states that in the case of threshold effects, for purposes of providing this reasonable certainty of no harm, "an additional tenfold margin of safety for the pesticide chemical residue and other sources of exposure shall be applied for infants and children to take into account potential pre- and post-natal toxicity and completeness of the data with respect to exposure and toxicity to infants and children. Notwithstanding such requirement for an additional margin of safety, the Administrator may use a different margin of safety for the pesticide residue only if, on the basis of reliable data, such margin will be safe for infants and children."

Pursuant to the language and intent of the FQPA directive regarding infants and children, the applicable toxicity database for azinphos methyl was evaluated by the Hazard Identification Assessment Review Committee (HIARC). **The final recommendation on the FQPA Safety Factor, however, will be made during risk characterization by the FQPA Safety Committee.**

Adequacy of data: The data included an acceptable two-generation reproduction study in rats and acceptable prenatal developmental toxicity studies in rats and rabbits, meeting the basic data requirements, as defined for a food-use chemical by 40 CFR Part 158. At the Hazard Identification Assessment Review Committee (HIARC) meeting on azinphos methyl (March 19, 1998) it was determined that a developmental neurotoxicity study was not required.

Susceptibility issues: The developmental toxicity studies in rats and rabbits showed no evidence of additional sensitivity of young rats or rabbits following *in utero* exposure to azinphos methyl. In the prenatal developmental toxicity study in rats, no evidence of developmental toxicity was seen even in the presence of maternal toxicity (cholinesterase inhibition).

In the two-generation reproduction study in rats, however, there was a suggestion of increased sensitivity to the offspring following pre-and/or postnatal exposure to azinphos methyl. In both the one- and two-generation studies, decreased pup survival in both early and late stages of lactation and pup weight reductions in late lactation were observed. In the two-generation study, these effects in the offspring were observed at a dietary level which was not systemically toxic to the parental animals. It was noted, however, that parental toxicity in the one-generation study was based upon decreased cholinesterase activity, while cholinesterase measurements were not conducted in the two-generation study, and the parental toxicity was based upon mortality, clinical signs, and body weight decrements (less sensitive indicators). **The HIARC, therefore, concluded that the suggested susceptibility of the offspring was an artifact of the study design.**

Comparative cholinesterase inhibition data for adult rats and their fetuses or pups did not identify increased susceptibility to the offspring. In the prenatal developmental toxicity study in rats, brain cholinesterase activity did not appear to be significantly inhibited in GD20 rat fetuses following *in utero* exposure, even at a dose which demonstrated marked brain cholinesterase inhibition in the dams on the same day of gestation. Brain cholinesterase inhibition in 5- and 28-day old pups of the one-generation reproduction study occurred at the highest dietary level tested; however, brain cholinesterase inhibition was also observed in maternal animals at this dose level at termination.

Uncertainty factor: The application of an additional uncertainty factor to ensure the protection of infants and children from exposure to azinphos methyl, as required by FQPA, will be determined by the FQPA Safety Factor Assessment Review Committee.

The HIARC, **based on the hazard assessment, recommends** to the FQPA Safety Committee, that the additional **10x** factor **should be removed** because:

(i) Developmental toxicity studies showed no increased sensitivity in fetuses as compared to maternal animals following *in utero* exposure in rats and rabbits.

(ii) Both a one- and a two-generation reproductive toxicity study in rats showed no increased susceptibility in pups when compared to adults.

(iii) There was no evidence of abnormalities in the development of the fetal nervous system in the pre/postnatal studies. Neither brain weight nor histopathology (nonperfused) of the nervous system was affected in the subchronic and chronic toxicity studies.

(iv) The toxicology data base is complete and there are no data gaps. There is no evidence to require a developmental neurotoxicity study.

b. Reference Dose (RfD) for Chronic Oral Exposure

On September 16, 1993, the Health Effects Division RfD/Peer Review Committee evaluated the toxicology database for azinphos methyl to establish a Reference Dose (RfD). **An RfD of 0.0015 mg/kg/day was derived, based on the NOEL of 0.15 mg/kg/day established in male dogs in a 1-year chronic toxicity study (MRID # 41804801) and using an uncertainty factor of 100** (10 for inter- and 10 for intra-species variations). The LOEL in this study, 0.69 mg/kg/day, was based on decreases in erythrocyte cholinesterase. The World Health Organization in 1991 established an Acceptable Daily Intake (ADI) of 0.005 mg/kg/day for azinphos-methyl.

c. Carcinogenicity Classification

At the September 1993, meeting of the RfD/Peer Review Committee, azinphos methyl was classified as a **"not likely"** human carcinogen. This classification was based on the lack of evidence of carcinogenicity in male and female CD-1 mice (MRID No. 00147895) and in male and female Wistar rats (MRID No. 41119901). In both studies, the highest dose tested was considered adequate for carcinogenicity testing based on cholinesterase inhibition. Treatment with azinphos methyl did not alter the tumor profile in the above strain of mice or rats. The HIARC concurred with these conclusions and re-affirmed the previous classification.

d. Dermal Absorption (85-3)

A 35% wettable powder formulation of azinphos-methyl was applied dermally to rats at 0.93, 9.3, and 93 $\mu g/cm^2$ exposure, equivalent to 0.056, 0.56, or 5.6 mg (a.i.)/kg. Duration of exposure for six groups of four male rats/dose was 1, 4, 10, 24, 72, or 168 hours. By 10 hours, 32.2, 22.1, and 23.7% of the applied doses of 0.056, 0.56, and 5.6 mg/kg, respectively, remained on the skin.

To simulate worker exposure, the test site of animals exposed for 24, 72, and 168 hours was wiped with a moistened gauze pad after 10 hours of exposure. Maximum systemic absorption occurred from the 168 hour exposure with 41.7, 21.9, and 18.3% of the applied dose recovered in blood, urine, feces, carcass, and cage wash combined for the 0.056, 0.56, and 5.6 mg/kg doses, respectively. **From these data, the value of 41.7% absorption was used as a measure of dermal absorption for azinphos-methyl (MRID # 42452701).**

e. Summary of Toxicological Endpoints for use in Human Risk Assessment

The Health Effects Division Hazard Identification Assessment Review Committee (HIARC) considered the available toxicology data for azinphos-methyl at a meeting held on March 19, 1998. Toxicology endpoints and dose levels of concern were identified for use in risk assessment corresponding to acute dietary exposure, short and intermediate term occupational and residential exposure, and chronic occupational and residential exposure. Percentage of dermal absorption was also determined.

1) Acute Dietary

To estimate acute (one-day) dietary risk, the endpoint selected was neurotoxicity. **An acute RfD of 0.003 mg/kg/day based on a LOEL of 1 mg/kg from an acute neurotoxicity** study in rats (MRID # 43360301) was identified for use in acute dietary risk assessments. This LOEL was selected based on neurobehavioral effects and inhibition of plasma, erythrocyte, and brain cholinesterase observed following a single dose. Because no NOEL was established for this study, an additional uncertainty factor of 3 to account for the lack of a NOEL in the critical study was applied to the existing uncertainty factor for inter-species extrapolation (10X) and intra-species variability (10X) resulting in a total uncertainty factor of 300 for the acute dietary risk assessment.

2) Chronic Dietary

The chronic RfD of 0.0015 mg/kg/day, based on the NOEL of 0.15 mg/kg/day established in male dogs in a 1-year chronic toxicity study and using an uncertainty factor of 100, will be used for chronic dietary risk assessments.

3) Dermal Absorption

Based on a dermal absorption study in rats (discussed above), a value of **41.7% absorption** was selected for use in risk calculations (MRID # 42452701).

4) Short and Intermediate Term Occupational and Residential

For short (1 to 7 days) term dermal exposure, the HIARC recommended use of the dermal absorption study in rats (MRID No. 42452701), which included a determination of ChE

inhibition, as appropriate for the Short-Term Occupational or Residential Exposure Risk Assessment. Previously, the 21-day dermal toxicity study in rabbits (MRID No. 00145715) was selected for the Short- and Intermediate-Term Occupational or Residential Exposure Risk Assessments. However, during the evaluation of the data base for azinphos methyl, the HIARC determined that the 21-day dermal toxicity study in rabbits was not appropriate (i.e., the rat toxicity data maybe more protective than the rabbit data).

For intermediate (7 days to several months) term exposure, the HIARC selected the one year toxicity study in dogs for this Exposure Risk Assessment. **Since an oral NOEL was selected a dermal absorption factor of 41.7% should be used for this risk assessment.** Application of the dermal absorption factor (0.42) to the above NOEL yields an equivalent dermal dose of 0.36 mg/kg/day. Previously, the 21-day dermal toxicity study in rabbits (MRID No. 00145715) was selected for the Short- and Intermediate-Term Occupational or Residential Exposure Risk Assessments. However, during the evaluation of the data base for azinphos methyl, the HIARC determined that the 21-day dermal toxicity study in rabbits was not appropriate (i.e., the rat toxicity data maybe more protective than the rabbit data).

For inhalation exposure (any time period), a 90-day inhalation toxicity study (MRID 00155011) was selected with a **NOEL of 0.0012 mg/L**. The endpoint was inhibition of plasma and erythrocyte cholinesterase was observed at the next highest dose of 0.0047 mg/l in both male and female rats.

5) Chronic Occupational and Residential (non-cancer)

Long-term dermal exposure via the dermal route is not expected based on the use pattern.

A summary of toxicological endpoints is given in table 3 below.

Table 3. Summary of Toxicological Endpoints for Azinphos methyl Risk Assessments

EXPOSURE SCENARIO	DOSE (mg/kg/day)	ENDPOINT	STUDY
Acute Dietary	LOEL = 1.0 UF = 300	Plasma, erythrocyte and brain cholinesterase inhibition	Acute Neurotoxicity-Rat
	Acute RfD = 0.003 mg/kg		
Chronic Dietary	NOEL= 0.149 UF = 100	Erythrocyte cholinesterase inhibition.	1-Year Toxicity- Dog
	Chronic RfD = 0.0015 mg/kg/day		

Table 3. Summary of Toxicological Endpoints for Azinphos methyl Risk Assessments			
EXPOSURE SCENARIO	DOSE (mg/kg/day)	ENDPOINT	STUDY
Short-Term (Dermal)	Dermal NOEL = 0.56	Erythrocyte cholinesterase inhibition.	Dermal Absorption Rat
	MOE = 100		
Intermediate-Term (Dermal)[a]	Oral NOEL = 0.149	Erythrocyte cholinesterase inhibition.	1-Year Toxicity-Dog
	MOE = 100		
Long-Term (Dermal)	Not Applicable	Not Applicable	Not Applicable
Inhalation (Any Time Period)	NOEL= 0.0012 mg/L	Plasma and erythrocyte cholinesterase inhibition.	90-Day Inhalation Rat
	MOE = 100		

[a] A 42% dermal absorption factor should be used for the intermediate-term risk assessment.

3. Dietary Exposure and Risk Assessment/Characterization

a. Dietary exposure (Food Sources)

The submitted residue chemistry data are adequate to support reregistration. The residue chemistry database is substantially complete; however, magnitude of the residue data are required for walnuts and cotton gin byproducts.

i. OPPTS GLN 860.1200: Directions for Use

A search of the Agency's Reference Files System (REFS) on 12/10/96 indicates that there are nine azinphos methyl end-use products (EPs) with food/feed uses registered to Bayer Corp. These EPs are presented below.

EPA Reg No.	Label Acceptance Date	Formulation Class	Product Name
3125-102 [a]	7/94	2 lb/gal EC	Guthion® 2L
3125-123 [b]	8/94	2 lb/gal EC	Guthion® 2S
3125-193 [c]	7/94	50% WP	Guthion® 50% Wettable Powder Crop Insecticide
3125-301 [d]	4/96	50% WP	Guthion Solupak® 50% Wettable Powder Insecticide
3125-338	7/94	3 lb/gal FlC	Guthion 3® Flowable Insecticide

3125-378	7/94	35% WP	Guthion® 35% Wettable Powder Insecticide
3125-379	8/94	35% WP	Guthion Solupak® 35% Wettable Powder Insecticide
3125-426	4/93	2 lb/gal EC	Guthion® 2L
3125-427	4/93	3 lb/gal FlC	Guthion 3® Flowable Insecticide

[a] Includes SLN Nos. MS840012, TX840005.
[b] Includes SLN Nos. CA900021, MA780002, OH810018.
[c] Includes SLN Nos. CA790139, NJ940002, OH810017, VT800004.
[d] Includes SLN Nos. CA790139, CA790149, CA800146, CA810074, CA900012, NJ940003.

Some labels still list uses the registrant does not intend to support (CBRS No. 16871, DP Barcode D222840, 6/28/96, F. Fort). These uses, including artichokes, cabbage, celery, eggplant, and peppers should be deleted from the labels.

Labels bearing uses on grapes should be revised to clarify specific use rates that correspond to the PHIs listed. The labels bearing use directions for filberts and pecans should specify a 45-day PHI; the reference to shuck-split for pecans should be deleted from the labels. The FlC labels should be revised to specify a maximum seasonal rate for cotton. (See Table A - Food/Feed Use Patterns Subject to Reregistration).

A comprehensive summary of the registered food/feed use patterns of azinphos methyl, based on the product labels registered to Bayer Corp., is presented in Table A (Appendix II). A tabular summary of the residue chemistry science assessments for reregistration of azinphos methyl is presented in Table B (Appendix III). The conclusions listed in Table B regarding the reregistration eligibility of azinphos methyl food/feed uses are based on the use patterns registered by the basic producer, Bayer Corp. When end-use product DCIs are developed (e.g., at issuance of the RED), RD should require that all end-use product labels (e.g., MAI labels, SLNs, and products subject to the generic data exemption) be amended such that they are consistent with the basic producer's labels.

ii. OPPTS GLN 860.1300: Nature of the Residue in Plants

The reregistration requirements for plant metabolism are fulfilled. Acceptable studies depicting the qualitative nature of the residue in or on apple, cotton, and potato have been submitted and evaluated. Based on these studies, it has been determined that the residue of concern in/on plant commodities is azinphos methyl *per se*. The current tolerance expression for plant commodities is appropriate.

iii. OPPTS GLN 860.1300: Nature of the Residue in Livestock

The reregistration requirements for animal metabolism are fulfilled. Acceptable studies, depicting the qualitative nature of the residue in ruminant and poultry have been submitted and evaluated. The HED Metabolism Committee has determined that the residue of concern in animal commodities is azinphos methyl per se. Tolerances are currently expressed in terms of parent only for residues in/on fat, meat, and meat byproducts of cattle, goats, horses and sheep and in terms of parent and its metabolites in milk. The current tolerance for milk must be changed to regulation of the parent only.

iv. OPPTS GLN 860.1340: Residue Analytical Methods

Adequate analytical methodology is available for data collection and enforcement of tolerances of azinphos methyl. A gas chromatograph (GC)/flame photometric detection (FPD) method No. 69523 has undergone a successful Agency validation trial and is recommended by HED for inclusion in PAM, Vol. II. Using method No. 69523, residues are extracted with acetone/water, partitioned into chloroform, purified using gel permeation chromatography and silica gel, and analyzed by GC/FPD. The spectrophotometric methods listed in PAM, Vol. II are not considered specific and are to be replaced.

Data from analysis of azinphos methyl residues in plant and animal matrices have been collected using Method No. 69523 or modifications as well as the non-specific spectrophotometric methods.

v. OPPTS GLN 860.1360: Multiresidue Method Testing

The FDA PESTDATA database indicates that azinphos methyl is completely recovered using FDA Multiresidue Protocol A, with a special GC/HPLC, and Protocol D for non-fatty foods (PAM, Vol. I Sections 242.2 and 232.4).

vi. OPPTS GLN 860.1380: Storage Stability Data

Requirements for storage stability data are satisfied for purposes of reregistration. Residues of azinphos methyl are stable for 18-24 months in representative commodities in frozen storage.

vii. OPPTS GLN 860.1500: Magnitude of the Residue in Crop Plants

For purposes of reregistration, requirements for magnitude of the residue in plants are fulfilled for the following crops: alfalfa, almonds, apples, blackberries, blueberries, boysenberries, citrus fruits, cottonseeds, cranberries, cucumbers, grapes, loganberries, melons, onions, nectarines, peaches, pecans, pistachios, plums, pomegranates, raspberries, rye, strawberries, sugarcane, and tomatoes. Adequate field trial data depicting azinphos methyl residues following applications made according to the maximum or proposed registered use patterns have been submitted for these commodities. Geographical representation is adequate and a sufficient number of trials reflecting representative formulation classes were conducted. Data on alfalfa will support the use on birdsfoot trefoil, data on plums will be used to support cherries, data on pecans will support filberts, and data on apples will support uses on pears and quinces. Additional data are forthcoming to fulfill outstanding requirements on walnuts.

IR-4 has submitted adequate field trial data to support the tolerances on broccoli. Additional field trial data are required to support cauliflower use. Additional field trials should be conducted in Regions 1, 5, and 12 for cauliflower. Alternatively, field trial data on cabbage conducted in Regions 1, 2, 3, 5, 6, and 10 may be done if the registrant desires a head and stem Brassica crop subgroup tolerance.

For purposes of reregistration, additional residue data are required on cotton gin byproducts. Data are required depicting azinphos methyl residues in/on cotton gin byproducts ginned from cotton harvested on the day after the last of multiple foliar applications of azinphos methyl at the maximum labeled rate and totaling 6 lb ai/A/season. The cotton must be harvested by commercial equipment (stripper and mechanical picker) to provide an adequate representation of plant residue from the ginning process. At least three field trials for each type of harvesting (stripper and picker) are needed, for a total of six field trials. Azinphos methyl residue data on cotton gin byproducts exist from previously conducted field trials. As an alternative to conducting new field trials, the registrant may identify and re-submit those data on cotton gin byproducts that were collected using acceptable harvesting techniques and analyzed using adequate GC method(s) and which reflect the currently registered use pattern.

viii. OPPTS GLN 860.1520: Magnitude of the Residue in Processed Food/Feed

The reregistration requirements for magnitude of the residue in processed food/feed commodities are fulfilled for apple, citrus, cottonseed, grape, potato, sugarcane, and tomato. Based on the available processing studies, separate tolerances are only required for citrus oil, cottonseed hulls, and wet apple pomace.

A tolerance should be established for citrus oil. An adequate processing study indicated that residues concentrated 7.45x in orange oil. Applying the concentration factor to the HAFT residues for oranges of 1.5 ppm, the expected residue in orange oil would be 11.2 ppm. A tolerance of 15 ppm would be sufficient to cover residues in citrus oil.

A tolerance should be established for wet apple pomace. An adequate processing study on apples indicated that residues concentrated 2x in wet apple pomace. Applying this concentration factor to the HAFT residues for apples of 1.7 ppm, the expected residue in apple pomace would be 3.4 ppm. A tolerance of 4 ppm would be sufficient to cover residues in wet apple pomace.

A tolerance should be established for cottonseed hulls. Residues concentrated 1.4x in cottonseed hulls. Applying this concentration factor to the HAFT residues for cottonseed of 0.5 ppm, the expected residue in cottonseed hulls would be 0.7 ppm. A tolerance of 1.0 ppm would be sufficient to cover residues in wet cottonseed hulls.

No processing study exists on rye grain or on any other small cereal grain. However, as residues on these crops were <0.01 ppm, one twentieth the tolerance, and the theoretical concentration factor is 10x, a processing study is not required.

ix. OPPTS GLN 860.1480: Magnitude of the Residue in Meat, Milk, Poultry, and Eggs

The maximum theoretical dietary intake of azinphos methyl by cattle is approximately 7 ppm, based on the diet calculated as follows:

Commodity	Tolerance (ppm)	Dry weight (%)	% Beef cattle diet	Residues in beef cattle diet (ppm)	% Diary cattle diet	Residues in dairy cattle diet (ppm)
Almond hulls	5 [a]	90	10	0.6	10	0.6
Alfalfa hay	5	89	60	3.4	60	3.4
Apple pomace (wet)	4 [b]	40	30	3	20	2
Cottonseed meal	0.5	88	--	--	10	0.06
Total				**7**		**6.06**

[a] Reassessed tolerance.
[b] New tolerance required.

Residues of azinphos methyl analyzed by currently accepted GC/FPD methods were <0.01 ppm in all tissues and milk at all feeding levels from 11 to 77 ppm (up to 11x) (MRID 00030303, report nos. 66448, 66450, 66451). Data collected using the non-specific colorimetric (fluorescence) methods (MRID 00090126) are disregarded. Because residues were nondetectable in milk and tissues at feeding levels up to 11x, a 40 CFR §180.6(a)(3) situation exists for azinphos methyl residues in ruminant tissues and milk and the tolerances should be revoked.

Results from the poultry metabolism studies indicate that a 40 CFR §180.6(a)(3) situation

exists for azinphos methyl residues in poultry tissues and eggs. Therefore tolerances are not needed on poultry commodities.

x. OPPTS GLN 860.1400: Magnitude of the Residue in Water, Fish, and Irrigated Crops

Azinphos methyl is presently not registered for direct use on potable water and aquatic food and feed crops; therefore, no residue chemistry data are required under these guideline topics.

xi. OPPTS GLN 860.1460: Magnitude of the Residue in Food-Handling Establishments

Azinphos methyl is presently not registered for use in food-handling establishments; therefore, no residue chemistry data are required under this guideline topic.

xii. OPPTS GLN 860.1850: Confined Accumulation in Rotational Crops

Chemical Review Management System (CRMS) cites a 1990 confined rotational crop study (MRID 41393601) and a review by EFED dated 1/2/92; the study was judged supplemental. Azinphos methyl was extensively metabolized in soil following application. At 30 days after treatment, 20% of the soil total radioactive residue (TRR) was accounted for by azinphos methyl and seven degradates were identified, none of which retained an intact organophosphate structure. After 70 and 135 days of aging $<10\%$ of the soil radioactivity was the parent compound and at 181 days and thereafter azinphos methyl was below the LOQ in soil (<0.04 ppm). Commodities of kale, wheat, and beets planted at the 30-day plant-back interval did not contain detectable azinphos methyl residues. [^{14}C]Residues in edible commodities planted 30 days after soil treatment were identified as soil residues and conjugates thereof; the metabolite profile in rotated crops was similar to that seen in a metabolism study on cotton.

The current product labels prohibit planting root crops for which azinphos methyl is not registered within 6 months of treatment; a plant-back restriction of 30 days is specified for all other crops for which azinphos methyl is not registered. This plant-back restriction is adequate. No residues of concern are expected in rotated crops. Therefore, field rotational crop studies and potential tolerances on rotated crops are not required.

xiii OPPTS GLN 860.1900: Field Accumulation in Rotational Crops

The EFED one-liner database included the following regarding a field rotational crop study:

> No residues were detected in grain, pod vegetables, or leafy vegetables planted 30 days after application of 8 lb ai/A.

The results of a confined rotational crop study indicate that residues of concern are not expected in rotated crops; therefore, field accumulation studies are not required.

xiv. Tolerance Reassessment/Codex Summary

Tolerances for residues of azinphos methyl in/on plant RACs are currently expressed in terms of azinphos methyl [40 CFR §180.154 (a) and (b)] or azinphos methyl and/or its metabolites [40 CFR §180.154a]. The HED Metabolism Committee has determined that the residue to be regulated is the parent, azinphos methyl. Food/feed additive tolerances have been established for residues of azinphos methyl in soybean oil [40 CFR §185.2225] and dried citrus pulp and sugarcane bagasse [40 CFR §185.2225].

A summary of the azinphos methyl tolerance reassessment and recommended modifications in commodity definitions are presented in Table 4.

Tolerances Listed Under 40 CFR §180.154 (a):

Sufficient data are available to ascertain the adequacy of the established tolerances on all listed commodities that are to be supported except for walnuts.

In accordance with 40 CFR §180.1 (h), the tolerance on peaches covers nectarines. Therefore, the individual tolerance on nectarines should be deleted.

A tolerance for "caneberries" is recommended, concomitant with deletion of individual tolerances on blackberries, boysenberries, loganberries, and raspberries. The tolerance for caneberries should be increased to 8 ppm, based on residues of 7.6 ppm in/on a loganberry sample harvested 3 days following application to the lower portion of the cane at 1x (MRID 42076801; CBRS No. 9195, DP Barcode D172624, 8/27/92, B. Cropp-Kohlligian).

The available data indicate that the tolerances established for almonds, grapes, and potatoes can be lowered to achieve compatibility with the corresponding Codex MRLs. Available data indicate that the 10.0 ppm tolerance for almond hulls can be lowered to 5.0 ppm. In addition, the tolerance for cranberries can be lowered to 0.5 ppm.

As there are no registered uses on apricots, barley, beans, clover, gooseberries, grass, kiwi fruit, oats, peas, soybeans, spinach, and wheat, the tolerances on these crops should be revoked. The following crops appear on current Bayer labels (see Table A), although the registrant has indicated that they do not intend to support these uses: artichoke, eggplant; peppers, cabbage, and celery. Bayer should remove from labels any use it does not intend to support; tolerances on these crops should be revoked.

IR-4 has submitted adequate field trial data to support to tolerances on broccoli. Additional field trial data are required to support cauliflower use. Additional field trials should be conducted in Regions 1, 5, and 12 for cauliflower. Alternatively, field trial data on cabbage conducted in Regions 1, 2, 3, 5, 6, and 10 may be done if the registrant desires a head and stem Brassica crop subgroup tolerance.

The available data indicate that finite residues are not expected in animal tissues (refer to the discussion under OPPTS GLN 860.1480); therefore the tolerances on animal tissues should be revoked.

Tolerances Listed Under 40 CFR §180.154 (b):

Sufficient data are available to ascertain the adequacy of the established tolerance with a regional registration on pomegranates.

Tolerances Listed Under 40 CFR §180.154a:

The available data indicate that finite residues are not expected in milk (refer to the discussion under OPPTS GLN 860.1480); therefore the tolerance for milk should be revoked and this section should be deleted.

Tolerances Listed Under 40 CFR §185.2225:

The established food additive tolerance for soybean oil should be revoked, as there is no registered use on soybeans.

Tolerances Listed Under 40 CFR §186.2225:

The established tolerance for dehydrated citrus pulp should be revoked, as an adequate orange processing study did not show concentration in dried orange pulp.

The established tolerance for sugarcane bagasse should be revoked, as this commodity is not considered a significant livestock feed item.

New Tolerances Needed Under 40 CFR §180.154 (a):

Residue data are required to determine a tolerance level for cotton gin byproducts.

New Tolerances Needed Under 40 CFR §185.2225:

A tolerance should be established for citrus oil, based on a concentration factor of 7.45x.

New Tolerances Needed Under 40 CFR §186.2225:

A tolerance should be established on wet apple pomace, based on a concentration factor of 2x. A tolerance of 1.0 ppm is needed for cottonseed hulls based on the 1.3x concentration factor and HAFT residues of 0.5 ppm.

Table 4. Tolerance Reassessment Summary for Azinphos methyl.			
Commodity	Current Tolerance (ppm)	Tolerance Reassessment (ppm)	Comment/*Correct Commodity Definition*
Tolerances listed under 40 CFR §180.154 (a):			
Alfalfa	2	2	
Alfalfa, hay	5	5	
Almonds	0.3	0.2	The U.S tolerance can be lowered to harmonize with the corresponding Codex MRL.
Almonds, hulls	10	5	The U.S tolerance can be lowered to harmonize with the corresponding Codex MRL.
Apples	2	2	
Apricots	2	Revoke	No registered use.
Artichokes	2	Revoke	Not supported. [a]
Barley, grain	0.2	Revoke	No registered use.
Barley, straw	2	Revoke	No registered use.
Beans, dry	0.3	Revoke	No registered use.
Beans, snap	2	Revoke	No registered use.
Birdfoot trefoil	2	2	
Birdfoot trefoil hay	5	5	
Blackberries, boysenberries, loganberries, raspberries	2	8	Residues of 7.6 ppm occurred from registered use on lower part of the cane with a 3-day PHI. *Caneberries*
Blueberries	5	5	
Broccoli	2	2	
Brussels sprout	2	Revoke	
Cabbage	2	TBD	Data forthcoming from IR-4.
Cattle, fat	0.1	Revoke	40 CFR §180.6(a)(3) situation exists.
Cattle, mbyp	0.1	Revoke	
Cattle, meat	0.1	Revoke	
Cauliflower	2	TBD	Data forthcoming from IR-4
Celery	2	Revoke	Not supported.
Cherries	2	2	
Citrus fruits	2	2	
Clover	2	Revoke	No registered use.
Clover, hay	5	Revoke	No registered use.
Cottonseed	0.5	0.5	
Crabapples	2	2	

Table 4. Tolerance Reassessment Summary for Azinphos methyl.			
Commodity	Current Tolerance (ppm)	Tolerance Reassessment (ppm)	Comment/*Correct Commodity Definition*
Cranberries	2	0.5	The U.S tolerance can be lowered to harmonize with the corresponding Codex MRL.
Cucumbers	2	2	
Eggplants	0.3	Revoke	Not supported.
Filberts	0.3	0.3	
Goats, fat	0.1	Revoke	40 CFR §180.6(a)(3) situation exists
Goats, mbyp	0.1	Revoke	
Goats, meat	0.1	Revoke	
Gooseberries	5	Revoke	No registered use.
Grapes	5	4	The U.S tolerance can be lowered to harmonize with the corresponding Codex MRL.
Grass, pasture (green)	2	Revoke	No registered use.
Grass, pasture, hay	5	Revoke	No registered use.
Horses, fat	0.1	Revoke	40 CFR §180.6(a)(3) situation exists
Horses, mbyp	0.1	Revoke	
Horses, meat	0.1	Revoke	
Kiwi fruit	10	Revoke	No registered use.
Melons	2	2	
Nectarines	2	Revoke	Covered by the tolerances for peaches.
Oats, grain	0.2	Revoke	No registered use.
Oats, straw	2	Revoke	No registered use.
Onions	2	2	
Parsley, leaves	5	5	
Parsley, roots	2	2	
Peaches	2	4	The U.S. tolerance can be increased to harmonize with the corresponding Codex MRL.
Pears	2	2	
Peas, black-eyed	0.3	Revoke	No registered use.
Pecans	0.3	0.3	
Peppers	0.3	Revoke	Not supported.
Pistachios	0.3	0.3	
Plums (fresh prunes)	2	2	

Table 4. Tolerance Reassessment Summary for Azinphos methyl.			
Commodity	Current Tolerance (ppm)	Tolerance Reassessment (ppm)	Comment/*Correct Commodity Definition*
Potatoes	0.3	0.2	The U.S tolerance can be lowered to harmonize with the corresponding Codex MRL.
Quinces	2	2	
Rye, grain	0.2	0.2	
Rye, straw	2	2	
Sheep, fat	0.1	Revoke	40 CFR §180.6(a)(3) situation exists.
Sheep, mbyp	0.1	Revoke	
Sheep, meat	0.1	Revoke	
Soybeans	0.2	Revoke	No registered use.
Spinach	2	Revoke	No registered use.
Strawberries	2	2	
Sugarcane	0.3	0.3	
Tomatoes (pre- and post-H)	2	2	*Tomatoes*
Walnuts	0.3	TBD	Additional data are forthcoming.
Wheat, grain	0.2	Revoke	No registered use.
Wheat, straw	0.2	Revoke	No registered use.
Tolerances listed under 40 CFR §180.154 (b):			
Pomegranates	0.1	0.1	
Tolerances listed under 40 CFR §180.154a:			
Milk	0.04	Revoke	40 CFR §180.6(a)(3) situation exists.
Tolerances listed under 40 CFR §185.2225:			
Soybean oil	1	Revoke	No registered use.
Tolerances listed under 40 CFR §186.2225:			
Dried citrus pulp	5	Revoke	Residues do not concentrate in this fraction.
Sugarcane bagasse	1.5	Revoke	Not a significant livestock feed item.
Tolerances needed under 40 CFR §180.154 (a):			
Cotton gin byproducts	none	TBD	Residue data required.
Tolerances needed under 40 CFR §185.2225:			
Citrus oil	none	15	
Tolerances needed under 40 CFR §186.2225:			
Apple, wet pomace	none	4	
Cottonseed hulls	none	1	

[a] CBRS No. 16871, DP Barcode D222840, 6/28/96, F. Fort.

[b] TBD = To be determined. Tolerance cannot be determined at this time because additional data are required.

Codex Harmonization

The Codex Alimentarius Commission has established maximum residue limits (MRLs) for azinphos methyl residues in/on various plant and animal commodities (see *Guide to Codex Maximum Limits For Pesticide Residues, Part A.1, 1995*). A comparison of the Codex MRLs and the corresponding U.S. tolerances is presented in Table 5.

The following conclusions can be made regarding efforts to harmonize the U.S. tolerances with the Codex MRLs: The U.S. tolerances for almonds, grapes, and potatoes can be decreased and the tolerance for peaches can be increased to harmonize with the Codex MRLs.

Table 5.Codex MRLs for azinphos methyl and applicable U.S. tolerances.

Codex			Reassessed U.S. Tolerance (ppm)	Recommendation and Comments
Commodity (As Defined)	MRL (mg/kg)	Step		
Alfalfa forage (green)	2	CXL	2	
Almonds	0.2	CXL	0.2	
Apricot	2	CXL	Revoked	No registered use in the U.S.
Broccoli	1	CXL	2	Additional data are required to assess the U.S. tolerance.
Brussels sprouts	1	CXL	2	Additional data are required to assess the U.S. tolerance.
Celery	2	CXL	Revoked	Not supported.
Cereal grains	0.2	CXL	0.2 (rye)	
Citrus fruit	2	CXL	2	
Cotton seed	0.2	CXL	0.5	The registered U.S. use pattern precludes lowering the tolerance to harmonize with the Codex MRL.
Fruits (except as otherwise noted)	1	CXL	2-5	The registered U.S. use patterns preclude lowering tolerances to harmonize with Codex MRLs.
Grapes	4	CXL	4	
Kiwifruit	4	CXL	Revoked	No registered use in U.S.
Melons, except watermelon	2	CXL	2	
Pea vines (green)	5	CXL	none	
Peach	4	CXL	4	

(continued)

Table 5.Codex MRLs for azinphos methyl and applicable U.S. tolerances.				
Codex			Reassessed U.S. Tolerance (ppm)	Recommendation and Comments
Commodity (As Defined)	MRL (mg/kg)	Step		
Potato	0.2	CXL	0.2	
Soya bean forage (green)	2	CXL	none	
Soya bean (dry)	0.2	CXL	Revoked	
Sunflower seed	0.2	CXL	none	
Vegetables (except as otherwise noted)	0.5	CXL	2-5	The registered U.S. use patterns preclude lowering tolerances to harmonize with Codex MRLs.

b. Dietary Risk Assessment (Food Sources)

i. Acute Dietary Risk (Tier 1/2/3)

The Agency uses a tiered approach to perform acute dietary exposure and risk assessments as outlined in the memorandum dated June 13, 1996 (D. Edwards). This approach allows the Agency to conserve resources.

Tier 1:

HED conducted a detailed acute dietary risk analysis estimating the distribution of single-day exposures for the overall U.S. population and certain subgroups. The analysis included all currently registered uses of azinphos methyl. The analysis evaluates individual food consumption as reported by respondents in the USDA 1977-78 Nationwide Food Consumption Survey (NFCS) and accumulates exposure to the chemical for each commodity. Each analysis assumes uniform distribution of azinphos methyl in the commodity supply. The assessment assumes tolerance level residues and that 100% of the crop is treated with azinphos methyl. The LOEL from the acute neurotoxicity study (1 mg/kg/day) was used to calculate the acute dietary risk.

The Margin of Exposure (MOE) is a measure of how close the exposure comes to the NOEL (the highest dose at which no effects were observed in the toxicology test), and is calculated as the ratio of the NOEL to the exposure [MOE = NOEL (mg/kg/day) ÷ Exposure (mg/kg/day)]. Generally, acute dietary MOEs greater than 100 tend to cause no concern when results are compared to animal-derived data. However, in the case of azinphos methyl, an additional UF of 3 is required for the acute dietary risk assessment, because the acute neurotoxicity study did not identify a NOEL. In place of a NOEL, the LOEL was used to calculate risk, and the ratio of the

LOEL to the exposure is compared to a MOE of 300 to account for the lack of a NOEL from the critical acute neurotoxicity study. At a tier 1 level of analysis, using the high-end exposure, presently registered commodities result in the following MOEs given in table 6. At the 95th percentile of exposure, presently registered commodities result in MOEs that are slightly higher, but still much less than the acceptable MOE of 300.

Table 6. Acute MOEs

Population Subgroups	High-End Exposure (mg/kg/day)	MOE
U.S. General Population	0.14	7
Infants and Children	0.3	3
Children (1-6 years old)	0.3	3
Females (13+ years)	0.08	12.5
Males (13+ years)	0.06	17

The results of this tier 1 analysis indicate that azinphos methyl in the diet represents a serious risk concern for acute exposure both for existing and proposed uses.

Tier 2:

Because of the risk estimates resulting at the tier 1 level of assessment, the tier 2 level was skipped, and an acute dietary assessment was performed by the registrant using Monte Carlo techniques (tier 3).

Tier 3:

The registrant submitted an acute dietary exposure assessment for azinphos methyl using Monte Carlo (MC) analysis. The exposure assessment has been reviewed by HED. **Exposure at the 99.9th percentile as calculated in the analysis exceed HED's levels of concern, i.e., all MOEs calculated for various populations were less than the acceptable MOE of 300.** Several deficiencies in the assessment were noted. These include: the use of Doane percent crop-treated (%CT) data (as opposed to BEAD's, in some cases, higher estimates), the miscalculation of 95th percentile monitoring data values, the inappropriate use of monitoring data for non-blended commodities, inadequate support for the use of processing data and processing factors, and lack of supporting residue data files (D. Miller, D245496, 4/29/98). HED believes the methodology used in the current assessment underestimates the dietary risk of azinphos methyl for all age groups. The MC analysis should be redone using EPA standard methodologies and assumptions (see memo D. Miller).

The residue values used in the exposure assessment were from monitoring data, which is based on composited samples. Residue data from composited samples are inappropriate for acute

dietary exposure assessments. A distribution of residues on individual pieces of fruit or vegetable treated with azinphos methyl would be the appropriate dataset for use in a Monte Carlo analysis for acute dietary exposure. Also, the consumption data used in the assessment were not provided. Therefore, this acute dietary exposure assessment is unacceptable and cannot be used for regulatory purposes.

ii. Chronic Dietary Risk

The chronic dietary exposure estimate is used to calculate the lifetime risk of consuming an average amount of azinphos methyl residues in the diet. The Dietary Risk Estimate System (DRES) analysis used to determine this exposure and risk used percent-crop-treated data and anticipated residue data to calculate the Anticipated Residue Concentration (ARC) for the general U.S. population and 22 population subgroups. This is not a worst-case estimate for chronic dietary exposure and risk, but a highly refined assessment using either FDA monitoring data or field trial data adjusted with percent crop-treated information. The appropriate toxicological endpoint used for a chronic dietary exposure and risk analysis is the RfD. As previously defined, the RfD is 0.0015 mg/kg/day. Existing tolerances (i.e., published tolerances) result in an ARC which represents 13% of the RfD for the U.S. general population. The most highly exposed subgroup, Non-Nursing Infants (<1 year old), occupies 54% of the RfD and Children (1-6 years old) occupies 33% of the RfD. Based on the risk estimates calculated in this analysis, it appears that the chronic risk contributed to the dietary risk from the registered uses of azinphos methyl, is not of concern.

Section 408(b)(2)(E) requires that if a tolerance relies on anticipated or actual residue levels, that the Agency make a determination every five years as to the reliability of the data, i.e., that the current residue levels are not above the levels relied on. To provide for the periodic evaluation of these anticipated residues, the Agency will require under Section 408(b)(2)(E) residue data to be submitted every 5 years as long as the tolerances remain in force.

Section 408(b)(2)(F) requires that if a tolerance relies on percent crop-treated data, that the Agency make a determination as to the reliability of the data. Percent crop-treated estimates are derived from federal and private market survey data. Typically, a range is assumed for the exposure assessment. By using this upper end estimate of percent crop treated, the Agency is reasonably certain that exposure is not understated for any significant population subgroup. Additionally, the DRES modeling used in estimating chronic dietary risk uses regional consumption information to estimate exposure for four population subgroups that are geographically based regions of the United States. To provide for the periodic evaluation of these estimates of percent crop-treated, the Agency will require under Section 408(b)(2)(F) percent crop-treated data to be submitted every 5 years as long as the tolerances remain in force.

c. Exposure from Drinking Water

There is no established Maximum Contaminant Level (MCL) for residues of azinphos methyl in

drinking water. No health advisory levels for azinphos methyl in drinking water have been established.

i. Ground water (modeling/monitoring)

A screening level assessment (tier 1) that provides estimates of the concentration of azinphos methyl in ground water was conducted. This tier 1 assessment used SCI-GROW, an empirical model based on actual ground-water monitoring data from small-scale prospective ground-water monitoring studies, to estimate upper bound concentrations of a chemical in vulnerable ground water. The SCI-GROW model estimated a 90-day peak average concentration of 0.325 ppb for azinphos methyl in ground water. This value was compared to drinking water levels of concern (DWLOCs) calculated for both acute and chronic effects of azinphos methyl. Because the concentration of pesticides in ground water is not expected to fluctuate widely, a single value was selected for acute and chronic exposure assessments.

ii. Surface water (modeling/monioring)

Model estimates for maximum concentrations of azinphos methyl in surface water were not used for acute exposure assessment because the exposure to azinphos methyl residues in food alone exceed HED's level of concern for acute dietary risk. Any additional exposure to azinphos methyl through drinking water would only cause acute risk estimates to further exceed our level of concern. The DWLOC for all subpopulations for acute exposure and effects of azinphos methyl is zero. Model estimates for average concentrations of azinphos methyl in surface water for comparison against drinking water levels of concern for chronic effects of azinphos methyl were not available.

d. Drinking Water Risk

The Agency has calculated drinking water levels of concern for acute and chronic exposures to azinphos methyl in drinking water for the general U.S. population, females (13+), children (1-6 years old), and non-nursing infants (< 1 year old), respectively.

For chronic (non-cancer) exposure to azinphos methyl, the drinking water levels of concern (DWLOCs) are: 45, 39, 10, and 7 ppb for the subpopulations listed above, respectively. To calculate the DWLOC for chronic (non-cancer) exposure relative to a chronic toxicity endpoint, the chronic dietary food exposure (from DRES) was subtracted from the RfD to obtain the acceptable chronic (non-cancer) exposure to azinphos methyl in drinking water. DWLOC values were then calculated using default body weights (70 kg for adult males, 60 kg for adult females, and 10 kg for children) and drinking water consumption figures (2 L/day for adults and 1 L/day for children).

In effect, for acute exposure to azinphos methyl, the drinking water level of concern (DWLOCs) for all subpopulations is zero. **Because the exposure to residues from food alone exceeds**

HED's level of concern for acute dietary exposure, any additional exposure to azinphos methyl in drinking water would lead to risk estimates that further exceed HED's level of concern. To calculate the DWLOC for acute exposure relative to an acute toxicity endpoint, the acute dietary food exposure (from the DRES analysis) was subtracted from the ratio of the acute NOEL (used for acute dietary assessments) to the "acceptable" MOE for aggregate exposure to obtain the acceptable acute exposure to azinphos methyl in drinking water. DWLOC values were calculated using default body weights and conumption values as described above.

Population Group	DWLOC (ppb) for Chronic Exposure Assessment	DWLOC (ppb) for Acute Exposure Assessment	Ground Water* Concentration Estimate (ppb)		Surface Water** Concentration Estimate (ppb)	
			max.	min.	max.	min.
General U.S./Hispanic	45	0	0.325		N/A	N/A
Females (13-19 years old)	39	0	0.325		N/A	N/A
Children (1-6 years old)	10	0	0.325		N/A	N/A
Infants. non-nursing (<1 year old)	7	0	0.325		N/A	N/A

* For ground water the maximum and minimum concentration estimate are considered the same for purposes of comparison against the DWLOC values. ** N/A = not available.

The estimated maximum concentration of azinphos methyl in ground water (from SCI-GROW) is 0.325 ppb. The estimated average concentration of azinphos methyl in ground water is also 0.325 ppb. [Note: For the purposes of the screening-level assessment, the maximum and average concentrations in ground water are not believed to vary significantly.] The estimated average concentration of azinphos methyl in ground water is less than HED's drinking water levels of concern for azinphos methyl in in all subpopulations. The estimated concentration of azinphos methyl in ground water for acute exposure assessments is also 0.325 ppb. As stated above, because the exposure to azinphos methyl from food sources alone exceeds HED's levels of concern for acute dietary risk, any additional exposure through drinking water is unacceptable.

Estimates of the concentration of azinphos methyl in surface water were not available for comparison against the DWLOC values for chronic exposure to azinphos methyl in drinking water.

4. Occupational and Residential Exposure and Risk Characterization

a. Use Patterns and Formulation Summary

Azinphos methyl, O,O-Dimethyl S-[(4-oxo-1,2,3-benzotriazin-3(4H)-

(49)

yl)methyl]phosphorodithioate is an organophosphate insecticide. Azinphos methyl is formulated as a liquid (10.0 to 34.9 percent active ingredient), a manufacturing product (88.1 percent active ingredient), and a wettable powder (35.0 to 54.9 percent active ingredient). Some wettable powder formulations are contained in water-soluble packaging. It is registered for use on a variety of terrestrial food/feed and on-food crops. **At this time, products containing azinphos methyl are intended only for agricultural uses (i.e., there are no residential uses).** There are no registered residential uses of azinphos methyl. Therefore, no exposure or risk calculations for residential uses are warranted. Azinphos methyl is a restricted use pesticide (RUP).

The following equipment is used to apply azinphos methyl: aircraft (both fixed-wing and helicopters), chemigation equipment, groundboom sprayer, airblast sprayer, low pressure handwand, high pressure sprayer, and backpack sprayer.

b. Applicator, Mixer-Loader, Handler Exposure and Assumptions

Short-term and intermediate-term dermal and inhalation exposure assessments were made using Pesticide Handlers Exposure Database (PHED) Version 1.1 surrogate data. ***No chemical-specific handler data were submitted.*** Ten major exposure scenarios were identified. For each scenario, exposures were determined for one or more crops, which were chosen to be representative of the typical range of the amount of active ingredient handled daily (ie., combination of application rate and area treated). While some larger application rates appear on some labels, it is believed that the rates used are more realistic for assessment purposes. Use of the larger rates might change the results in some cases, but not substantially. The treatment scenario (specific crops, application rates, and acres treated) used for each of 10 major exposure scenarios identified are given below:

(1a) mixing/loading liquids for aerial/chemigation application (cotton treated with 0.13 - 0.75 lb ai/A and tomatoes treated with 0.375 - 1.5 lb ai/A, 350 acres treated for each scenario);
(1b) mixing/loading liquids for groundboom application (potatoes treated with 0.375 - 0.75 lb ai/A over 80 acres, and tomatoes treated with 0.375 - 1.5 lb ai/A over 50 acres);
(1c) mixing/loading liquids for airblast sprayer application (pecans treated with 1.5 - 2 lb ai/A, citrus treated with 1.25 - 2 lb ai/A, grapes treated with 0.75 - 1 lb ai/A, apples treated with 0.5 - 1 lb ai/A, and stone fruits treated with 0.875 - 2 lb ai/A, 20 acres treated for all scenarios);
(2a) mixing/loading wettable powders for aerial application/chemigation irrigation (alfalfa treated with 0.25 - 0.5 lb ai/A, tomatoes treated with 0.375 - 1.5 lb ai/A, over 350 acres) ;
(2b) mixing/loading wettable powders for groundboom application (potatoes treated with 0.375 - 0.75 lb ai/A over 80 acres, and tomatoes treated with 0.375 - 1.5 lb ai/A over 50 acres);
(2c) mixing/loading wettable powders for airblast sprayer application (almonds treated with 1.5 - 2 lb ai/A, citrus treated with 1.25 - 2 lb ai/A, grapes treated with 0.75 - 1 lb ai/A, apples treated with 1 - 1.5 lb ai/A, and stone fruits treated with 0.875 -2 lb ai/A, 20 acres treated for each scenario);

(3) applying sprays with fixed-wing aircraft (cotton treated with 0.13 - 0.75 lb ai/A and tomatoes treated with 0.375 - 1.5 lb ai/A, both scenarios over 350 acres);
(4) applying sprays with helicopter (cotton and tomatoes with same treatment scenario as in (3) above) ;
(5) applying sprays using a groundboom sprayer (potatoes treated with 0.375 - 0.75 lb ai/A over 80 acres, and tomatoes treated with 0.375 - 1.5 lb ai/A over 50 acres);
(6) applying sprays using an airblast sprayer (same treatment scenario as in (2c) above);
(7) mixing/loading/applying sprays using a low pressure hand wand, spot treatment (ornamentals treated with 0.01 - 0.04 lb ai/gal. at 40 gallons);
(8) mixing/loading/applying sprays using a high pressure hand wand, greenhouse (ornamentals treated with 0.01 - 0.04 lb ai/gal. at 1000 gallons);
(9) mixing/loading/applying sprays using a backpack sprayer, spot treatment (same scenario as (7) above);
(10) flagging during aerial application, sprays (cotton treated with 0.13 -0.75 lb ai/A over 350 acres).

Table 7 provides **short-term and intermediate-term dermal exposure and risk estimates** for each of the 10 major exposure scenarios. Table 8 provides **short-term and intermediate-term inhalation exposure and risk estimates** for each of the 10 major exposure scenarios. A range of risks (MOEs), based on minimum and maximum application rates, is given for each of the scenarios with baseline exposure, exposure with additional protective clothing (PPE), and with engineering controls. For the baseline exposure, the worker is assumed to be wearing long pants, long sleeve shirt, no gloves, and there is open mixing/loading, and an open cab tractor. Additional PPE includes a double layer of clothing and gloves (used in scenarios 1,2,5,6,7,8, and 9), or include a double layer of clothing, only (scenario 10). The engineering controls varied for each scenario as follows:

Scenario 1: Closed mixing system, single layer of clothing with chemical resistant gloves.
Scenario 2: Water soluble packets no gloves.
Scenario 3 and 4: Enclosed cockpit, single layer clothing, no gloves.
Scenario 5: Enclosed cab, single layer clothing no gloves.
Scenario 6: Enclosed cab, single layer clothing and chemical resistant gloves.
Scenario 10: Enclosed cab, single layer clothing no gloves.

Potential daily exposure is calculated using the following formula:

Daily Exp. (mg ai/day) = Unit Exp. (mg ai/lb ai) x Max. Appl. Rate (lb ai/acre) x Max. Area Treated (acres/day)

These calculations of daily exposure to azinphos methyl by handlers are used to calculate the daily dose to those handlers.

The daily dose is calculated using the following formula:

Daily Dose (mg ai/kg/day) = Daily Exp. (mg ai/day)/ body weight (kg)

These calculations of daily dose of azinphos methyl received by handlers are used to assess the dermal risk to those handlers. The short-term and intermediate-term MOEs were calculated using the following formula:

MOE = NOEL (mg/kg/day)/ Daily Dose (mg/kg/day)

c. Occupational Risk Assessment/Characterization

i. Risk from Dermal and Inhalation Exposures

These calculations of daily dose of azinphos methyl by handlers are used to assess the risk to those handlers. For the short-term dermal risk assessment, a NOEL of 0.56 mg/kg/day (taken directly from the 21-day dermal toxicity study in rats) was used along with a 70 kg body weight. For the short-term dermal assessment, no dermal absorption factor was used because the toxicological endpoint was from a dermal study. For the intermediate-term dermal risk assessment, an equivalent dermal dose of 0.36 mg/kg/day was derived by using the NOEL from a one year oral toxicity study in dogs (0.146 mg/kg/day) and applying a dermal absorption factor (0.42) from a dermal absorption study. The inhalation risk assessment used a NOEL of 0.32 mg/kg/day* and a 70 kg body weight. No inhalation absorption data are available, therefore 100 percent absorption was assumed. *[Note:The inhalation endpoint (0.0012 mg/L) taken directly from the subchronic inhalation study in rats, was converted for use in the inhalation risk assessments through the following equation: [(0.0012 mg/L/day) (8.46 L/hr.) (6 hrs.) ÷ (0.190 kg)] = 0.32 mg/kg/day. The 0.190 kg is the body weight of the test animal (rat).

Table 7 below provides short-term (based on a NOEL of 0.56 mg/kg/day) and intermediate-term (based on an equivalent dermal dose of 0.36 mg/kg/day) dermal risk estimates for the 10 scenarios.

Table 7. Short- and Intermediate-Term Dermal Risk Estimates for Mixer/Loader, Handlers of Azinphos Methyl									
Exposure Scenario	Unit of Exposure: Baseline (2.9 mg/ lb ai)			Unit of Exposure: Additional PPE (0.025 mg/lb ai)			Unit of Exposure: Eng. Controls (0.009 mg/lb ai)		
	Dose range (mg/kg/day)	MOE Range		Dose range (mg/kg/day)	MOE Range		Dose range (mg/kg/day)	MOE Range	
		short-term	interm-term		short-term	interm-term		short-term	interm-term
1(a)	10.9 - 21.8	All <1	All <1	0.1 - 0.19	3 - 6	2 - 4	0.006 - 0.0675	8 - 93	5 - 60
1(b)	2.5 - 3.1	All <1	All <1	0.021 - 0.027	21 - 27	13 - 17	0.008 - 0.01	56 - 70	36 - 45
1(c)	0.8 - 1.7	All <1	All <1	0.007 - 0.014	40 - 80	26 - 51	0.0025 - 0.005	112 - 224	72 - 140
Exposure Scenario	Unit of Exposure: Baseline (3.8 mg/lb ai)			Unit of Exposure: Additional PPE (0.089 mg/lb ai)			Unit of Exposure: Eng. Controls (0.02 mg/lb ai)		
	Dose range (mg/kg/day)	MOE Range		Dose range (mg/kg/day)	MOE Range		Dose range (mg/kg/day)	MOE Range	
		short-term	interm-term		short-term	interm-term		short-term	interm-term
2(a)	9.5 - 28.5	All <1	All <1	0.22 - 0.67	0.6 - 3	< 2	0.05 - 0.15	3 - 11	2 - 7
2(b)	3.3 - 4.1	All <1	All <1	0.08 - 0.10	6 - 7	3 - 4	0.02	28	18
2(c)	1.1 - 2.2	All <1	All <1	0.025 - 0.05	11 - 22	14 - 7	0.006 - 0.01	56 - 93	36 - 60
Exposure Scenario	Unit of Exposure: Baseline (mg/lb ai)			Unit of Exposure: Additional PPE (mg/lb ai)			Unit of Exposure: Eng. Controls (0.005 mg/lb ai)		
	Dose range (mg/kg/day)	MOE Range		Dose range (mg/kg/day)	MOE Range		Dose range (mg/kg/day)	MOE Range	
								short-term	interm-term
3	See Eng. Controls	See Eng. Controls		See Eng. Controls	See Eng. Controls		0.02 - 0.038	15 - 28	9 - 18
Exposure Scenario	Unit of Exposure: Baseline (mg/lb ai)			Unit of Exposure: Additional PPE (mg/lb ai)			Unit of Exposure: Eng. Controls (0.0021 mg/lb ai)		
	Dose range (mg/kg/day)	MOE Range		Dose range (mg/kg/day)	MOE Range		Dose range (mg/kg/day)	MOE Range	
								short-term	interm-term
4	See Eng. Controls	See Eng. Controls		See Eng. Controls	See Eng. Controls		0.008 - 0.016	35 - 70	23 - 45

Table 7. Short- and Intermediate-Term Dermal Risk Estimates for Mixer/Loader. Handlers of Azinphos Methyl									
Exposure Scenario	Unit of Exposure: Baseline (0.015 mg/lb ai)			Unit of Exposure: Additional PPE (0.01 mg/lb ai)			Unit of Exposure: Eng. Controls (0.0067 mg/lb ai)		
	Dose range (mg/kg/day)	MOE Range		Dose range (mg/kg/day)	MOE Range		Dose range (mg/kg/day)	MOE Range	
		short-term	interm-term		short-term	interm-term		short-term	interm-term
5	0.013 - 0.016	35 - 43	23 - 28	0.009 - 0.011	51 - 62	33 - 40	0.006 - 0.007	80 - 93	51 - 60
Exposure Scenario	Unit of Exposure: Baseline (0.36 mg/lb ai)			Unit of Exposure: Additional PPE (0.122 mg/lb ai)			Unit of Exposure: Eng. Controls (0.016 mg/lb ai) (gloves)		
	Dose range (mg/kg/day)	MOE Range		Dose range (mg/kg/day)	MOE Range		Dose range (mg/kg/day)	MOE Range	
		short-term	interm-term		short-term	interm-term		short-term	interm-term
6	0.10 - 0.21	2 - 5	1 - 3	0.035 - 0.07	8 - 16	5 - 10	0.005 - 0.009	62 - 112	40 - 72
Exposure Scenario	Unit of Exposure: Baseline (103.8 mg/lb ai)			Unit of Exposure: Additional PPE (3.2 mg/lb ai)			Unit of Exposure: Eng. Controls (mg/lb ai) NONE		
	Dose range (mg/kg/day)	MOE Range		Dose range (mg/kg/day)	MOE Range		Dose range (mg/kg/day)	MOE Range	
		short-term	interm-term		short-term	interm-term		short-term	interm-term
7	2.4	<1	<1	0.073	7	5	None	None	None
Exposure Scenario	Unit of Exposure: Baseline (3.4 mg/lb ai)			Unit of Exposure: Additional PPE (1.3 mg/lb ai)			Unit of Exposure: Eng. Controls (mg/lb ai) NONE		
	Dose range (mg/kg/day)	MOE Range		Dose range (mg/kg/day)	MOE Range		Dose range (mg/kg/day)	MOE Range	
		short-term	interm-term		short-term	interm-term		short-term	interm-term
8	1.9	<1	<1	0.743	<1	<1	None	None	None
Exposure Scenario	Unit of Exposure: Baseline (2.5 mg/lb ai)			Unit of Exposure: Additional PPE (1.26 mg/lb ai)			Unit of Exposure: Eng. Controls (mg/lb ai) NONE		
	Dose range (mg/kg/day)	MOE Range		Dose range (mg/kg/day)	MOE Range		Dose range (mg/kg/day)	MOE Range	
		short-term	interm-term		short-term	interm-term		short-term	interm-term
9	0.06	9	6	0.03	19	12	None	None	None

Table 7. Short- and Intermediate-Term Dermal Risk Estimates for Mixer/Loader, Handlers of Azinphos Methyl									
Exposure Scenario	Unit of Exposure: Baseline (0.01 mg/lb ai)			Unit of Exposure: Additional PPE (0.007 mg/lb ai)			Unit of Exposure: Eng. Controls (0.0002 mg/lb ai)		
	Dose range (mg/kg/day)	MOE Range		Dose range (mg/kg/day)	MOE Range		Dose range (mg/kg/day)	MOE Range	
		short-term	interm-term		short-term	interm-term		short-term	interm-term
10	0.0375	15	9	0.03	19	12	0.0008	700	450

The calculations of **dermal** risk in the above table indicate that the MOEs **are** equal to, or greater than 100 at **baseline** for short-term or intermediate-term risk for **NO** scenarios:

With **Additional PPE** MOEs **are** equal to, or greater than 100 for short-term or intermediate-term risk for **NO** scenarios.

Using **Engineering Controls** MOEs for the following scenarios **are** equal to, or greater than 100:

(for short-term risk)

- (1c) mixing/loading liquids for airblast application (all rates analyzed);
- (6) applying sprays with an airblast sprayer (at 1 lbs ai/acre);
- (10) flagging liquid sprays for aerial application (at 0.75 lbs ai/acre).

(For intermediate-term risk)

- (1c) mixing/loading liquids for airblast application (at 1.25 lbs ai/acre);
- (10) flagging liquid sprays for aerial application (at 0.75 lbs ai/acre).

The calculations of risk indicate that the MOEs **are not** equal to, or greater than 100 despite maximum mitigation measures including additional PPE and engineering controls (where appropriate) for all remaining scenarios.

There were no data for:

- (3) Baseline and additional PPE for liquids aerial application with a fixed-wing aircraft.
- (4) Baseline and additional PPE for liquids aerial application with a helicopter.

Table 8 below provides **inhalation risk** estimates for the 10 major exposure scenarios for any time period of exposure.

Table 8. Inhalation Risk Estimates (Any Time Period) for Mixer/Loader, Handlers of Azinphos Methyl						
Exposure Scenario	Unit of Exposure: Baseline (1.2 ug/ lb ai)		Unit of Exposure: Additional PPE (0.24 ug/lb ai)		Unit of Exposure: Eng. Controls (0.08 ug/lb ai)	
	Dose range (mg/kg/day)	MOE Range	Dose range (mg/kg/day)	MOE Range	Dose range (mg/kg/day)	MOE Range
1(a)	0.0045 - 0.009	36 - 71	0.0009 - 0.0018	178 - 356	0.0003 - 0.0006	533 - 1067
1(b)	0.001	320	0.0002 - 0.0003	1600 - 1067	0.00007-0.00009	3556-4571
1 (c)	0.0003 - 0.0007	457 - 1067	0.0024 - 0.0096	2286-4571	0.00002-0.00005	6400-16000
Exposure Scenario	Unit of Exposure: Baseline (43.4 ug/lb ai)		Unit of Exposure: Additional PPE (8.68 ug/lb ai)		Unit of Exposure: Eng. Controls (0.24 ug/lb ai)	
	Dose range (mg/kg/day)	MOE Range	Dose range (mg/kg/day)	MOE Range	Dose range (mg/kg/day)	MOE Range
2(a)	0.109 - 0.326	1 - 3	0.02 - 0.065	5 - 16	0.0006 - 0.0018	178 - 533
2(b)	0.037 - 0.047	7 - 9	0.007 - 0.009	35 - 46	0.0002 - 0.0003	1067 - 1600
2 (c)	0.012 - 0.025	13 - 27	0.0025 - 0.005	64 - 128	0.00007- 0.00014	2286 - 4571
Exposure Scenario	Unit of Exposure: Baseline (ug/lb ai)		Unit of Exposure: Additional PPE (ug/lb ai)		Unit of Exposure: Eng. Controls (0.068 ug/lb ai)	
	Dose range (mg/kg/day)	MOE Range	Dose range (mg/kg/day)	MOE Range	Dose range (mg/kg/day)	MOE Range
3	See Eng. Controls	See Eng. Controls	See Eng. Controls	See Eng. Controls	0.0003 - 0.0005	640 - 1067
Exposure Scenario	Unit of Exposure: Baseline (ug/lb ai)		Unit of Exposure: Additional PPE (ug/lb ai)		Unit of Exposure: Eng. Controls (0.0018 ug/lb ai)	
	Dose range (mg/kg/day)	MOE Range	Dose range (mg/kg/day)	MOE Range	Dose range (mg/kg/day)	MOE Range
4	See Eng. Controls	See Eng. Controls	See Eng. Controls	See Eng. Controls	7×10^{-6}- 1.4×10^{-5}	22K - 45K
Exposure Scenario	Unit of Exposure: Baseline (0.7 ug/lb ai)		Unit of Exposure: Additional PPE (0.14 ug/lb ai)		Unit of Exposure: Eng. Controls (ug/lb ai) NA	
	Dose range (mg/kg/day)	MOE Range	Dose range (mg/kg/day)	MOE Range	Dose range (mg/kg/day)	MOE Range
5	0.0006 - 0.0007	457 - 533	0.0001 - 0.00015	2133 - 3200	NA	NA

Table 8. Inhalation Risk Estimates (Any Time Period) for Mixer/Loader. Handlers of Azinphos Methyl						
Exposure Scenario	Unit of Exposure: Baseline (4.5 ug/lb ai)		Unit of Exposure: Additional PPE (0.9 ug/lb ai)		Unit of Exposure: Eng. Controls (0.4 ug/lb ai)	
	Dose range (mg/kg/day)	MOE Range	Dose range (mg/kg/day)	MOE Range	Dose range (mg/kg/day)	MOE Range
6	0.0013 - 0.0025	128 - 246	0.00025-0.0005	640 -1280	0.0001 - 0.0002	1600 - 3200
Exposure Scenario	Unit of Exposure: Baseline (31.2 ug/lb ai)		Unit of Exposure: Additional PPE (ug/lb ai) NA		Unit of Exposure: Eng. Controls (ug/lb ai) NA	
	Dose range (mg/kg/day)	MOE Range	Dose range (mg/kg/day)	MOE Range	Dose range (mg/kg/day)	MOE Range
7	0.0007	457	NA	NA	NA	NA
Exposure Scenario	Unit of Exposure: Baseline (117 ug/lb ai)		Unit of Exposure: Additional PPE (23.4 ug/lb ai)		Unit of Exposure: Eng. Controls (ug/lb ai) NONE	
	Dose range (mg/kg/day)	MOE Range	Dose range (mg/kg/day)	MOE Range	Dose range (mg/kg/day)	MOE Range
8	0.067	5	0.013	25	None	None
Exposure Scenario	Unit of Exposure: Baseline (30.2 ug/lb ai)		Unit of Exposure: Additional PPE (ug/lb ai) NA		Unit of Exposure: Eng. Controls (ug/lb ai) NA	
	Dose range (mg/kg/day)	MOE Range	Dose range (mg/kg/day)	MOE Range	Dose range (mg/kg/day)	MOE Range
9	0.0007	457	NA	NA	NA	NA
Exposure Scenario	Unit of Exposure: Baseline (0.28 ug/lb ai)		Unit of Exposure: Additional PPE (0.056 ug/lb ai)		Unit of Exposure: Eng. Controls (ug/lb ai) NA	
	Dose range (mg/kg/day)	MOE Range	Dose range (mg/kg/day)	MOE Range	Dose range (mg/kg/day)	MOE Range
10	0.001	320	0.0002	1600	NA	NA

The calculations of **inhalation risk** in the above table indicate that the MOEs **are** equal to, or greater than 100 at **baseline** for risk (any time period) for the following scenario:

- (1b) mixing/loading liquids for groundboom application (at 0.75 to 1.5 lbs ai/acre);
- (1c) mixing/loading liquids for airblast application (at 1.0 to 2.0 lbs ai/acre);
- (5) applying liquids with a groundboom sprayer (at 0.75 to 1.5 lbs ai/acre);
- (6) applying liquids sprays with an airblast sprayer (at 1.0 lbs ai/acre);
- (7) mixing/loading/applying liquids with a low pressure handwand (at 0.04 lbs ai/gal);

- (9) mixing/loading/applying liquids with a backpack sprayer (at 0.04 lbs ai/gal) and,
- (10) flagging liquid aerial applications (at 0.75 lbs ai/acre).

With **Additional PPE** MOEs for the following additional scenarios **are** equal to, or greater than 100 with for risk (any time period):

- (1a) mixing/loading liquids for aerial/chemigation application (at 0.75 lbs ai/acre);
- (2c) mixing/loading wettable powders for airblast sprayer application (at 1.0 lbs ai/acre);
- (5) applying sprays using a groundboom sprayer (potatoes treated with 0.375 - 0.75 lb ai/A over 80 acres, and tomatoes treated with 0.375 - 1.5 lb ai/A over 50 acres);
- (6) applying liquid sprays with an airblast sprayer (at 1.0 and 2.0 lbs ai/acre);
- (10) flagging during aerial application, sprays (cotton treated with 0.13 -0.75 lb ai/A over 350 acres).

Using **Engineering Controls** MOEs for the following additional scenarios **are** equal to, or greater than 100 risk (any time period):

- (2a) mixing/loading wettable powders for aerial/chemigation application (at 0.5 lbs ai/acre);
- (2b) mixing/loading wettable powders for groundboom application (at 0.75 and 1.5 lbs ai/acre);
- (2c) mixing/loading wettable powders for airblast sprayer application (at 1.5 to 2.0 lbs ai/acre);
- (3) applying liquids with a fixed-wing aircraft (at 0.5 and 4.0 lbs ai/acre);
- (4) applying liquids with a helicopter (at all rates); and,

Despite maximum mitigation measures including additional PPE and engineering controls (where appropriate) MOEs for the following scenarios **are not** more than 100:

- (8) mixing/loading applying liquids with a high pressure handwand (1000 gal/day).

There were no data for the following scenarios:

- (3) Baseline and additional PPE data for liquids aerial application with a fixed-wing

aircraft. There are engineering controls data for this scenario.

- (4) Baseline and additional PPE data for liquids aerial application with a helicopter. There are engineering controls for this scenario.

ii. Risk from Aggregating Dermal and Inhalation Exposure

Because the same same toxicity endpoint (i.e., RBC cholinesterase inhibition) is applicable to both inhalation and dermal risks, it is appropriate to add these risks together to obtain a total risk for occupational exposure. As seen under i. above, the only scenarios that have acceptable MOEs are (1c), (6) and (10). Since all other scenarios result in unacceptable MOEs, aggregating dermal and inhalation risks for these will only result in even less acceptable MOEs. Therefore, only the individually acceptable scenarios will be aggregated to assess whether the risks posed by both routes together remain acceptable. The fomula used to aggregate the risks is as follows:

$$\frac{1}{\frac{1}{MOE_{dermal}} + \frac{1}{MOE_{inhalation}}}$$

Using this formula, the aggregate risk is:

(for short-term risk)

- **MOE = 111** for (1c) mixing/loading liquids for airblast application (all rates analyzed);
- **MOE = 104** for (6) applying sprays with an airblast sprayer (at 1 lbs ai/acre);
- **MOE = 220** for (10) flagging liquid sprays for aerial application (at 0.75 lbs ai/acre; with engineering controls for dermal exposure, but baseline for inhalation).

(For intermediate-term risk)

- **MOE = 107** for (1c) mixing/loading liquids for airblast application (at 1.25 lbs ai/acre);
- **MOE = 187** for (10) flagging liquid sprays for aerial application (at 0.75 lbs ai/acre; with engineering controls for dermal exposure, but baseline for inhalation).

d. Exposure and Risk from Post-Application Exposures

Azinphos methyl is widely used on crops such as apples, cotton, almonds, pears, peaches, walnuts and cherries.

A chemical-specific study, "Review of Guthion Foliar Dislodgeable Residue Study" (EPA MRID No. 408998-01) was conducted to determine the dislodgeable foliar residue (DFR) for azinphos methyl residues on apple, grape, potato, and tomato leaves. An airblast sprayer was used for application to apples and a backpack sprayer was used for all other crops in this study. In the case of grapes, it would have been more appropriate that an airblast sprayer be used (instead of the backpack sprayer). Despite the many problems with this study, HED will use portions of this data set to create a post application exposure assessment. The raw DFR data was developed into a graph which displays the Best Fit DFR for each formulation (Guthion 2S and WP50) and each crop (apples, grapes, potato, and tomato). HED has decided to primarily use data for which the R value is above 0.75. The R value is the relationship between the independent and dependent variables.

i. Post-Application Risk for Tomatoes (Cotton)

In the first tomato study, azinphos methyl, formulated as *Guthion 2S*, was applied 4 times to tomatoes at 8 to 10 day intervals at a rate of 24 oz ai/acre (ie., 1.5 lbs ai/acre) using a backpack sprayer. DFR residues were measured on 0, 1, 2, 5, 7, 14, 21, 28, and 35 DAT. The residues for the leaf samples collected were "single-sided" leaves. The table below outlines the best fit DFR and associated risk. A transfer coefficient of 750 cm^2/hr was assumed for tomatoes (equivalent to 1500 cm^2/hr of a "double-sided" leaf).

REENTRY CALCULATIONS FOR TOMATOES TREATED WITH GUTHION 2S AT 1.5 LBS AI/ACRE

Days After Treatment	Best Fit DFR ($\mu g/cm^2$)[a]	Tc (cm^2/hr)[b]	Exposure (mg/day)[c]	Dose (mg/kg/day)[d]	Short-term MOE[e]
0	0.18	750	1.08	0.015	37
2 Current REI	0.1376	750	0.8256	0.01179	48
7	0.0702	750	0.4212	0.0060	93
8	0.0613	750	0.3678	0.0053	106

a = Best Fit DFR (ug/cm^2) = foliar dislodgeable residues.
b = Transfer Coefficient (cm^2/hr) assumed 750 for high exposure crops such as tomatoes.
c = Exposure (mg/day) = [Best Fit DFR x Transfer Coefficient / 1000 (ug/mg conversion)] x 8 hours/day
d = Dose (mg/kg/day) = Exposure (mg/day) / BW (70 kg)
e = MOE = NOEL (0.56 mg/kg/day) / Daily Dose (mg/kg/day)

(60)

In a second tomato study, azinphos methyl, formulated as *Guthion WP50*, was applied 4 times to tomatoes at 8 to 10 day intervals at a rate of 24 oz ai/acre (ie., 1.5 lbs ai/acre) using a backpack sprayer. DFR residues were measured on 0, 1, 2, 5, 7, 14, 21, 28, and 35 DAT. The residues for the leaf samples collected were "single sided" leaves. The table below outlines the best fit DFR and associated risk. A transfer coefficient of 750 cm^2/hr was assumed for tomatoes (equivalent to 1500 cm^2/hr of a "double-sided" leaf).

REENTRY CALCULATIONS FOR TOMATOES TREATED WITH GUTHION 50WP AT 1.5 LBS AI/ACRE.

Days After Treatment	Best Fit DFR ($\mu g/cm^2$)[a]	Tc (cm^2/hr)[b]	Exposure (mg/day)[c]	Dose (mg/kg/day)[d]	Short-term MOE[e]
0	0.066	750	0.396	0.0057	98
1	0.062	750	0.372	0.0053	106
2	0.058	750	0.348	0.005	112
7	0.042	750	0.252	0.0036	156

a = Best Fit DFR (ug/cm^2) = foliar dislodgeable residues.
b = Transfer Coefficient (cm^2/hr) assumed 750 for high exposure crops such as tomatoes.
c = Exposure (mg/day) = [Best Fit DFR x Transfer Coefficient / 1000 (ug/mg conversion)] x 8 hours/day
d = Dose (mg/kg/day) = Exposure (mg/day) / BW (70 kg)
e = MOE = NOEL (0.56 mg/kg/day) / Daily Dose (mg/kg/day)

Discussion/Conclusions:

Acceptable short-term MOEs for this maximum application rate and crop begin on day 8 post-application for the 2S product and on day 1 post-application for the 50WP product. This means that for the 50WP, the current REI of 2 days post-application for tomatoes (1 day for cotton) is acceptable for other potentially necessary maintenance activities (eg., hoeing, scouting, thinning, staking). These study results may be implied for cotton because of the similarity of crop profile and cotton's, even lower, application rate.

ii. Post-Application Risk for Potatoes

In the first potato study, azinphos methyl, formulated as *Guthion 2S*, was applied 3 times to potatoes at 14 day intervals at a rate of 24 oz ai/acre (ie., 1.5 lbs ai/acre) using a groundboom sprayer. DFR residues were measured on 0, 1, 2, 7, 21, 28, and 35 DAT. The residues for the leaf samples collected were "single sided" leaf. The table below outlines the best fit DFR and associated risk. A transfer coefficient of 250 cm^2/hr was assumed for potatoes (equivalent to 500 cm^2/hr of a "doubles sided" leaf.

(61)

REENTRY CALCULATIONS FOR POTATOES TREATED WITH GUTHION 2S AT 1.5 LBS AI/ACRE.					
Days After Treatment	Best Fit DFR (μg/cm^2)[a]	Tc (cm^2/hr)[b]	Exposure (mg/day)[c]	Dose (mg/kg/day)[d]	Short-term MOE[e]
0	1.06	250	2.12	0.030	19
2	0.810	250	1.62	0.023	24
3	0.7088	250	1.42	0.020	28
4	0.621	250	1.02	0.015	37
13	0.187	250	0.37	0.005	112

REENTRY CALCULATIONS FOR POTATOES TREATED WITH GUTHION 2S AT 1.5 LBS AI/ACRE (WITH DFR VALUES PRORATED TO 0.75 LBS AI/ACRE)					
Days After Treatment	Best Fit DFR (μg/cm^2)[a]	Tc (cm^2/hr)[b]	Exposure (mg/day)[c]	Dose (mg/kg/day)[d]	Short-term MOE[e]
0	0.53	250	1.06	0.015	37
2	0.405	250	0.81	0.012	47
3	0.354	250	0.71	0.010	56
4	0.311	250	0.51	0.0075	75
8	0.182	250	0.36	0.005	112

a = Best Fit DFR (ug/cm^2) = foliar dislodgeable residues.
b = Transfer Coefficient (cm^2/hr) assumed 250 for low exposure crops such as potatoes.
c = Exposure (mg/day) = [Best Fit DFR x Transfer Coefficient / 1000 (ug/mg conversion] x 8 hours/day
d = Dose (mg/kg/day) = Exposure (mg/day) / BW (70 kg)
e = MOE = NOEL (0.56 mg/kg/day) / Daily Dose (mg/kg/day)

Discussion/Conclusions:

Short-term MOEs are not acceptable until day 13 post-application under the use conditions of the study. The actual maximum use rate is only 0.75 lbs ai/acre, and when the DFR values are prorated to this level, the MOE is acceptable at day 8. This means that the current REI of 2 days is unacceptable.

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In a second potato study, azinphos methyl, formulated as *Guthion WP50*, was applied 3 times to potatoes at 14 day intervals at a rate of 24 oz ai/acre (ie., 1.5 lbs ai/acre) using a groundboom sprayer. DFR residues were measured on 0, 1, 2, 7, 21, 28, and 35 DAT. The residues for the leaf samples collected were "single sided" leaves. The table below outlines the best fit DFR and associated risk. A transfer coefficient of 250 cm^2/hr was assumed for potatoes (equivalent to 500 cm^2/hr of a "double sided" leaf).

REENTRY CALCULATIONS FOR POTATOES TREATED WITH GUTHION WP50 AT 1.5 LBS AI/ACRE.

Days After Treatment	Best Fit DFR ($\mu g/cm^2$)[a]	Tc (cm^2/hr)[b]	Exposure (mg/day)[c]	Dose (mg/kg/day)[d]	Short-term MOE[e]
0	1.97	250	7.92	0.11	5
10	0.85	250	1.7	0.024	23
12	0.72	250	1.44	0.021	27
13	0.66	250	1.32	0.019	29
28	0.189	250	0.38	0.005	112

REENTRY CALCULATIONS FOR POTATOES TREATED WITH GUTHION WP50 AT 1.5 LBS AI/ACRE (WITH DFR VALUES PRORATED TO 0.75 LBS AI/ACRE).

Days After Treatment	Best Fit DFR ($\mu g/cm^2$)[a]	Tc (cm^2/hr)[b]	Exposure (mg/day)[c]	Dose (mg/kg/day)[d]	Short-term MOE[e]
0	0.985	250	1.97	0.028	20
2	0.831	250	1.66	0.024	23
3	0.765	250	1.53	0.022	26
4	0.703	250	1.41	0.020	28
10	0.425	250	0.85	0.012	47
12	0.36	250	0.72	0.010	56
13	0.33	250	0.66	0.009	62
20	0.185	250	0.37	0.005	112

REENTRY CALCULATIONS FOR POTATOES TREATED WITH GUTHION WP50 AT 1.5 LBS AI/ACRE (WITH DFR VALUES PRORATED TO 0.5 LBS AI/ACRE).					
Days After Treatment	Best Fit DFR ($\mu g/cm^2$)[a]	Tc (cm^2/hr)[b]	Exposure (mg/day)[c]	Dose (mg/kg/day)[d]	Short-term MOE[e]
0	0.66	250	1.32	0.019	30
2	0.55	250	1.12	0.016	35
3	0.51	250	1.02	0.015	37
4	0.47	250	0.94	0.013	43
10	0.28	250	0.56	0.008	70
12	0.24	250	0.48	0.007	80
13	0.22	250	0.44	0.006	93
15	0.187	250	0.37	0.005	112

a = Best Fit DFR (ug/cm^2) = foliar dislodgeable residues.
b = Transfer Coefficient (cm^2/hr) assumed 250 for low exposure crops such as potatoes.
c = Exposure (mg/day) = [Best Fit DFR x Transfer Coefficient / 1000] x 8 hours/day
d = Dose (mg/kg/day) = Exposure (mg/day) / BW (70 kg)
e = MOE = NOEL (0.56 mg/kg/day) / Daily Dose (mg/kg/day)

Discussion/Conclusions

In this study, acceptable short-term MOEs were not achieved until day 15 (after prorating the application rate to 0.5 lbs ai/acre), indicating that the current 2-day REI would not be acceptable. The same is also true after prorating the results of the study to the actual maximum use rate (0.75 lbs ai/acre).

iii. Post-Application Risk for Orchard and Citrus Crops

Measurements of field worker exposure (transfer factors) while exposed to azinphos methyl treated orchard and citrus crops have been measured by the California Department of Pesticide Regulation (CDPR). The transfer factors developed by the CDPR will be used in this assessment. The transfer factors developed by CDPR were generated using double-sided residues. However, the transfer factors were adjusted to reflect the single-sided DRF measurements collected by the registrant. It is recommended that the reentry exposure be reevaluated when the newly generated DFR data and reentry exposure database become available.

To address reentry exposure to deciduous orchard crops treated with azinphos methyl, the Apple DFR data have been used. The DFRs are presented based on a best fit regression analysis of the wettable powder formulation. The apple DRFs were the result of apples trees treated with 4 applications of 1.5 pounds active ingredient per acre. The DFRs presented in the following

tables have been prorated to reflect various application rates ranging from 2 to 0.5 pounds active per acre. According to the registrant, 1 pound active per acre is the typical rate for apples. However because the label has higher rates for apples and other orchard crops, and azinphos is acutely toxic, all rates are being considered in this assessment. The use of lower rates for potential risk mitigation if feasible should be considered. However, with a short-term dermal NOEL of 0.56 mg/kg/day, MOE's for the orchard uses are well below the Agency's recommended 100 for many uses even with the long existing reentry intervals.

Reentry tasks identified for the orchard crops are harvesting, thinning, and propping. Harvester exposure is estimated based on the range of preharvest intervals for each crop (eg., 7 days, 14 days, 21 days), as well as restricted-entry intervals imposed on the registrant by CDPR. Exposure while thinning and propping has been estimated based on the interim 48 hour Restricted Entry Interval (REI) imposed by the Agency's Worker Protection Standard (WPS). The use of poles to prop-up tree limbs with heavy fruit set is common in stone fruit crops such as plums. These exposures are much lower than those encountered while thinning fruit and harvesting.

REENTRY EXPOSURE FOR DECIDUOUS ORCHARD CROPS TREATED WITH 2 POUNDS ACTIVE INGREDIENT PER ACRE

DAT	DFR $\mu g/cm^2$	Task	Transfer Factor cm^2/hr	Estimated Exposure mg/kg/day	Short-term MOE
2	3.12	propper	90	0.03	19
2	3.12	thinner	1650	0.58	1
7	2.5	harvester	2090	0.6	0.9
14	2.2	harvester	2090	0.52	1
21	1.4	harvester	2090	0.33	2

REENTRY EXPOSURE FOR DECIDUOUS ORCHARD CROPS TREATED WITH 1.5 POUNDS ACTIVE INGREDIENT PER ACRE

DAT	DFR $\mu g/cm^2$	Task	Transfer Factor cm^2/hr	Estimated Exposure mg/kg/day	Short-term MOE
2	2.34	propper	90	0.024	23
2	2.34	thinner	1650	0.44	1.3

REENTRY EXPOSURE FOR DECIDUOUS ORCHARD CROPS TREATED WITH 1.5 POUNDS ACTIVE INGREDIENT PER ACRE

DAT	DFR µg/cm²	Task	Transfer Factor cm²/hr	Estimated Exposure mg/kg/day	Short-term MOE
7	1.9	harvester	2090	0.45	1.2
14	1.4	harvester	2090	0.33	1.7
21	1.1	harvester	2090	0.25	2.2

REENTRY EXPOSURE FOR DECIDUOUS ORCHARD CROPS TREATED WITH 1 POUND ACTIVE INGREDIENT PER ACRE

DAT	DFR µg/cm²	Task	Transfer Factor cm²/hr	Estimated Exposure mg/kg/day	Short-term MOE
2	1.56	propper	90	0.02	28
2	1.56	thinner	1650	0.29	2
7	1.26	harvester	2090	0.30	2
14	0.93	harvester	2090	0.22	2.6
21	0.7	harvester	2090	0.17	3

REENTRY EXPOSURE FOR DECIDUOUS ORCHARD CROPS TREATED WITH 0.75 POUNDS ACTIVE INGREDIENT PER ACRE

DAT	DFR µg/cm²	Task	Transfer Factor cm²/hr	Estimated Exposure mg/kg/day	Short-term MOE
2	1.17	propper	90	0.01	56
2	1.56	thinner	1650	0.29	2
7	1.26	harvester	2090	0.30	1.9
14	0.93	harvester	2090	0.22	2.6
21	0.53	harvester	2090	0.125	4.5

REENTRY EXPOSURE FOR DECIDUOUS ORCHARDS TREATED WITH 0.5 POUNDS ACTIVE INGREDIENT PER ACRE					
DAT	DFR $\mu g/cm^2$	Task	Transfer Factor cm^2/hr	Estimated Exposure mg/kg/day	Short-term MOE
2	0.77	propper	90	0.008	70
2	0.77	thinner	1650	0.15	3.7
7	0.63	harvester	2090	0.15	3.7
14	0.47	harvester	2090	0.11	5
21	0.35	harvester	2090	0.08	7

iv. Post-Application Risk for Citrus Crops

Recent DFR data following azinphos methyl applications to citrus crops are not available. However, in the CDPR Draft Azinphos Methyl Assessment, DFR's were presented based on a study submitted to California by the registrant (Chemagro at the time) that was conducted in 1970. The DFRs are reported as double sided in the CDPR report. Therefore, the corresponding transfer factor, used in the above deciduous orchard crop tables, reflects that change. The PHI and REI for citrus is 7 days except in California which has an REI of 30 days.

REENTRY EXPOSURE FOR CITRUS TREATED WITH 3.75 POUNDS ACTIVE INGREDIENT PER ACRE (WITH DFR VALUES PRORATED TO 2 POUNDS ACTIVE INGREDIENT PER ACRE)					
DAT	DFR $\mu g/cm^2$	Task	Transfer Factor cm^2/hr	Estimated Exposure mg/kg/day	Short-term MOE
7	0.59	harvester	4180	0.28	2
30	0.32	harvester	4180	0.15	3.7

v. Post-Application Risk for Caneberries and Blueberries

To address reentry exposure while harvesting caneberries and blueberries, DFR data following treatment of grapes with 0.25 pounds active per acre were used. The data were prorated to reflect the higher rate of 0.5 pounds active ingredient per acre. Some label rates reach a maximum rate of 0.75 pounds ai/acre for blueberries, and 1 pound ai/acre for caneberries. However, using these

atypically higher rates in the calculation will only worsen an already unacceptably low MOE at the 0.5 pound rate.

REENTRY EXPOSURE FOR CANEBERRIES AND BLUEBERRIES TREATED WITH 0.5 POUNDS ACTIVE INGREDIENT PER ACRE

DAT	DFR µg/cm²	Task	Transfer Factor cm²/hr	Estimated Exposure mg/kg/day	Short-term MOE
2	6.19	tying, training, topping	900	0.64	0.9
7	5.13	harvesting	900	0.52	1.1

REENTRY EXPOSURE FOR CANEBERRIES AND BLUEBERRIES TREATED WITH 0.25 POUNDS ACTIVE INGREDIENT PER ACRE

DAT	DFR µg/cm²	Task	Transfer Factor cm²/hr	Estimated Exposure mg/kg/day	Short-term MOE
2	3.1	tying, training, topping	900	0.32	1.8
7	2.56	harvesting	900	0.26	2.2

vi. Post-Application Risk for Grapes

REENTRY EXPOSURE FOR GRAPES TREATED WITH 0.5 POUNDS ACTIVE INGREDIENT PER ACRE

DAT	DFR µg/cm²	Task	Transfer Factor cm²/hr	Estimated Exposure mg/kg/day	Short-term MOE
2	6.19	cane throwing, leaf pulling, girdling	9000	6.36	0.1
7	5.13	harvesting	9000	5.28	0.1
21	3.01	harvesting	9000	3.1	0.2

REENTRY EXPOSURE FOR GRAPES TREATED WITH 0.25 POUNDS ACTIVE INGREDIENT PER ACRE

DAT	DFR µg/cm^2	Task	Transfer Factor cm^2/hr	Estimated Exposure mg/kg/day	Short-term MOE
2	3.09	cane throwing, leaf pulling, girdling	9000	3.18	0.2
7	2.56	harvesting	9000	2.62	0.2
21	1.51	harvesting	9000	1.55	0.4

Despite these limitations, the data reflect similar levels of dislodgeable residues found in other studies and reveal the slow dissipation rate for which azinphos methyl is known. The registrant is a member of the Agricultural Reentry Task Force (ARTF) which is developing a generic worker reentry exposure database. The registrant is currently conducting dislodgeable foliar residue (DFR) data on apples and cotton representing approximately 75 percent of the usage. These data are being generated in response to the Agricultural Data Call-In issued by the Agency in 1995.

Occupational Risk Characterization

Summary of handler risks

HED has serious concerns regarding occupational exposures and risks for a number of exposure scenarios during application for **pesticide handlers**. The estimated risks consider baseline protection (long pants and a long-sleeved shirt, no gloves, and an open cab or tractor), additional personal protective equipment (PPE, which includes a double layer of clothing and gloves), and engineering controls (closed application and mixing systems, and water soluble packets). For **dermal short-term and intermediate-term** exposures using baseline protection, risks expressed as MOEs were > 100 for none of the 14 major applicator/handler scenarios. Risks did not improve using additional PPE, with still no MOEs > 100 for the 14 major scenarios. Using engineering controls, short-term MOEs were > 100 for 3 out of 10 major scenarios for which engineering controls were applicable; but, only two of these have acceptable MOEs for intermediate-term exposures. **This still leaves 11 occupational exposure scenarios for which MOEs are < 100 and exceed HED's level of concern despite maximum mitigation measures.**

For **inhalation exposures (any time period)** using baseline protection, risks expressed as MOEs were > 100 for 9 out of 14 major applicator/handler scenarios. Risks improved using additional PPE with MOEs > 100 for 10 out of 14 major scenarios. Using engineering controls, MOEs were > 100 for all 9 major scenarios for which engineering controls were applicable. **However,**

(69)

Incidents

this leaves 1 occupational exposure scenario (mixing/loading/applying sprays using high pressure handwands, as in greenhouses) for which the MOE is less than 100 and exceeds HED's level of concern despite maximum mitigation measures.

When inhalation and dermal risks are aggregated, 11 occupational exposure scenarios produce unacceptable MOEs (i.e., <100).

Summary of post-application risks

In summary, **post-applicator risks** from the use of azinphos methyl WP50 formulation on **tomatoes and cotton** at the maximum labelled rate (1.5 lbs. a.i./A) result in acceptable MOEs (i.e., >100) at existing 2-day and 1-day restricted entry intervals (REIs), respectively. Post-applicator risks for uses of the 2S formulation of azinphos methyl on **potatoes** at the actual maximum application rate of 0.75 lbs. a.i./A and at the existing 2-day REI are unacceptable. Uses of the WP50 formulation on potatoes at 0.75 lbs. a.i./A, also result in unacceptable MOEs at the existing 2-day REI. Based on **apple** data, post-applicator risks for orchard crops were calculated for harvesting, propping, and thinning activities. MOEs calculated for propper activities were unacceptable, i.e., < 100, for all application rates > 1.0 lbs. a.i./A. MOEs were unacceptable for all harvesting and thinning activities regardless of the application rates and REIs. MOE calculations were unacceptable for all post-applicator risks for **citrus, grape, and berry** uses of azinphos methyl at all labelled use rates and existing REIs.

HED has serious concern for reentry workers and the post-application exposure and risk associated with all uses of azinphos methyl except its use in the WP50 formulation on cotton and tomatoes at 1.5 lbs ai/acre. Risks expressed as MOEs associated with harvesting and tending activities for all other analyzed crops were well below 100.

e. Residential and Other Non-Occupational Exposures and Risks

At this time, products containing azinphos methyl are intended only for agricultural uses. There are no registered residential uses of azinphos methyl. Therefore, no exposure or risk calculations for residential uses are warranted. Azinphos methyl is a restricted use pesticide (RUP).

f. Incident Reports

Azinphos methyl was one of 28 chemicals for which Poison Control Center data were requested. When both Poison Control Center (PCC) and California data were considered, azinphos methyl ranked sixth among 28 pesticides selected on the basis of a high incidence of pesticide poisonings, relatively high toxicity, and high usage. All of the 28 pesticides were either carbamate or organophosphate insecticides. In California it had the third highest ratio (1982-1989) for cases when the pesticide was considered the primary cause of poisoning of fieldworkers per 1,000 applications. Azinphos methyl ranked fifth on percentage of

occupational PCC cases requiring hospitalization. In terms of ratio of PCC hospital admitted cases per 1,000 pounds reported in use, azinphos methyl ranked fourth and in terms of exposures and treatment per reported use it ranked fifth.

Detailed descriptions of 134 cases submitted to the California Pesticide Illness Surveillance Program (1982-1990) were reviewed. In 62 of these cases, azinphos methyl was used alone and was judged to be responsible for the health effects. Only cases with a definite, probable or possible relationship were reviewed. Azinphos methyl ranked 20th as a cause of systemic poisoning in California and 40th as a cause of hospitalization. One individual was hospitalized in the period 1982 to 1990. A total of 53 persons had systemic illnesses or 85.5% of 62 persons. Where the crop was identified, 85% of the cases were related to tree crop use. Thirty-one of these cases occurred in 1987 including twenty-five systemic illnesses from non-occupational miscellaneous exposure due to azinphos methyl being applied to an orchard that drifted nearby to residential areas. A summary of the types of illnesses reported are given in Table 1. Most of the cases described below are reentry violations or spray drift violations. The type of spray equipment and personal protective equipment (PPE) used were not reported frequently enough to determine whether that was a factor in the incidences or not.

Table 1: Cases Due to Azinphos methyl Exposure in California Reported by Type of Illness and Year, 1982-1990

	Illness Type					
Year	*Systemic	Eye	Skin	Respir.	**Combined	Total
1982	4	-	-	-	-	4
1983	4	-	-	-	-	4
1984	3	2	-	-	-	5
1985	6	-	-	-	-	6
1986	-	1	-	-	-	1
1987	31	-	1	-	-	32
1988	3	-	-	-	-	3
1989	1	-	1	-	2	4
1990	1				2	3
Total	53	3	2	-	4	62

* Category includes cases where skin, eye, or respiratory effects were also reported

** Category includes eye/skin or eye/respiratory illnesses

California reported 9 cases of systemic poisoning due to azinphos methyl from 1990 through 1994 and one possible case of a skin rash in a worker picking pears. Four of the nine cases involved applicators. Cholinesterase tests were available for only one of these cases and was in the normal range. All four cases were considered "possible" in terms of azinphos methyl causing the reported symptoms. Four cases involved exposure to residues in a recently treated field. Two workers thinning peaches were exposed from reentering one day prior to the expiration of the reentry interval. An irrigator and a man operating a mower were also exposed apparently prior to expiration of the reentry interval. In the remaining case a traffic officer responding to a chemical spill was exposed to azinphos methyl and developed symptoms of headache and salivation. Direct overspray of azinphos methyl on a residential population resulted in 40 cases of mild to moderate poisoning symptoms. California reported four cases involving reentry into a treated field, though apparently each case involved a violation of reentry time restrictions.

In summary, an earlier review of azinphos methyl incident data (for the period 1982-1990) concluded it was a significant problem, especially for fieldworker poisoning. Many of the reported cases have involved violation of the reentry interval or exposure to spray drift. The most recent five years of data from California have shown a significant drop from the earlier 1982-1990 data. It is not clear how much of this decline is due to safer work practices and how much is due to a 1990 California requirement which calls for all applications of azinphos methyl to be reported. This latter reporting requirement might result in a decreased poisoning/application ratio. Similar drops in poisoning/application ratios for related pesticides suggest that reporting of usage for other pesticides did increase, and may be responsible for reduced incidences.

Among 28 organophosphate and carbamate pesticides, azinphos methyl was on the borderline between the top five and the other 22 in terms of various measures used to rank the hazard. Measures to reduce spray drift and enforce reentry standards are recommended to prevent poisoning from this pesticide. Other measures to reduce applicator exposure and exposure in other handlers (e.g. closed mixing/loading systems) should be considered and made consistent with requirements for the other organophosphate and carbamate insecticides that are often used as alternatives or substitutes for azinphos methyl and for each other.

5. Food Quality Protection Act Considerations

a. Cumulative Risk

Azinphos methyl is a member of the organophosphate class of pesticides. All pesticides of this class contain phosphorus and other members of this class of pesticide are numerous and include mevinphos, phorate, disulfoton, dichlorvos, monocrotophos, dimethoate, dicrotophos, oxydemeton methyl, and methamidophos, to name a few.

Section 408(b)(2)(D)(v) of the Food Quality Protection Act requires that, when considering

whether to establish, modify, or revoke a tolerance, the Agency consider "available information" concerning the cumulative effects of a particular pesticide's residues and "other substances that have a common mechanism of toxicity". The Agency believes that "available information" in this context might include not only toxicity, chemistry, and exposure data, but also scientific policies and methodologies for understanding common mechanisms of toxicity and conducting cumulative risk assessments. For most pesticides, although the Agency has some information in its files that may turn out to be helpful in eventually determining whether a pesticide shares a common mechanism of toxicity with any other substances, EPA does not at this time have the methodologies to resolve the complex scientific issues concerning common mechanism of toxicity in a meaningful way. EPA has begun a pilot process to study this issue further through the examination of particular classes of pesticides. The Agency hopes that the results of this pilot process will increase the Agency's scientific understanding of this question such that EPA will be able to develop and apply scientific principles for better determining which chemicals have a common mechanism of toxicity and evaluating the cumulative effects of such chemicals. The Agency anticipates, however, that even as its understanding of the science of common mechanisms increases, decisions on specific classes of chemicals will be heavily dependent on chemical-specific data, much of which may not be presently available.

Although at present the Agency does not know how to apply the information in its files concerning common mechanism issues to most risk assessments, there are pesticides as to which the common mechanism issues can be resolved. These pesticides include pesticides that are toxicologically dissimilar to existing chemical substances (in which case the Agency can conclude that it is unlikely that a pesticide shares a common mechanism of activity with other substances) and pesticides that produce a common toxic metabolite (in which case common mechanism of activity will be assumed).

HED does not have, at this time, available data to determine whether azinphos methyl has a common mechanism of toxicity with other substances or how to include this pesticide in a cumulative risk assessment. For the purposes of this reregistration action, therefore, HED has not assumed that azinphos methyl has a common mechanism of toxicity with other substances.

b. Aggregate Risk

Acute Aggregate Risk

The acute aggregate risk assessment for azinphos methyl will include risks associated with dietary exposure through food and water, only. Because exposure to azinphos methyl from food sources alone exceed HED's level of concern for acute dietary risk, any additional exposure through drinking water would lead to risk estimates that further exceed HED's level of concern. HED defers a calculation of aggregate risk as a result of exposures to azinphos methyl in food and water until exposures through food alone have been reduced to an acceptable level. At that time, the OPP can reconsider the extent of the contribution, if any, of azinphos methyl residues in drinking water to the acute expsoure and aggregate risk.

Chronic Aggregate Risk

The chronic aggregate risk assessment for azinphos methyl will include risks associated with dietary exposure through food and water, only, because azinphos methyl has no registered residential uses, and therefore, HED has minimal concern regarding residential exposures to azinphos methyl. Anticipated residues and percent crop-treated data for commodities with published tolerances result in an exposure to azinphos methyl through food which represents 13% of the RfD for the U.S. general population. The highest subgroup, Non-Nursing Infants (<1 year old) occupies 54% of the RfD and Children (1-6 years old) occupies 33% of the RfD. Conservative model estimates of the average concentration of azinphos methyl in ground water indicate that exposure through drinking water will be minimal. The estimated average concentration in ground water (0.325 ppb) does not exceed drinking water levels of concern (DWLOCs) for the general U.S. population, females (13+), children (1-6 years old), and infants, non-nursing (<1 year old), 45, 39, 10, and 7 ppb ppb, respectively. The estimated average concentration in ground water is much lower than the calculated DWLOCs for chronic exposure and risk assessments. Based on the risk estimates calculated in this analysis, it appears that the chronic aggregate risk from azinphos methyl in the diet and in drinking water from registered uses of azinphos methyl, is not of concern.

Therefore, taking into account estimated concentrations in ground water only, HED concludes with reasonable certainty that residues of azinphos methyl in drinking water (when considered along with other sources of exposure for which HED has reliable data) would not result in unacceptable levels of aggregate **chronic human health risk** at this time.

The Agency bases this determination on a comparison of estimated concentrations of azinphos methyl in ground water to back-calculated "levels of concern" for azinphos methyl in drinking water. These levels of concern in drinking water were determined after HED has considered all other non-occupational human exposures for which it has reliable data, including all current uses, and uses considered in this action. The estimate of azinphos methyl in ground water is derived from a water quality model that uses conservative assumptions (health-protective) regarding the pesticide transport from the point of application to ground water. Because HED considers the aggregate risk resulting from multiple exposure pathways associated with a pesticide's uses, levels of concern in drinking water may vary as those uses change. If new uses are added in the future, HED will reassess the potential impacts of azinphos methyl on drinking water as a part of the aggregate risk assessment process.

An estimate of the average concentration of azinphos methyl in surface water was not available at the time of this writing; however, residues of azinphos methyl in either ground- or surface-water-sourced drinking water are not expected to significantly impact the chronic aggregate risk assessment.

c. Endocrine Disruption

EPA is required to develop a screening program to determine whether certain substances (including all pesticides and inerts) "may have an effect in humans that is similar to an effect produced by a naturally occurring estrogen or such other endocrine effect..." The Agency is currently working with interested stakeholders, including other government agencies, public interest groups, industry and research scientists in developing a screening and testing program and a priority setting scheme to implement this program. Congress has allowed 3 years from the passage of FQPA (August 3, 1996) to implement this program. At that time, EPA may require further testing of this active ingredient and end use products for endocrine disruptor effects.

d. Special Sensitivity to Infants and Children

The application of a FQPA factor to ensure the protection of infants and children from exposure to azinphos methyl, as required by FQPA, will be determined by the FQPA Safety Factor Assessment Review Committee.

The HIARC, **based on the hazard assessment, recommends** to the FQPA Safety Committee, that the additional **10x** factor **should be removed** because:

(i) Developmental toxicity studies showed no increased sensitivity in fetuses as compared to maternal animals following *in utero* exposure in rats and rabbits.

(ii) Both a one- and a two-generation reproductive toxicity study in rats showed no increased susceptibility in pups when compared to adults.

(iii) There was no evidence of abnormalities in the development of the fetal nervous system in the pre/postnatal studies. Neither brain weight nor histopathology (nonperfused) of the nervous system was affected in the subchronic and chronic toxicity studies.

(iv) The toxicology data base is complete and there are no data gaps. There is no evidence to require a developmental neurotoxicity study.

The final recommendation on the FQPA Safety Factor, however, will be made during risk characterization by the FQPA Safety Committee.

III. RISK MANAGEMENT AND REREGISTRATION DECISION

A. Use Pattern/Labeling Rationale/Dietary Risk Mitigation Measures

THIS SECTION IS DEFERRED PENDING A MEETING/DECISION WITH SRRD ON ACUTE DIETARY RISK MITIGATION AND/OR SUBMISSION OF AN ACCEPTABLE PROBABILISTIC (MONTE CARLO) ACUTE DIETARY EXPOSURE ASSESSMENT.

B. Occupational and Residential Labeling Rationale/Risk Mitigation Measure

THIS SECTION IS DEFERRED PENDING A MEETING/DECISION WITH SRRD ON HANDLER AND POST-APPLICATION RISK MITIGATION.

IV. ACTIONS REQUIRED BY REGISTRANTS

A. Additional Generic Data Requirements

1. Toxicology Studies

None.

2. Chemistry Studies

a. Product Chemistry

Additional data are required for the Makhteshim 85% T and 85% FI (OPPTS 830.1750, 830.6313, and 830.7050) and for the Bayer 85% T (OPPTS 830.1750 and 830.7050). All product chemistry data remain outstanding for the Gowan 94% T and the Bayer 85% FI.

b. Residue Chemistry

Residue trial data are required for cauliflower, walnuts and cotton gin byproducts.

3. Occupational and Residential Exposure Studies

a. Handler Safety Requirements

Based on the risk assessment of the current uses of azinphos methyl, additional handler exposure studies are not required. The Agency is considering a dialogue with the registrant to discuss alternative mitigation possibilities for those scenarios where mitigation techniques used in the risk assessment presented here were insufficient to produce acceptable risks.

b. Post-Application Safety Requirements

Additional studies are currently being conducted by the Registrant. Pending the outcome of those studies, no additional studies are required at this time. Additional clarification of the use of this pesticide on ornamental crops would be helpful. Depending on the use scenarios, the transfer coefficients (and therefore the REIs) may range from minimal (e.g.., Christmas trees) to high (e.g., greenhouse-grown transplants). It is not clear from the current labels the extent and type of use this pesticide has on ornamentals.

B. Labeling Requirements for End-Use Products

1. Residue Chemistry

Labels bearing uses on grapes should be revised to clarify specific use rates that correspond to the PHIs listed. The labels bearing use directions for filberts and pecans should specify a 45-day PHI; the reference to shuck-split for pecans should be deleted from the labels. The FlC labels should be revised to specify a maximum seasonal rate for cotton.

2. Dietary Exposure

ADDITIONAL LABELING REQUIREMENTS MAY BE NECESSARY PENDING A MEETING/DECISION WITH SRRD ON ACUTE DIETARY RISK MITIGATION.

3. Occupational Exposure and Residential Exposure

ADDITIONAL LABELING REQUIREMENTS MAY BE NECESSARY PENDING A MEETING/DECISION WITH SRRD ON HANDLER AND POST-APPLICATION RISK MITIGATION.

APPENDIX I.

Product Chemistry Data Summary

Case No. 0235
Chemical No. 058001

Case Name: Azinphos methyl
Registrant: Gowan Company
Product(s): 94% T (EPA Reg. No. 10163-95)

PRODUCT CHEMISTRY DATA SUMMARY

Guideline Number	Requirement	Are Data Requirements Fulfilled? [1]	MRID Number
830.1550	Product Identity and Disclosure of Ingredients	N	
830.1600	Starting Materials and Manufacturing Process	N	
830.1620			
830.1650			
830.1670	Discussion of Formation of Impurities	N	
830.1700	Preliminary Analysis	N	
830.1750	Certification of Ingredient Limits	N	
830.1800	Analytical Methods to Verify the Certified Limits	N	
830.6302	Color	N	
830.6303	Physical State	N	
830.6304	Odor	N	
830.6313	Stability	N	
830.6314	Oxidation/Reduction	N	
830.6315	Flammability	N	
830.6316	Explodability	N	
830.6317	Storage Stability	N	
830.6319	Miscibility	N	
830.6320	Corrosion Characteristics	N	
830.7000	pH	N	
830.7050	UV/Visible Absorption	N [2]	
830.7100	Viscosity	N	
830.7200	Melting Point/Melting Range	N	
830.7220	Boiling Point/Boiling Range	N	
830.7300	Density/Relative Density/Bulk Density	N	
830.7370	Dissociation Constant in Water	N	
830.7550	Partition Coefficient (Octanol/Water)	N	
830.7560			
830.7570			
830.7840	Solubility	N	
830.7860			
830.7950	Vapor Pressure	N	

[1] Y = Yes; N = No; N/A = Not Applicable.

[2] The OPPTS Series 830, Product Properties Test Guidelines require data pertaining to UV/visible absorption for the

PRODUCT CHEMISTRY DATA SUMMARY

Guideline Number	Requirement	Are Data Requirements Fulfilled? [1]	MRID Number [2]
830.1550	Product Identity and Disclosure of Ingredients	Y	40158701, CSF 2/3/88, CSF 10/31/94
830.1600 830.1620 830.1650	Starting Materials and Manufacturing Process	Y	40158701
830.1670	Discussion of Formation of Impurities	Y	40502301
830.1700	Preliminary Analysis	Y	40502302, **44121302, 44121303**
830.1750	Certification of Ingredient Limits	N [3]	40502302, **44121302, 44121303,** CSF 2/3/88, CSF 10/31/94
830.1800	Analytical Methods to Verify the Certified Limits	Y	40502302, **44121301**
830.6302	Color	Y	40158702
830.6303	Physical State	Y	40158702
830.6304	Odor	Y	40158702
830.6313	Stability	N [4]	40502303
830.6314	Oxidation/Reduction	Y	40200501
830.6315	Flammability	N/A [5]	
830.6316	Explodability	Y	40200501
830.6317	Storage Stability	Y	40502304
830.6319	Miscibility	N/A [5]	
830.6320	Corrosion Characteristics	Y	40200501, 40502303
830.7000	pH	N/A [6]	
830.7050	UV/Visible Absorption	N [7]	
830.7100	Viscosity	N/A [5]	
830.7200	Melting Point/Melting Range	Y	40158702
830.7220	Boiling Point/Boiling Range	N/A [5]	
830.7300	Density/Relative Density/Bulk Density	Y	40200501
830.7370	Dissociation Constant in Water	N/A [6]	
830.7550 830.7560 830.7570	Partition Coefficient (Octanol/Water)	Y	40158702
830.7840 830.7860	Solubility	Y	40158702
830.7950	Vapor Pressure	Y	40158702

[1] Y = Yes; N = No; N/A = Not Applicable. CBRS has determined, based on comparison of the CSFs (dated 2/3/88 for the 85% T and 10/31/94 for the 85% FI), that the composition of the Makhteshim 85% FI is identical to the composition of the Makhteshim 85% T; thus, the 85% FI should be identified as a technical product, and data requirements for the 85% FI will be fulfilled by data submitted for the 85% T.

[2] **Bolded** references were reviewed under CBRS No. 17844, 4/2/97, F. Fort; all other references were reviewed in

the Azinphos methyl Reregistration Standard Update dated 1/8/91 for the 85% T, except for the CSF dated 1/31/94 for the 85% FI which was obtained from the product jacket.

[3] A revised certified limits for the active ingredient must be proposed.

[4] Additional data are required concerning the stability of the TGAI upon exposure to metals and metal ions.

[5] Data are not required because the TGAI/MP is a solid at room temperature.

[6] Data are not required because the TGAI/MP is not dispersible in water.

[7] The OPPTS Series 830, Product Properties Test Guidelines require data pertaining to UV/visible absorption for the PAI.

APPENDIX II

TABLE A. FOOD/FEED USE PATTERNS SUBJECT TO REREGISTRATION FOR Azinphos methyl (CASE 0235).

Site Application Type Application Timing Application Equipment	Formulation [EPA Reg. No./ SLN No.]	Max. Single Application Rate (ai)	Maximum # of Apples./crop [a]	Minimum Retreatment Interval (Days)	Use Limitations [b]
Food/Feed Uses					
Alfalfa					
Foliar broadcast Ground and aerial equipment	35% WP [3125-378] [3125-379] 50% WP [3125-193] [3125-301]	0.5 lb/A	1 (per cutting)	N/A [c]	PHI: 14 days at ≤0.38 lb ai/A; 16 days at 0.5 lb ai/A. Not for use on alfalfa grown for seed. 10 gal/A ground, 1 gal/A aerial
	3 lb/gal FlC [3125-338] [3125-427]	0.75 lb/A	2 (per cutting) at <0.25 lb ai/A	10	PHI: 14 days at ≤0.38 lb ai/A; 21 days at 0.5 lb ai/A; 28 days at >0.5 lb ai/A.
Almonds					
Foliar broadcast Ground and aerial equipment	2 lb/gal EC [3125-426]	2 lb/A	2	30	60-day PHI Do not apply after husks split
	35% WP [3125-378] [3125-379] 50% WP [3125-301] [3125-193]		2	28	28-day PHI Do not apply within 25 ft of an aquatic site 400 gal/A ground, 20 gal/A aerial

Table A. Continued.

Site Application Type Application Timing Application Equipment	Formulation [EPA Reg. No./ SLN No.]	Max. Single Application Rate (ai)	Maximum # of Apples./crop [a]	Minimum Retreatment Interval (Days)	Use Limitations [b]
Apples					
Foliar broadcast Ground and aerial equipment	35% WP [3125-378] [3125-379] 50% WP [3125-193] [3125-301] [VT800004]	1.5 lb/A	4	7	7-day PHI Apply up to 6 lb/A/season
	3 lb/gal FlC [3125-338] [3125-427]	0.75 lb ai/A			7-day PHI 3 lb ai/A/season
Artichokes					
Foliar broadcast Ground equipment	2 lb/gal EC [3125-426]	1.5	3	14	30-day PHI
Birdsfoot trefoil (East of the Mississippi River only)					
Foliar broadcast Ground and aerial equipment	35% WP [3125-378] [3125-379] 50% WP [3125-193] [3125-301]	0.5 lb/A	1 (per cutting)	N/A	PHI: 14 days at ≤0.38 lb ai/A; 16 days at 0.5 lb ai/A. 10 gal/A ground, 1 gal/A aerial

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Table A. Continued.

Site Application Type Application Timing Application Equipment	Formulation [EPA Reg: No./ SLN No.]	Max. Single Application Rate (ai)	Maximum # of Apples./crop [a]	Minimum Retreatment Interval (Days)	Use Limitations [b]
Blackberries, boysenberries, loganberries, raspberries Eastern and North Central U.S. only)					
Foliar broadcast Ground and aerial equipment	35% WP [3125-378] [3125-379] 50% WP [3125-193] [3125-301] 2 lb/gal EC [3125-102] [3125-123] [3125-426]	0.5 lb/A	2	NS [c]	14-day PHI Apply aerially in a minimum of 1 gal/A. A 3-day PHI is specified for 2 applications to the lower part of canes at 0.5 lb ai/A.
Blueberries					
Foliar broadcast Ground and aerial equipment	35% WP [3125-378] [3125-379] 50% WP [3125-193] [3125-301] 2 lb/gal EC [3125-102] [3125-123] [3125-426]	0.75 lb/A	3	10	7-day PHI

Table A. Continued.

Site Application Type Application Timing Application Equipment	Formulation [EPA Reg. No./ SLN No.]	Max. Single Application Rate (ai)	Maximum # of Apples./crop [a]	Minimum Retreatment Interval (Days)	Use Limitations [b]
Broccoli					
Drench at planting and foliar broadcast Ground equipment	35% WP [3125-378] [3125-379] 50% WP [3125-193] [3125-301] 2 lb/gal EC [3125-102] [3125-123] [3125-426]	0.75 lb/A	3	NS	15-day PHI
Brussels sprouts					
Drench at planting and foliar broadcast Ground equipment	35% WP [3125-378] [3125-379] 50% WP [3125-193] [3125-301] 2 lb/gal EC [3125-102] [3125-123] [3125-426]	0.75 lb/A	3	NS	7-day PHI

Table A. Continued.

Site Application Type Application Timing Application Equipment	Formulation [EPA Reg. No./ SLN No.]	Max. Single Application Rate (ai)	Maximum # of Apples./crop [a]	Minimum Retreatment Interval (Days)	Use Limitations [b]
Cabbage					
Drench at planting and foliar broadcast Ground equipment	35% WP [3125-378] [3125-379] 50% WP [3125-193] [3125-301] 2 lb/gal EC [3125-102] [3125-123] [3125-426]	0.75 lb/A	3	NS	21-day PHI
Cauliflower					
Drench at planting and foliar broadcast Ground equipment	35% WP [3125-378] [3125-379] 50% WP [3125-193] [3125-301] 2 lb/gal EC [3125-102] [3125-123] [3125-426]	0.75 lb/A	3	NS	15-day PHI

Table A. Continued.

Site Application Type Application Timing Application Equipment	Formulation [EPA Reg. No./ SLN No.]	Max. Single Application Rate (ai)	Maximum # of Apples./crop [a]	Minimum Retreatment Interval (Days)	Use Limitations [b]
Celery					
Foliar broadcast Ground equipment	35% WP [3125-378] [3125-379] 50% WP [3125-193] [3125-301] 2 lb/gal EC [3125-102] [3125-123] [3125-426] [OH810017]	0.5 lb/A	3	NS	14-day PHI
Cherries					
	35% WP [3125-378] [3125-379] 50% WP [3125-193] [3125-301]	0.75 lb/A	2	14	15-day PHI In CA apply only after harvest Maximum of 3 lb ai/A/season
	3 lb/gal FlC [3125-338] [3125-427]	East of Rocky Mts 0.75 lb/A West of Rocky Mts 0.5 lb/A	4 2	14	21-day PHI (east) 7-day PHI (west)

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Table A. Continued.

Site Application Type Application Timing Application Equipment	Formulation [EPA Reg. No./ SLN No.]	Max. Single Application Rate (ai)	Maximum # of Apples./crop [a]	Minimum Retreatment Interval (Days)	Use Limitations [b]
Citrus fruits					
Foliar broadcast Ground equipment	35% WP [3125-378] [3125-379] 50% WP [3125-193] [3125-301] 2 lb/gal EC [3125-102] [3125-123] [3125-426]	2 lb/A	2	NS	7-day PHI for 1 appl 28-day PHI for 2 appl
Cotton					
Foliar broadcast Ground and aerial equipment (conventional or low volume)	2 lb/gal EC [3125-102] [3125-123] [3125-426]	0.5 lb/A	12	NS	0-day PHI for machine harvesting For hand picking, 1-day PHI at ≤0.5 lb/A, 17-day PHI at >0.5 lb/A Maximum seasonal rate 6 lb ai/A for ECs No maximum specified for FICs
	3 lb/gal FIC [3125-338] [3125-427]	0.5 lb ai/A 0.75 west of Rocky Mts			
Foliar broadcast Ground and aerial equipment (Ultra low volume)	2 lb/gal EC [3125-102] [3125-123] [3125-426] [CA810074] [MS840012] [TX840005] [TX900011]	0.25			0-day PHI for machine harvesting For hand picking, 2-day PHI Maximum seasonal rate 3 lb ai/A

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Table A. Continued.

Site Application Type Application Timing Application Equipment	Formulation [EPA Reg. No./ SLN No.]	Max. Single Application Rate (ai)	Maximum # of Apples./crop [a]	Minimum Retreatment Interval (Days)	Use Limitations [b]
Crabapples					
Foliar broadcast Ground and aerial equipment	35% WP [3125-378] [3125-379] 50% WP [3125-193] [3125-301]	1.5 lb/A	4	7	7-day PHI Apply up to 6 lb/A/season
Cranberries					
Foliar broadcast Ground and aerial equipment	35% WP [3125-378] [3125-379] 50% WP [3125-193] [3125-301] 2 lb/gal EC [3125-426] [MA780002]	1 lb/A	3	14	A 21-day PHI is specified.
Cucumbers					
Foliar broadcast Ground equipment	35% WP [3125-378] [3125-379] 50% WP [3125-193] [3125-301] 2 lb/gal EC [3125-102] [3125-123] [3125-426]	0.5 lb/A	3	7	A 1-day PHI is specified.

Table A. Continued.

Site Application Type Application Timing Application Equipment	Formulation [EPA Reg. No./ SLN No.]	Max. Single Application Rate (ai)	Maximum # of Apples./crop [a]	Minimum Retreatment Interval (Days)	Use Limitations [b]
Eggplant					
Foliar broadcast Ground equipment	2 lb/gal EC [3125-426]	0.5 lb/A	3	7	A 21-day PHI is specified.
Filberts (pacific northwest only)					
Foliar broadcast Ground equipment	35% WP [3125-378] [3125-379] 50% WP [3125-193] [3125-301] 2 lb/gal EC [3125-102] [3125-123] [3125-426]	2 lb/A	3	14	A 45-day PHI is specified on 3125-378, -379, -and -102. A 30-day PHI remains on 3125-193, -301, and -426.
Grapes					
Foliar broadcast Ground equipment	35% WP [3125-378] [3125-379] 50% WP [3125-193] [3125-301] 2 lb/gal EC [3125-102] [3125-123] [3125-426] [CA800146]	1 lb/A	3	14	0-day PHI for application at 0.75 lb ai/A. 10-day PHI is specified for 1 lb ai/A.

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Table A. Continued.

Site Application Type Application Timing Application Equipment	Formulation [EPA Reg. No./ SLN No.]	Max. Single Application Rate (ai)	Maximum # of Apples./crop [a]	Minimum Retreatment Interval (Days)	Use Limitations [b]
Melons					
Foliar broadcast Ground equipment	35% WP [3125-378] [3125-379] 50% WP [3125-193] [3125-301] 2 lb/gal EC [3125-102] [3125-123] [3125-426]	0.5 lb/A	3	5	A 7-day PHI is specified.
Nectarines and Peaches					
Foliar broadcast Ground equipment	35% WP [3125-378] [3125-379] 50% WP [3125-193] [3125-301] 2 lb/gal EC [3125-102] [3125-123] [3125-426]	1.125 lb/A (Eastern U.S.) 2 (West of the Rocky Mts)	NS	14	A 21-day PHI is specified A total of 3.38 lb ai/A per crop season may be applied.

Table A. Continued.

Site Application Type Application Timing Application Equipment	Formulation [EPA Reg. No./ SLN No.]	Max. Single Application Rate (ai)	Maximum # of Apples./crop [a]	Minimum Retreatment Interval (Days)	Use Limitations [b]
Onions (green and dry)					
Foliar broadcast Ground and aerial equipment	35% WP [3125-378] [3125-379] 50% WP [3125-193] [3125-301] 2 lb/gal EC [3125-102] [3125-123] [3125-426]	0.75 lb/A	3	7 (bulb) 10 (green)	PHIs of 28 days (dry) and 14 days (green) are specified.
Parsley (root and moss curled)					
Foliar broadcast Ground equipment	50% WP [NJ940002] [NJ940003] [OH810017]	0.5 lb/A	3	NS	A PHI of 21 days is specified
Pears					
Foliar broadcast Ground equipment	35% WP [3125-378] [3125-379] 50% WP [3125-193] [3125-301]	1.5 lb/A	4	7	7-day PHI Apply up to 6 lb/A/season
	3 lb/gal FIC [3125-338] [3125-427]	0.75 lb/A			7-day PHI Apply up to 3 lb/A/season

Table A. Continued.

Site Application Type Application Timing Application Equipment	Formulation [EPA Reg. No./ SLN No.]	Max. Single Application Rate (ai)	Maximum # of Apples./crop [a]	Minimum Retreatment Interval (Days)	Use Limitations [b]
Pecans					
Foliar broadcast Ground and aerial equipment	35% WP [3125-378] [3125-379] 50% WP [3125-193] [3125-301] 2 lb/gal EC [3125-102] [3125-123] [3125-426]	2 lb/A	3	7	45-day PHI listed on 3125-378, -379, -102 No PHI listed on 3125-193, -301, 426. "Do not apply after shuck-split" specified on 3125-193, -301, -426.
Peppers					
Foliar broadcast Ground equipment	2 lb/gal EC [3125-426]	0.5 lb/A	3	7	A 21-day PHI is specified.
Plums/fresh prunes					
Foliar broadcast Ground equipment	35% WP [3125-378] [3125-379] 50% WP [3125-193] [3125-301] 2 lb/gal EC [3125-102] [3125-123] [3125-426]	1.5 lb/A (Eastern U.S.) 2 lb/A (West of the Rocky Mts)	NS	10	A 15-day PHI is specified. A total of 3.38 lb ai/A may be applied per crop season

Table A. Continued.

Site Application Type Application Timing Application Equipment	Formulation [EPA Reg. No./ SLN No.]	Max. Single Application Rate (ai)	Maximum # of Apples./crop [a]	Minimum Retreatment Interval (Days)	Use Limitations [b]
Pistachios					
Foliar broadcast Ground equipment	50% WP [CA790149]	2.5 lb/A	1	N/A	A 21-day PHI is specified. Apply prior to 10% hull split.
Pomegranates					
Foliar broadcast Ground equipment	2 lb/gal EC [CA900021]	1 lb ai/A	2	30	A 55-day PHI is specified.
Potatoes					
Foliar broadcast Ground and aerial equipment	35% WP [3125-378] [3125-379] 50% WP [3125-193] [3125-301] 2 lb/gal EC [3125-102] [3125-123] [3125-426] 3 lb/gal FlC [3125-338] [3125-427]	0.75 lb/A	3	7	A 7-day PHI is specified.
Quinces					
Foliar broadcast Ground equipment	50% WP [CA900012]	1.5 lb/A	4	7	7-day PHI Apply up to 6 lb/A/season

Table A. Continued.

Site Application Type Application Timing Application Equipment	Formulation [EPA Reg. No./ SLN No.]	Max. Single Application Rate (ai)	Maximum # of Apples./crop [a]	Minimum Retreatment Interval (Days)	Use Limitations [b]
Rye					
Foliar broadcast Ground equipment	35% WP [3125-378] [3125-379] 50% WP [3125-193] [3125-301] 2 lb/gal EC [3125-102] [3125-123] [3125-426]	0.5 lb/A	1	N/A	A 30-day PHI/PGI is specified.
Strawberries					
Foliar broadcast Ground equipment	35% WP [3125-378] [3125-379] 50% WP [3125-193] [3125-301] 2 lb/gal EC [3125-102] [3125-123] [3125-426]	0.5 lb/A	4	5	A 5-day PHI is specified.

Table A. Continued.

Site Application Type Application Timing Application Equipment	Formulation [EPA Reg. No./ SLN No.]	Max. Single Application Rate (ai)	Maximum # of Apples./crop [a]	Minimum Retreatment Interval (Days)	Use Limitations [b]
Sugarcane					
Foliar broadcast Ground and aerial equipment Conventional and ultra low volume sprays	2 lb/gal EC [3125-102] [3125-123] [3125-426] 3 lb/gal FIC [3125-338] [3125-427]	0.75 lb/A	5 (TX, FL) 2 (LA)	21 (LA)	A 30-day PHI is specified. For use in FL, LA, and TX only. In LA, do not apply within 100 ft of lakes, reservoirs, rivers, permanent streams, marshes, ponds, canals, estuaries, or commercial fish farm ponds. 3125-426 and 3425-427 not for use in LA.
Tomatoes					
Foliar broadcast Ground and aerial equipment	35% WP [3125-378] [3125-379] 50% WP [3125-193] [3125-301] 2 lb/gal EC [3125-102] [3125-123] [3125-426]	1.5 lb/A	4	7	A 0-day PHI is specified for rates ≤0.75 lb ai/A A 14-day PHI is specified for rates >0.75 lb ai/A

Table A. Continued.

Site Application Type Application Timing Application Equipment	Formulation [EPA Reg. No./ SLN No.]	Max. Single Application Rate (ai)	Maximum # of Apples./crop [a]	Minimum Retreatment Interval (Days)	Use Limitations [b]
Walnuts					
Foliar broadcast Ground and aerial equipment	35% WP [3125-378] [3125-379] 50% WP [3125-193] [3125-301] 2 lb/gal EC [3125-102] [3125-123] [3125-426]	2 lb/A	3	14	A 21-day PHI is specified.

[a] Label-specified maximum number of applications, regardless of rate.

[b] The following restrictions appear on end-use product labels:

Rotational crops: A 6-month plant-back interval (PBI) is specified for root crops not having azinphos methyl uses, and a 30-day PBI is specified for all other crops not having azinphos methyl uses [all labels].

Restricted entry interval (REI): 24 hours [3125-426 and -427]. 48 hours (72 hours in areas where average rainfall is <25 in/yr) [all other labels]

Pregrazing interval: Do not graze livestock in treated orchards or groves for 21 days after treatment [all labels].

Do not treat greenhouse-grown crops [all labels].

[c] N/A = not applicable; NS = not specified.

APPENDIX III

Table B. Residue Chemistry Science Assessments for Reregistration of Azinphos methyl.

OPPTS GLN: Data Requirements	Current Tolerances, ppm [40 CFR]	Must Additional Data Be Submitted?	References[1]
860.1200: Directions for Use	N/A	Yes[2]	See Table A.
860.1300: Nature of the Residue			
- Plants	N/A	No	00100826 00107018 00112112 00155026 00155065 **40581701** **40581702** **40581703** **40755801** 43221701[3] 43221702[3] 43221704[3] 43750501[3] GS0235008
- Livestock	N/A	No	00090275 00090278 00155019 00155020 00155021 **40581704** **40581705** 43221703[3] 43834501[4]
860.1340: Residue Analytical Methods	N/A	No	00030303 00080102 00089642 00089740 00090126 00090127 00090274 00090277 00090279 00090946 00093572 00106832 00107018 00107020 00112052 00112054 00112074 00112083 00112093 00112114 00112116 00112120 00112145 00141541 00155064 00158905 00158906 05004211 GS0235014 GS0235015 **41456132** **41456134**
860.1360: Multiresidue Method	N/A	No	
860.1380: Storage Stability	N/A	No	00030303 00090127 00090275 00112078 00155064 43738901[5] 43890001[6]
860.1500: Magnitude of the Residue in Crop Plants			
Root and Tuber Vegetables Group			
- Parsley, root	2 [§180.154(a)]	No	00112073

OPPTS GLN: Data Requirements	Current Tolerances, ppm [40 CFR]	Must Additional Data Be Submitted?	References[1]
- Potatoes	0.3 [§180.154(a)]	No	00112039 00112053 40814701[7]
Bulb Vegetables (*Allium spp.*) Group			
- Onions	2 [§180.154(a)]	No	00112111 **41456111 41456112**
Leafy Vegetables (Except Brassica Vegetables) Group			
- Celery	2 [§180.154(a)]	No[8]	00107018
- Parsley	5 [§180.154(a)]	No	00112073
- Spinach	2 [§180.154(a)]	No[9]	00089740
Brassica (Cole) Leafy Vegetables Group			
- Broccoli	2 [§180.154(a)]	No[10]	00080143 00080144 00107020 00112116 00154989 44035402[11]
- Brussels sprouts	2 [§180.154(a)]	No[8]	00090127 00154989
- Cabbage	2 [§180.154(a)]	No[10]	00112116 00107020
- Cauliflower	2 [§180.154(a)]	Yes[10]	00112116 00107020 44035401[12]
Legume Vegetables (Succulent or Dried) Group			
- Beans, dry	0.3 [§180.154(a)]	No[9]	00087512 00089740 00090946 00107019 00112052 00154989
- Beans, succulent	2.0 [§180.154(a)]	No[9]	00087512 00089740 00090946 00107019 00112052 00154989
- Peas, blackeyed	0.3 [§180.154(a)]	No[9]	00107019 00112035 00112052
- Soybeans	0.2 [§180.154(a)]	No[9]	00107020 00112039 00112052 00112086 00112151
Fruiting Vegetables (Except Cucurbits) Group			
- Eggplant	0.3 [§180.154(a)]	No[8]	
- Peppers	0.3 [§180.154(a)]	No[8]	00107020 **41456114**
- Tomatoes	2.0 [§180.154(a)]	No	00080143 00089740 00112120 00154996 00154989 **41456113**
Cucurbit Vegetables Group			
- Cucumbers	2.0 [§180.154(a)]	No	00107019 **41456110**
- Melons	2.0 [§180.154(a)]	No	00107018 **41456101 41456102 41456103**

OPPTS GLN: Data Requirements	Current Tolerances, ppm [40 CFR]	Must Additional Data Be Submitted?	References[1]
Citrus Fruits Group	2.0 [§180.154(a)]	No	00090126 00106832 00112037 00112139 00112143 00112145 **41456104 41456105 41456106 41456130**
Pome Fruits Group			
- Apples	2.0 [§180.154(a)]	No	00087512 00100824 00112113 00112137 00154989 40224401[13] **41456115**
- Crabapples	2.0 [§180.154(a)]	No[14]	
- Pears	2.0 [§180.154(a)]	No[14]	00087512 00100824 00155064 00154989
- Quinces	2.0 [§180.154(a)]	No[14]	
Stone Fruits Group			
- Apricots	2.0 [§180.154(a)]	No[9]	00100824 00154989 **41456120**
- Cherries	2.0 [§180.154(a)]	No[15]	00107020 00112145 00154989 40679301[16]
- Nectarines	2.0 [§180.154(a)]	No[17]	00154989 **41456117**
- Peaches	2.0 [§180.154(a)]	No	00100824 00154989 **41456121**
- Plums	2.0 [§180.154(a)]	No	00107020 00154989 **41456119**
Berries Group			
- Blackberries, boysenberries, loganberries, raspberries	2.0 [§180.154(a)]	No	0089890 00112142 00112143 42076801[18]
- Blueberries	5.0 [§180.154(a)]	No	00089740 00127018 00112143 **41456118**
- Gooseberries	5.0 [§180.154(a)]	Yes[19]	
Tree Nuts Group			
- Almonds	0.3 [§180.154(a)]	No	00109278 00112159 00158908 40167201[20]
- Almond hulls	10.0 [§180.154(a)]		**41135501**
- Filberts	0.3 [§180.154(a)]	No[21]	00089740 00112117
- Pecans	0.3 [§180.154(a)]	No	00112126 **41456107**
- Walnuts	0.3 [§180.154(a)]	Yes[22]	00112052 **41456108**
Cereal Grains Group			
- Barley, grain	0.2 [§180.154(a)]	No[9]	00093570 00093572
- Oats, grain	0.2 [§180.154(a)]	No[9]	00093570 00093572

OPPTS GLN: Data Requirements	Current Tolerances, ppm [40 CFR]	Must Additional Data Be Submitted?	References[1]
- Rye, grain	0.2 [§180.154(a)]	No	00093572
- Wheat, grain	0.2 [§180.154(a)]	No[9]	00080143 00080144 00093570 00093572 00154989
Forage, Fodder, and Straw of Cereal Grains Group			
- Barley forage and straw	2.0 [§180.154(a)]	No[9]	00093570 00093572
- Oats forage, hay, and straw	2.0 [§180.154(a)]	No[9]	00093570 00093572
- Rye forage, hay, and straw	2.0 [§180.154(a)]	No	00093572
- Wheat forage, hay, and straw	2.0 [§180.154(a)]	No[9]	00080143 00080144 00093570 00093572 00154989
Grass Forage, Fodder, and Hay Group			
- Grasses, forage	2.0 [§180.154(a)]	No[9]	00070492 00112035 00117750
- Grasses, hay	5.0 [§180.154(a)]	No[9]	00070492 00112035 00117750
Nongrass Animal Feeds (Forage, Fodder, Straw, and Hay) Group			
- Alfalfa, forage	2.0 [§180.154(a)]	No	00035980 00067494 00090273 00090276 00090280 00154989 **41456125**
- Alfalfa, hay	5.0 [§180.154(a)]	No	00035980 00067494 00090273 00090276 00090280 00154989 **41456125**
- Birdsfoot trefoil, forage	2.0 [§180.154(a)]	No[23]	
- Birdsfoot trefoil, hay	5.0 [§180.154(a)]	No[23]	
- Clover, forage	2.0 [§180.154(a)]	No[24]	00090273 00090280 **41456124**
- Clover, hay	5.0 [§180.154(a)]	No[24]	00090273 00090280 **41456124**

OPPTS GLN: Data Requirements	Current Tolerances, ppm [40 CFR]	Must Additional Data Be Submitted?	References[1]
Miscellaneous Commodities			
- Artichokes	2.0 [§180.154(a)]	No[8]	00089740 **41456109**
- Cottonseed	0.5 [§180.154(a)]	Yes[25]	00029078 00045038 00080143 00080144 00087511 00098957 00102272 00122299 00112027 00112039 00112054 00112071 00112110 00112112 00112114 00141541 00154989
- Cranberries	2 [§180.154(a)]	No	00089740 **41456122** 43878001[26]
- Grapes	5 [§180.154(a)]	No	00089642 00112108 00112143 00154989 **41456116**
- Kiwi fruit	10 [§180.154(a)]	No[9]	00112072 00158909
- Pistachios	0.3 [§180.154(a)]	No	00112074
- Pomegranates	0.1 [§180.154(b)]	No	40581701[27] 40755801[27]
- Strawberries	2 [§180.154(a)]	No	00107020 **41456123**
- Sugarcane	0.3 [§180.154(a)]	No	00091562 00112024 00112026 00112083 00112115
- Tobacco	NA	No	
860.1520: Magnitude of the Residues in Processed Food/Feed			
- Apple	None	No[28]	00154989 00100824 **41456127**
- Barley	None	No	
- Citrus	5 [§186.2225]	No[29]	00090126 00112037 00112143 **41456130**
- Cottonseed	None	No	00102272 00112039 00112054 00112112 00112071 **41456126**
- Grape	None	No	00089642 00112108 00112143 00154989 **41456129**
- Oats	None	No	
- Plum	None	No	**41456119**
- Potato	None	No	00154989 **41456128** 43957101[30]

OPPTS GLN: Data Requirements	Current Tolerances, ppm [40 CFR]	Must Additional Data Be Submitted?	References[1]
- Rye	None	No[31]	
- Soybean (oil)	1 [§185.2225]	No[32]	
- Sugarcane (bagasse)	1.5 [§186.2225]	No[33]	
- Tomato	None	No	**41456131**
- Wheat	None	No	
860.1480: Magnitude of the Residue in Meat, Milk, Poultry, and Eggs		No	
- Cattle, goats, horses, sheep: meat, fat, mbyp	0.1 [§180.154(a)]	No[34]	00030303 00090126
- Milk	0.04 [**§180.154a**]	No[34]	00030303 00090126
860.1400: Magnitude of the Residue in water, fish, and irrigated crops	N/A	N/A	
860.1460: Magnitude of the Residue in Food Handling Establishments	N/A	N/A	
860.1850: Confined Accumulation in Rotational Crops	N/A	No	41393601
860.1900: Field Accumulation in Rotational Crops	None	No	00030279

1: Non-bolded references were cited in the Azinphos methyl Guidance Document dated 9/86. **Bolded** references were reviewed/cited in the Azinphos methyl Reregistration Standard Update dated 1/91. Underlined references were reviewed by EFED, but have not been reviewed by CBRS. Other references were reviewed as noted.

2. The recommended label amendments are listed in the SUMMARY OF SCIENCE FINDINGS, under OPPTS GLN 860.1200: Directions for Use.

3. CBRS Nos. 16463/16388, DP Barcodes D220772/D219719, 12/19/95, S. Knizner.

4. CBRS No. 17510, DP Barcode D229091, 2/9/97, F. Fort.

5. CBRS No. 16383, DP Barcode D220423, 12/12/95, S. Knizner.

6. CBRS No. 16871, DP Barcode D222840, 6/28/96, F. Fort.

7. CBRS No. 4449, 11/30/88, L. Propst.

8. Although the registrant does not intend to support this use (CBRS No. 16871, DP Barcode D222840, 6/28/96, F. Fort), this crop remains on some product label(s). These labels should be revised to delete this use site.

9. There is no registered use on this crop; therefore, the established tolerance should be revoked.

10. IR-4 has submitted adequate field trial data to support tolerances on broccoli. Additional field trial data are required to support cauliflower use. Additional field trials should be

conducted in Regions 1, 5, and 12 for cauliflower. Alternatively, field trial data on cabbage conducted in Regions 1, 2, 3, 5, 6, and 10 may be done if the registrant desires a head and stem Brassica crop subgroup tolerance.

11. CBRS No. 17846, DP Barcode D234678, 3/27/97, F. Fort

12. CBRS No. 17845, DP Barcode D234677, 4/2/97, F. Fort

13. CBRS No. 2552, 9/29/87, W. Anthony.

14. Data on apples support the tolerances on crabapples, pears, and quinces.

15. Data submitted for plums are being used to support the use on cherries.

16. CBRS No. 5592, 9/28/89, K. Dockter.

17. Data from peaches will be used to support nectarines.

18. CBRS No. 9195, DP Barcode D172624, 8/27/92, B. Cropp-Kohlligian.

19. Although the registrant has stated their intent to support the tolerance on gooseberries (CBRS No. 16871, DP Barcode D222840, 6/28/96, F. Fort), there are no registered uses. The registrant may propose use directions or request deletion of the tolerance. The data submitted for blueberries may be translated to gooseberries.

20. CBRS No. 2215, 8/19/87, W. Anthony.

21. Data on pecans will be used to support filberts.

22. Bayer Corp. intends to submit additional residue data (CBRS No. 16871, DP Barcode D222840, 6/28/96, F. Fort).

23. Data on alfalfa will used to support birdsfoot trefoil.

24. Although the registrant has stated the intent to support the tolerances on clover (CBRS No. 16871, DP Barcode D222840, 6/28/96, F. Fort), there are no registered uses. The registrant may propose use directions or the request deletion of the tolerance. The data submitted for alfalfa may be translated to clover.

25. For purposes of reregistration, additional residue data are required on cotton gin byproducts. Data are required depicting azinphos methyl residues in/on cotton gin byproducts ginned from cotton harvested on the day after the last of multiple foliar applications of azinphos methyl at the maximum labeled rate and totaling 6.0 lb ai/A/season. The cotton must be harvested by commercial equipment (stripper and mechanical picker) to provide an adequate representation of plant residue from the ginning process. At least three field trials for each type of harvesting (stripper and picker) are needed, for a total of six field trials.

26. CBRS No. 16870, DP Barcode D222919, 4/18/96, F. Fort.

27. CB No. 4505, no DP Barcode, 4/19/89, M. Nelson.

28. Residues concentrated 2x in wet apple pomace; a feed additive tolerance must be proposed.

29. An adequate processing study on citrus indicated that residues do not concentrate in dried citrus pulp; therefore the established tolerance should be revoked. Residues concentrated 7.5x in citrus oil; a food additive tolerance must be proposed.

30. CBRS No. 17164, DP Barcode D225279, 6/5/96, F. Fort.

31. No processing study exists on rye grain or on any other small cereal grain. However, as residues were <0.01 ppm, one twentieth the tolerance, and the theoretical concentration factor is 10x, a processing study is not required.

32. As there is no registered use on soybeans, the FAT for soybean oil should be revoked.

33. Sugarcane bagasse is not a significant livestock feed item; therefore the FAT for this commodity should be revoked.

34. A 40 CFR §180.6(a)(3) situation exists for azinphos methyl residues in ruminant tissues and milk and the tolerances should be revoked.

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