

US EPA ARCHIVE DOCUMENT

Azinphos-Methyl Technical Briefing



Azinphos-Methyl Case Study
Staff Paper 38a

April 27, 1999

Introduction and Background Information



Introduction

Purpose of Briefing

- Present Comprehensive Overview of Azinphos-Methyl Risk Estimates:
 - Prototype of OP "Technical Briefing"
 - Illustrate azinphos-methyl progress through the TRAC process
 - Identify where to focus mitigation

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Introduction (*con't*)

Azinphos-Methyl Risk Assessments Consider:

- Dietary risk:
 - food, drinking water, and aggregate
- Worker risk:
 - applicators, handlers, and harvesters (re-entry)
- Ecological risks:
 - birds, mammals, fish, and aquatic species

Not Included in Azinphos-Methyl Assessment:

- Azinphos-methyl has no residential or Public Health uses:
 - currently developing method to address secondary exposure

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Introduction (*con't*)

TRAC Pilot Public Participation Process for Azinphos-Methyl

Phase	Health Effects Assessment	Ecological Assessment
① "Error Only" Review	7/98	11/98
② Public Docket Opened	8/98	1/99
③ Comment Period Completed	10/98	3/99
④ Revised Assessment Sent to USDA	3/99	
⑤ Solicit Risk Management Options		
⑥ Develop Risk Management Strategy		

Introduction (*con't*)

Phase 1: "Error Only" Review by Registrant

- No substantive corrections to health effects assessment.
- No substantive corrections to ecological assessment.

Phase 2: Open Public Docket

- 60-day public comment period.

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Introduction (*con't*)

Phase 3: Public Comment

- Comments received from registrant, public interest groups, growers, USDA
- Importance to agriculture
- Used extensively in IPM programs
- Few alternatives for some crop/pests combinations
- Growers comments noted:
 - importance for codling moth control on cherries;
 - lack of good alternatives on apples;
 - important quarantine use for almonds.
- Additional data received from registrants, growers

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Introduction (*con't*)

<h3>New Data Received During Comment Period</h3> <ul style="list-style-type: none"> • Information on use practices 	<h3>New Data Received After Comment Period Closed</h3> <ul style="list-style-type: none"> • Dermal exposure studies <ul style="list-style-type: none"> – cotton – apples • Revised Monte-Carlo with data files
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Introduction (*con't*)

Phase 4: Revise Assessments, Solicit Comments from USDA

- Revisions to acute dietary assessment including:
 - Use of probabilistic model (Monte-Carlo)
 - Use of monitoring data (PDP & FDA)
 - Updated consumption data and percent crop treated
- Revisions to worker risk assessment include:
 - Use of Agricultural Task Force data to calculate REIs
- Preliminary comments from USDA on health effects assessment
- Comments and revisions to EFED assessment
 - In progress

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Introduction (*con't*)

Already Made Substantial Advances

- Used available monitoring data for dietary assessment
- Developed in-house Monte-Carlo capabilities
- Ability to perform sensitivity analysis
- Incorporated worker exposure data from industry task force

Work-in-Progress

- Considering comments on environmental assessment
- Revising assessment based on revised labels

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Introduction (*con't*)

Phase 4: Revise Assessments, Solicit Comments from USDA

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 - In progress

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Regulatory History

Registration Standard

Louisiana Sugarcane Agreement

Acute Worker Risk Strategy

California Emergency Regulations

Amended Labels

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Use Profile

- First Registered for Food Use in 1959
- Currently Registered Uses
 - About 50 food uses
- Sources of Use Data
 - USDA/NASS
 - California
 - Other sources

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Use Profile (*con't*)

Usage

- Two million pounds used per year (on average)
 - About 50% on fruit trees
 - About 15% on nut crops
 - About 20% on cotton

High-Use Food Crops

- > 50% crop treated for apples, pears, and cherries
- > 25% crop treated blueberries, almonds, pistachios, and cranberries

Major Use Regions

- California and Pacific Northwest on tree crops
- Delta states and Texas on tree crops and cotton

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Use Profile (*con't*)

Use Practices

- Application Methods
 - ground boom
 - airblast
 - aerial
- Use Rates
 - number of applications
 - pounds per acre
- Reentry Intervals

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Use Profile (*con't*)

Examples of Use Information Incorporated into Risk Assessments

Crop	% Crop Treated		Application Rate (lb. ai)		Number of Applications		PHI (days)	REI (days)
	Max.	Wt. Avg.	Max.	Typical	Max.	Typical		
Cotton	11	6	1.0	0.6	4	2.4	2	2
Tomatoes (fresh)	10	6	1.5	1.2	4	1.0	14	2
Apples	88	71	1.5	0.7	4	3.2	14	14
Peaches	30	21	2.0	0.7	NS	2.9	14	14
Pears	91	70	2.0	1.0	NS	2.5	14	14

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Use Profile (*con't*)

Use Practices

- Application Methods
 - ground boom
 - airblast
 - aerial
- Use Rates
 - number of applications
 - pounds per acre
- Reentry Intervals

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Human Health Risk Assessment



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Risk Assessment Components

- Dietary
 - Food
 - Drinking Water
- Aggregate
- Occupational

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Basic Risk Equation

- Risk = Hazard x Exposure, where
Exposure = Consumption x Residue

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Dietary Risk Assessments Conducted for Azinphos-Methyl

Acute

- Risk assessment reflecting one-day dietary exposures to pesticide residues

Chronic

- Risk assessment reflecting lifetime (long-term) exposures to pesticide residues

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Acute Hazard (toxicity)

- **From:** Rat acute neurotoxicity study
- **Endpoint** (*toxic effect*):
 - plasma, RBC, and brain cholinesterase inhibition
- **NOAEL:** not determined
- **LOAEL:** 1.0 mg/kgBW/day

Endpoints from this study most accurately reflect toxicity which could result from one-day dietary exposure to azinphos-methyl.

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Chronic Hazard (toxicity)

- **From:** 1-year chronic toxicity study in dogs
- **Endpoint** (*toxic effect*):
 - RBC cholinesterase inhibition
- **NOAEL:** 0.15 mg/kgBW/day
- **LOAEL:** 0.70 mg/kgBW/day

Endpoints from this study most accurately reflect toxicity which could result from long-term dietary exposure to azinphos-methyl.

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Uncertainty Factors

- 10X Interspecies Variability
- 10X Intraspecies Sensitivity
- 3X Lack of a NOAEL (acute only)
- Removed FQPA Safety Factor
- 300X Total for Acute
- 100X Total for Chronic

This would have been a typical type of uncertainty analysis, even before FQPA.

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Reference Doses for Azinphos-Methyl

$\frac{\text{LOAEL}}{\text{UF}} = \text{acute RfD} = 0.003 \text{ mg/kgBW/day}$

$\frac{\text{NOAEL}}{\text{UF}} = \text{chronic RfD} = 0.0015 \text{ mg/kgBW/day}$

$$\% \text{RfD} = \frac{\text{Exposure}}{\text{RfD}} \times 100$$

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Analysis of Special Sensitivity of Infants and Children

- No developmental effects in fetuses below maternally toxic doses.
- No increased sensitivity in pups relative to adults.
- No abnormalities in developing fetal nervous system.
- No neuropathology.
- Complete toxicity database.
- Good Data -- unlikely that exposures are underestimated.

Determination made not to require developmental neurotoxicity study (however, issue of requiring DNT for a much broader category of pesticides is being considered by the Agency).

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Exposure -- *Consumption*

- USDA's Continuing Survey of Food Intake by Individuals (CSFII) 1989-91 Data.
 - 1994-96 data are being validated for use in the near future.
 - Supplemental children's consumption data.
 - Due in December 1999

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Chronic Dietary Risk Assessments

- Chronic dietary risks were below levels of concern using high-end residues from field trials.
- Any further refinement of exposure estimates using monitoring data would lower risk estimates.
- Chronic risk estimate stopped and focus shifted to acute dietary risk assessment.

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Chronic Dietary Analysis Results

Risk Estimates as a Percentage of the cRfD (Tier 2/3)

Population	% cRfD
General U.S.	13%
Infants < 1 year	30%
Children 1-6	33%
Children 7-12	22%

Tier 2/3 used high-end residue data from field trials, some FDA monitoring data, and incorporated percent crop treated information. The chronic dietary risk assessment was done using DRES (the Dietary Risk Evaluation System).

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Types of Risk Assessment: *Azinphos-Methyl*

- **Acute Dietary:** Conducted tier 1 (non-probabilistic) and tier 3 (probabilistic) assessments.
 - Tier 1 assumed tolerance level residues and 100% of crop treated.
 - Tier 3 used monitoring data and incorporated information on percent of crop treated.
- **Monitoring Data Used:**
 - USDA’s Pesticide Data Program (PDP) Data
 - Statistically designed for dietary risk assessment
 - Important infant’s and children’s food sampled
 - Prepared as in the home (e.g., washing and peeling)
 - FDA Surveillance Monitoring Data
 - Designed for tolerance enforcement
 - Large number of samples and types of food

Note: Measured residues in composite samples -- samples are comprised of many individual serving size items.

Exposure -- Residues

Tier	Residue Data Used
1	Tolerance level residues
2	Field Trial Residues
3	Monitoring Data: USDA PDP data FDA data Market basket data

As we move through the tiers, we refine our risk estimates because we use residue data closer to the point of consumption.

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Two Types of Acute Dietary Risk Assessments

Non-Probabilistic

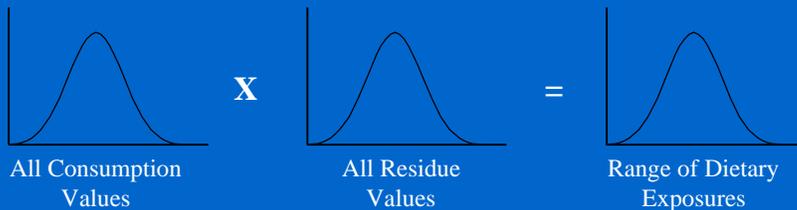


Assumes that every piece of fruit or vegetable consumed has residues at a high level. Therefore, a consumer's chance of consuming a high-residue piece of fruit or vegetable depends entirely on whether he or she eats that fruit or vegetable.

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Two Types of Acute Dietary Risk Assessments (*con't*)

Probabilistic



Assumes that any one piece of fruit or vegetable consumed can have residues anywhere in the range of residues observed. Therefore, a consumer's chance of consuming a high-residue piece of fruit or vegetable depends both on how much of the item he or she eats AND how frequently that item is found to have high residues.

More realistic exposure estimates.

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Azinphos-Methyl: Residue Data Used for Acute Dietary

- USDA Pesticide Data Program (PDP) Data } ~ 80% of foods
- FDA Surveillance Monitoring Data } >80% consumption
- Field Trial Data: (19 food types, low consumption foods, e.g., green cabbage, savoy cabbage)
- Processing Data: (e.g. processing factor for wheat grain to flour)

NOTE: Monitoring data were translated to similar crops if the crops had similar use patterns (e.g., orange juice to tangerine juice).
See Handout for Details.

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Acute Dietary Analysis Results (Food Only)

Risk Estimates As A Percentage
Of The Acute Rfd (%aRfD)

Population	Percentile		
	*95 th	°99.9 th (sent to USDA)	°99.9 th (current)
General U.S.	4670%	85%	68%
Infants < 1 yr	10,000%	331%	105%
Children 1-6	10,000%	202%	135%
Children 7-12	NR	129%	98%

*Tier 1 non-probabilistic. Risk @ 95th percentile of exposure

°Tier 3 probabilistic. Risk @ 99.9th percentile of exposure

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Acute Dietary Analysis Results (Food Only)

Risk Estimates As A Percentage
Of The Acute Rfd (%aRfD)

Population	Percentile @ Tier 3		Percentile @ 100 %aRfD
	99.9 th (current)	99.0 th (current)	
General U.S.	68%	23%	NA
Infants < 1 yr	105%	31%	99.89 th
Children 1-6	135%	41%	99.83 th
Children 7-12	98%	33%	NA

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Acute Dietary Results to Date

Refinements between assessment provided to USDA and current assessment

- New percent crop-treated for many commodities
- Use of new single-serving pear data
- Revised assessment for canned fruit

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Acute Dietary Results to Date (*con't*)

Contributors to Risk Estimates:

- Major contributors: apples, peaches, pears, cherries
- Minor contributors: tomatoes, grapes, almonds, citrus, beans

Non-Detectable Residues:

- Assuming all ND residues were zeros had an insignificant impact on risk

• Percent Crop-Treated:

- Sensitivity analysis in progress

Very Labor Intensive

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Acute Dietary Risk Assessment: *Summary*

- Methodology developed allowing use of PDP and FDA monitoring data for 80% of foods treated with azinphos-methyl, including major contributors to risk.
- Used most current information on percent of crop treated for all foods.
- Completed sensitivity analysis to determine that contribution of non-detectable residues to total risk for certain commodities was negligible.
- Completed analyses for various population subgroups including infants and children.
- Sensitivity analysis of tail of exposure values above 99.9th percentile to assess if the values are representative of real consumption/residue patterns -- in progress.

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Drinking Water Risk Assessment

- Assessment conducted because of azinphos-methyl's use pattern and environmental fate profile.
- Environmental fate data indicate azinphos-methyl can get into surface water and ground water to some extent.
- Available monitoring data are limited and there are some uncertainties associated with it.
- We relied on model estimates for the drinking water assessment.
- We expect some exposure in drinking water, therefore, we expect some contribution to risk.
- Concerns raised in the preliminary assessment warrant additional monitoring.

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Acute Dietary Risk Assessment: *Summary*

- Methodology developed allowing use of PDP and FDA monitoring data for 80% of foods treated with azinphos-methyl, including major contributors to risk.
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Drinking Water Risk Assessment (*con't*)

- Determined exposure to AZM in food first, then considered any remaining allowable exposure in drinking water.
- Example:
 - For children 1-6, 33% of chronic RfD used by exposure through food
 - 67% of the chronic RfD remaining for exposure through drinking water
- Drinking water exposure based on model estimates were less than 67% of chronic RfD.
- Conclude: chronic exposure to AZM in drinking water not a concern.
- Screening-level assessment considered health-protective because drinking water exposures based on model estimates are higher than actual exposures expected.

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Aggregate Risk Assessment

- Includes exposures from various sources:
 - food,
 - drinking water,
 - and residential and other non-occupational.
- No registered residential and non-occupational uses of azinphos-methyl.
 - For example, it is not used in homes, lawns, golf courses, etc.
- Aggregate risk assessment for azinphos-methyl includes food and drinking water only.

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Aggregate Risk Assessment (*con't*)

- Acute aggregate risk assessment was not done, because our risk estimates for exposures through food alone exceed EPA's level of concern.
- Chronic aggregate risk assessment:
 - Combined food exposures and estimates of exposure from models for drinking water are not of concern.

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Occupational Risk Assessments Conducted for Azinphos-Methyl

Handlers

– includes professional pesticide applicators and farmer/growers who mix, load and apply pesticides.

Post-Application Workers

– includes workers who prune, thin, hoe, prop, and harvest crops following pesticide application.

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Occupational Assessment (*con't*)

Factors Forming the Basis for Handler Risk Assessment

- Formulation and application equipment (e.g., wettable powder, airblast sprayer)
- Unit exposure (mg ai/lb ai handled)
- Rate of application (lb ai/acre)
- Areas treated per day (e.g., acres/day)
- Toxicity endpoint (mg/kg/day)
- Levels of protection

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Occupational Assessment (con't)

Handler Risk Calculation

$$\text{Dose} = \frac{(\text{unit exposure}) \times (\text{appl. rate}) \times (\text{acres/day}) \times (\text{dermal absorption\%})}{\text{Body Weight}}$$

$$\text{MOE} = \frac{\text{NOAEL}^* (\text{mg/kg/day})}{\text{Dose (mg/kg/day)}}$$

* From a 21-day dermal study; therefore, a dermal absorption factor is not needed.

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Occupational Assessment (con't)

Handler Scenarios: (includes representative crops, and maximum mitigation measures assessed)

Mixing/Loading Liquids for:

- (1a) aerial application on cotton and tomatoes;
- (1b) groundboom application on potatoes and tomatoes;
- (1c) airblast sprayer application on pecans, citrus, grapes, apples, and plums/prunes/peaches

Closed mixing system, single layer of clothing, chemical resistant gloves.

Mixing/Loading Wettable Powders for:

- (2a) aerial application on alfalfa and tomatoes;
- (2b) groundboom application on potatoes and tomatoes
- (2c) airblast sprayer application on almonds, citrus, grapes, apples, and plums/prunes/peaches

Water soluble packets, no gloves.

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Occupational Assessment (*con't*)

Handler Scenarios (*con't*)

Applying Liquid Spray by:

- (3) fixed-wing aircraft on cotton and tomatoes
Enclosed cockpit, single layer of clothing, no gloves.
- (4) helicopter on cotton and tomatoes
Enclosed cockpit, single layer of clothing, no gloves.
- (5) groundboom on potatoes and tomatoes
Enclosed cab, single layer of clothing, no gloves.
- (6) airblast sprayer on almonds, citrus, grapes, apples and plums/prunes/peaches
Enclosed cab, single layer of clothing, chemical resistant gloves.

Occupational Assessment (*con't*)

Handler Scenarios (*con't*)

Mixing/Loading/Applying by:

- (7) low pressure handwand on ornamentals
 - (8) high pressure handwand on ornamentals
 - (9) backpack sprayer on ornamentals
- Double layer of clothing, chemical resistant gloves.*

Flagging for:

- (10) Aerial application on cotton
Enclosed cab, single layer of clothing, no gloves.

Occupational Assessment (*con't*)

Results for Short- and Intermediate-Term Handler Risks:

- Out of the 14 handler scenarios, only one has an MOE above 100 when considering short and intermediate exposure.

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Occupational Assessment (*con't*)

Factors Forming the Basis for Post-Application Worker Risk

- Dislodgeable Foliar Residues (DFR):
 - amount of residue that workers could contact in field.
- Transfer Coefficient (Tc):
 - indicator of amount that workers actually contact during various field activities.

Post-Application Worker Risk Calculation

$$\text{Dose} = \frac{\text{DFR} (\lambda\text{g/cm}^2) \times \text{Tc} (\text{cm}^2/\text{hour}) \times 8 \text{ hours}}{\text{Body Weight (kg)}}$$

$$\text{MOE} = \frac{\text{NOAEL (mg/kg/day)}}{\text{Dose (mg/kg/day)}}$$

NOTE: A Re-entry Interval (REI): Period of time following application during which workers may not enter the fields.

Occupational Assessment (*con't*)

Sources of Information

DFR Data:

- Data used from studies on tomatoes, potatoes, apples, grapes, and cotton submitted by registrant.
- Most recent data on apples and cotton from studies submitted by registrant under a large Agricultural Data Call-In (DCI) issued by the Agency in 1995.

Transfer Coefficients:

- For orchard and citrus crops:
 - developed by California Department of Pesticide Regulation (CDPR) from azinphos-methyl exposure studies.

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Occupational Assessment (*con't*)

Post-Application Risk Assessment Results

- Risk estimates for reentry workers for all uses of azinphos-methyl (except its use in the WP50 formulation on tomatoes at 1.5 lbs ai/acre) pose serious risk concerns based on current application rates and REIs.
- Many REIs are currently two days (except for stone and pome fruits and nut crops at 14 days, grapes at 21 days, and citrus at 30 days).
- Some Results for Other Crops Studied:

Crop	MOE	Day and Application Rate
Potatoes	>100	Day 8; following 0.75 lb ai/acre
Apples	0.9	Day 21; following 1 lb ai/acre
Citrus	4	Day 30 following 2 lb ai/acre
Grapes	0.4	Day 21 following 0.25 lb ai/acre
Cotton	>100	Day 7 following 0.25 lb ai/acre

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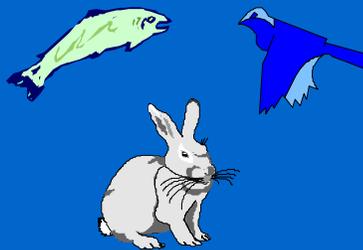
Occupational Assessment (*con't*)

Incidence Information:

- California Pesticide Illness Surveillance Program (1982 -1990)
- American Association of Poison Control Centers
- Cases of Illness:
 - Among:
 - Mixers/loaders
 - Re-entry Workers
 - Applicators
 - Spray Drift
 - Effects:
 - Systemic
 - Eye
 - Skin
 - Respiratory

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Ecological Assessment



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Public Comments

Public Comment Period on Preliminary Assessment Closed 3/99

Comments Received:

- Registrant:
 - Focused on Fate and Water Issues
- Grower Groups:
 - Focused on Typical Application Methods
- Washington State Department of Agriculture:
 - Focused on Toxicity to Bees

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Ecological Concerns

Concern for Aquatic Organisms Based on:

- Calculated estimates exceed levels of concern
- Extensive reported incidents
 - Many fish kills reports relative to other pesticides
 - Many fish killed in individual incidents
 - About 50% of incidents in OPP's data base are associated with azinphos-methyl use
 - Primarily associated with sugarcane and cotton uses.
- Efforts made to address concern
 - Prescriptive use on sugarcane
 - Reduction in maximum number of applications

Concern for Terrestrial Organisms Based on:

- Exceedence of both acute and chronic LOCs

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Summary and Conclusion



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Summary of Acute Dietary Risk Assessment

- Some risks of concern at 99.9 percentile
- Probabilistic assessment used predominately PDP and FDA monitoring data.
- New methodology used is being refined and will be Peer Reviewed.
- Assessment does not include potential additional contributions to risk estimates from drinking water.

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Summary of Worker Risk Assessment

Handler Exposure (Mixer/Loader/Applicator)

- Risk of concern for most scenarios.
- No chemical specific data available, so PHED data was used.
- Combined dermal & inhalation risks were calculated based on the maximum PPE and/or engineering controls.
- Risk mitigation proposed by registrants will help; however, risk estimates still remain of concern.

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Summary of Worker Risk Assessment (*con't*)

Post-Application Reentry Exposure

- Risk of concern for most scenarios.
- Chemical-specific studies were used for estimating post-application worker exposure.
- New Dislodgeable Foliar Residue Studies were used in the assessment.
- Transfer coefficients used showed how readily residues transfer from foliage to workers who contact treated foliage.
- Risk to reentry workers is still above EPA's level of concern for several crops; therefore, further mitigation is needed. 62

Summary of Preliminary Ecological Assessment

Aquatic

- Calculated risk estimates are high
- Fish kill incidents
- Some use restriction already in place

Terrestrial

- Calculated risk estimates are high

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Additional Data

Acute Dietary Exposure

- Refinements of % crop treated data (complete)
- USDA PDP single serving pear data (complete)
- Applesauce residue monitoring study-U.S. Apple Assoc. (2Q/00)
- New apple processing study-Bayer (2Q/99)
- Cherry processing study-Cherry Marketing Institute (2Q/99)
- USDA PDP single serving on apples-USDA(4Q/99)
- Single serving market basket survey focusing on "kid's foods"-Bayer (2Q/00)
- Reduction of residues study in "packing houses"-Bayer (2Q/99)
- New field trials on apples using lower application rate-Bayer (3Q/99)
- Surface & Ground Water Monitoring Studies are needed for the Drinking Water Risk Assessment

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Additional Data (*con't*)

Acute Dietary Toxicological Endpoint

- Human oral study (submitted 3/22/99, in review)

Worker Exposure

- Label Changes (Complete)
- Occupational monitoring study needed to verify reduced exposure with closed systems (Suggested)

Acute Worker Toxicological Endpoint

- Human dermal study (submitted 3/5/99, in review)

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Outstanding Issues

Acute Dietary Risk Assessment

Questions about the Inputs

- Calculation and use of estimated maximum % crop treated
- Calculation and use of decomposited distribution
- Documenting methods and SOPs

Questions about the Outputs

- Whether 99.9th percentile is driven by outliers (unreasonable values for consumption or residues)
- Documenting stability and reproducibility of results
- Sensitivity Analysis
- Providing Transparency and Clarity in Risk Characterizations

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Outstanding Issues (*con't*)

Worker Risk Assessment

- Current risk estimates for several crops for mixer/loader/appliator workers may possibly be mitigated by a reduction in application rates.
- For some crops, increases in Reentry Intervals (REIs) will still not alleviate risk concerns.
- The toxicological endpoint is driving the risk estimates.
- Compare with California risk assessment.

Ecological

- Evaluate comments and revise as appropriate

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