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Environmental Protection  
Agency

Prevention, Pesticides  
And Toxic Substances  
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# **Report on FQPA Tolerance Reassessment Progress and Interim Risk Management Decision for Fenitrothion**



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

OFFICE OF  
PREVENTION, PESTICIDES  
AND TOXIC SUBSTANCES

**CERTIFIED MAIL**

July 5, 2000

Dear Registrant:

This is to inform you that the Environmental Protection Agency (hereafter referred to as EPA or the Agency) has completed its review of the available data and public comments received concerning the revised risk assessment for the organophosphate pesticide fenitrothion. The public comment period on the revised risk assessment phase of the tolerance reassessment process is closed. The attached document summarizes the Agency's assessment of dietary risk from fenitrothion as part of the tolerance reassessment process for this chemical, presents a summary of the revised food tolerances for fenitrothion, and provides the Agency's current risk management position, based on the risk assessment. Fenitrothion is not registered for use on food or feed crops in the U.S. It has only one import tolerance, for wheat gluten imported from Australia, and the dietary risk analysis indicates that the risk is below the Agency's level of concern. Therefore, no mitigation is necessary at this time.

A Notice of Availability for this "Report on FQPA Tolerance Reassessment Progress and Interim Risk Management Decision for Fenitrothion" will be published in the *Federal Register*. This document and supporting technical documents are available for viewing in the Office of Pesticide Programs' Public Docket and can also be found on the Agency's web page, "[www.epa.gov/opp/op](http://www.epa.gov/opp/op)."

This document presents an update of the Reregistration Eligibility Decision (RED), which was issued in July 1995, taking into account the provisions of the Food Quality Protection Act (FQPA) of 1996. The docket includes background information on the risk assessments. No comments affecting the risk assessments were received during the Phase 3 or Phase 5 public comment periods. Therefore, the risk assessments were not revised.

This document and the process used to develop it are the results of a pilot process to facilitate greater public involvement and participation in the reregistration and/or FQPA tolerance reassessment decisions on pesticides. As part of the Agency's effort to involve the public in the implementation of the FQPA, the Agency is undertaking a special effort to maintain open public dockets on the organophosphate pesticides and to engage the public in the reregistration and tolerance reassessment processes for these chemicals. The idea of using such an open process was developed by the Tolerance Reassessment Advisory Committee (TRAC), a large multi-stakeholder advisory body which advised the Agency on implementing the new provisions of the FQPA. The reregistration and tolerance reassessment reviews for the organophosphate pesticides are following this new process.

Please note that the fenitrothion risk assessment concerns only this particular organophosphate. Because the FQPA directs the Agency to consider available information on cumulative risk from substances sharing a common mechanism of toxicity, such as the toxicity expressed by the organophosphates through a common biochemical interaction with cholinesterase, the Agency will evaluate the cumulative risk posed by the entire organophosphate class of chemicals, after completing risk assessments for the individual organophosphates. The Agency is working to complete a methodology to assess cumulative risk, and individual assessments of each organophosphate are likely to be necessary elements of any cumulative assessment. The Agency has decided to move forward with individual assessments and to identify mitigation measures, where necessary. The Agency will issue the final tolerance reassessment decision for fenitrothion once the cumulative assessment for all of the organophosphates is complete.

If you have questions on this document, please contact the Special Review and Reregistration Division representative for fenitrothion, Stephanie Nguyen at (703) 605-0702.

Lois A. Rossi, Director  
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Attachment

Report on FQPA Tolerance Reassessment Progress  
and Interim Risk Management Decision  
for  
Fenitrothion

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## Glossary of Terms and Abbreviations

|        |  |
|--------|--|
| AE     | Acid Equivalent  |
| a.i.   | Active Ingredient  |
| AGDCI  | Agricultural Data Call-In  |
| ai     | Active Ingredient  |
| aPAD   | Acute Population Adjusted Dose   |
| AR     | Anticipated Residue  |
| ARC    | Anticipated Residue Contribution   |
| BCF    | Bioconcentration Factor  |
| CAS    | Chemical Abstracts Service   |
| CI     | Cation   |
| CNS    | Central Nervous System   |
| cPAD   | Chronic Population Adjusted Dose   |
| CSF    | Confidential Statement of Formula  |
| CFR    | Code of Federal Regulations  |
| CSFII  | USDA Continuing Surveys for Food Intake by Individuals   |
| DCI    | Data Call-In   |
| DEEM   | Dietary Exposure Evaluation Model  |
| DFR    | Dislodgeable Foliar Residue  |
| DRES   | Dietary Risk Evaluation System   |
| DWEL   | Drinking Water Equivalent Level (DWEL) The DWEL represents a medium specific (i.e., drinking water) lifetime exposure at which adverse, noncarcinogenic health effects are not anticipated to occur. |
| DWLOC  | Drinking Water Level of Comparison.  |
| EC     | Emulsifiable Concentrate Formulation   |
| EEC    | Estimated Environmental Concentration. The estimated pesticide concentration in an environment, such as a terrestrial ecosystem.   |
| EP     | End-Use Product  |
| EPA    | U.S. Environmental Protection Agency   |
| FAO    | Food and Agriculture Organization  |
| FDA    | Food and Drug Administration   |
| FIFRA  | Federal Insecticide, Fungicide, and Rodenticide Act  |
| FFDCA  | Federal Food, Drug, and Cosmetic Act   |
| FQPA   | Food Quality Protection Act  |
| FOB    | Functional Observation Battery   |
| G      | Granular Formulation   |
| GENEEC | Tier I Surface Water Computer Model  |
| GLC    | Gas Liquid Chromatography  |
| GLN    | Guideline Number   |
| GM     | Geometric Mean   |
| GRAS   | Generally Recognized as Safe as Designated by FDA  |

|                  |  |
|------------------|--|
| HA               | Health Advisory (HA). The HA values are used as informal guidance to municipalities and other organizations when emergency spills or contamination situations occur.   |
| HAFT             | Highest Average Field Trial  |
| HDT              | Highest Dose Tested  |
| IR               | Index Reservoir  |
| LC <sub>50</sub> | Median Lethal Concentration. A statistically derived concentration of a substance that can be expected to cause death in 50% of test animals. It is usually expressed as the weight of substance per weight or volume of water, air or feed, e.g., mg/l, mg/kg or ppm.       |
| LD <sub>50</sub> | Median Lethal Dose. A statistically derived single dose that can be expected to cause death in 50% of the test animals when administered by the route indicated (oral, dermal, inhalation). It is expressed as a weight of substance per unit weight of animal, e.g., mg/kg. |
| LEL              | Lowest Effect Level  |
| LOC              | Level of Concern   |
| LOD              | Limit of Detection   |
| LOAEL            | Lowest Observed Adverse Effect Level   |
| MATC             | Maximum Acceptable Toxicant Concentration  |
| MCLG             | Maximum Contaminant Level Goal (MCLG) The MCLG is used by the Agency to regulate contaminants in drinking water under the Safe Drinking Water Act.   |
| mg/kg/day        | Milligram Per Kilogram Per Day   |
| mg/L             | Milligrams Per Liter   |
| MOE              | Margin of Exposure   |
| MP               | Manufacturing-Use Product  |
| MPI              | Maximum Permissible Intake   |
| MRID             | Master Record Identification (number). EPA's system of recording and tracking studies submitted.   |
| N/A              | Not Applicable   |
| NAWQA            | USGS National Water Quality Assessment   |
| NOEC             | No Observable Effect Concentration   |
| NOEL             | No Observed Effect Level   |
| NOAEL            | No Observed Adverse Effect Level   |
| NPDES            | National Pollutant Discharge Elimination System  |
| NR               | Not Required   |
| OP               | Organophosphate  |
| OPP              | EPA Office of Pesticide Programs   |
| OPPTS            | EPA Office of Prevention, Pesticides and Toxic Substances  |
| Pa               | pascal, the pressure exerted by a force of one newton acting on an area of one square meter.   |
| PAD              | Population Adjusted Dose   |
| PADI             | Provisional Acceptable Daily Intake  |
| PAG              | Pesticide Assessment Guideline   |
| PAM              | Pesticide Analytical Method  |

|                  |   |
|------------------|---|
| PCA              | Percent Crop Area   |
| PDP              | USDA Pesticide Data Program   |
| PHED             | Pesticide Handler's Exposure Data   |
| PHI              | Preharvest Interval   |
| ppb              | Parts Per Billion   |
| PPE              | Personal Protective Equipment   |
| ppm              | Parts Per Million   |
| PRN              | Pesticide Registration Notice   |
| PRZM/EXAMS       | Tier II Surface Water Computer Model  |
| Q <sub>1</sub> * | The Carcinogenic Potential of a Compound, Quantified by the EPA's Cancer Risk Model           |
| RAC              | Raw Agriculture Commodity   |
| RBC              | Red Blood Cell  |
| RED              | Reregistration Eligibility Decision   |
| REI              | Restricted Entry Interval   |
| RfD              | Reference Dose  |
| RQ               | Risk Quotient   |
| RS               | Registration Standard   |
| RUP              | Restricted Use Pesticide  |
| SAP              | Science Advisory Panel  |
| SCI-GROW         | Tier I Ground Water Computer Model  |
| SF               | Safety Factor   |
| SLC              | Single Layer Clothing   |
| SLN              | Special Local Need (Registrations Under Section 24© of FIFRA)                                 |
| TC               | Toxic Concentration. The concentration at which a substance produces a toxic effect.          |
| TD               | Toxic Dose. The dose at which a substance produces a toxic effect.                            |
| TEP              | Typical End-Use Product   |
| TGAI             | Technical Grade Active Ingredient   |
| TLC              | Thin Layer Chromatography   |
| TMRC             | Theoretical Maximum Residue Contribution  |
| torr             | A unit of pressure needed to support a column of mercury 1 mm high under standard conditions. |
| TRR              | Total Radioactive Residue   |
| UF               | Uncertainty Factor  |
| µg/g             | Micrograms Per Gram   |
| µg/L             | Micrograms Per Liter  |
| USDA             | United States Department of Agriculture   |
| USGS             | United States Geological Survey   |
| UV               | Ultraviolet   |
| WHO              | World Health Organization   |
| WP               | Wettable Powder   |
| WPS              | Worker Protection Standard  |

## **Executive Summary**

The U.S. Environmental Protection Agency (hereafter referred to as EPA or the Agency) has completed its review of public comments on the risk assessment for fenitrothion, and is, in this document, issuing its interim decision on the risk mitigation for this chemical. This risk assessment is based on review of the required target data base supporting the single fenitrothion import tolerance and information received during the public comment periods in the open process developed through the Tolerance Reassessment Advisory Committee (TRAC). Fenitrothion is registered in the U.S. for use in ant and roach baits. There are no food uses registered in the U.S. The product is manufactured by Sumitomo Chemical Corporation.

EPA's revised risk assessment for fenitrothion indicates that the dietary risk does not exceed the Agency's level of concern; therefore, no risk mitigation is necessary at this time. This assessment does not address residential, ecological, drinking water, or worker risks, because little or no exposure to residents, workers, or the environment is likely from the current limited domestic use of fenitrothion in ant and roach baits.

The tolerance reassessment decision for fenitrothion will be issued once the cumulative assessment for all of the organophosphates is completed. The Agency may need to issue risk management measures for fenitrothion at the time the organophosphate cumulative assessment is finalized.

## **I. Introduction**

This report on the progress toward tolerance reassessment of fenitrothion is the result of the pilot process developed through the TRAC to facilitate greater public involvement in the ongoing Federal Insecticide, Fungicide, and Rodenticide Act (FIFRA) reregistration and FQPA tolerance reassessment initiatives on pesticides. A Reregistration Eligibility Document (RED) was issued in July 1995. This assessment presents an update of the RED, taking into account the provisions of the Food Quality Protection Act of 1996. Fenitrothion is not used on food or feed crops in the U.S. It has only one tolerance, for wheat gluten imported from Australia. This assessment does not address residential, ecological, drinking water, or worker risks, because little or no exposure to residents, workers, or the environment is likely from the current limited domestic use of fenitrothion in ant and roach baits. Thus, this assessment relates only to the requirements of FQPA. However, some history and background of FIFRA is included here for informational purposes and to provide a discussion of the existing laws requiring action on pesticides.

The FIFRA was amended in 1988 to accelerate the reregistration of products with active ingredients registered prior to November 1, 1984. The amended act calls for the development and submission of data to support the reregistration of an active ingredient, as well as a review of all submitted data by the Agency. Reregistration involves a thorough review of the scientific database underlying a pesticide's registration. The purpose of the Agency's review is to reassess all potential hazards arising from the currently registered uses of the pesticide; determine the need for additional data on health and environmental effects; and determine whether the pesticide meets the "no unreasonable adverse effects" criteria of FIFRA.

On August 3, 1996, the FQPA was signed into law. This Act amends FIFRA to require tolerance reassessment during reregistration. It also requires that, by August 2006, EPA review all tolerances in effect on the day before the date of the enactment of the FQPA. FQPA amends both FIFRA and the Federal Food, Drug, and Cosmetic Act (FFDCA), but does not amend any of the existing reregistration deadlines. Therefore, the Agency is continuing its reregistration program while it resolves remaining issues associated with the implementation of FQPA. The Agency is also continuing its progress toward tolerance reassessment as required by FQPA for all of the organophosphate chemicals, whether or not they are subject to the reregistration process. While the methodology for completion of the cumulative assessment for all of the organophosphates is being developed, individual risk assessments and risk mitigation measures, where appropriate, are being conducted. The Fenitrothion RED, reflecting decisions of the reregistration process, was issued in July 1995. The revised individual dietary assessment for fenitrothion has been completed, and will be used in the cumulative assessment of all of the organophosphate chemicals, in order to satisfy the requirements of FQPA.

The import tolerance for fenitrothion is subject to the requirements of FQPA; therefore, a dietary risk assessment was completed. This document presents the Agency's dietary risk assessment for fenitrothion, as part of the tolerance reassessment process. Note that there is no comment period

for this document. As part of the process developed by the TRAC, which sought to open up the process to interested parties, the Agency's risk assessment for fenitrothion has already been subject to numerous public comment periods, and a further comment period was deemed unnecessary. A Notice of Availability for this document is published in the *Federal Register*. Phase 6 of the pilot process does not include a public comment period. However, for some chemicals, the Agency may provide another comment period, depending on the content of the risk management decision.

Implementation of FQPA has required the Agency to revisit some of its existing policies relating to the determination and regulation of dietary risk, and has also raised a number of new issues for which policies need to be created. These issues were refined and developed through collaboration between the Agency and the Tolerance Reassessment Advisory Committee (TRAC), which was composed of representatives from industry, environmental groups, and other interested parties. TRAC identified the following science policy issues it believed were key to the implementation of FQPA and tolerance reassessment:

- C Applying the FQPA 10-Fold Safety Factor
- C Whether and How to Use "Monte Carlo" Analyses in Dietary Exposure Assessments
- C How to Interpret "No Detectable Residues" in Dietary Exposure Assessments
- C Refining Dietary (Food) Exposure Estimates
- C Refining Dietary (Drinking Water) Exposure Estimates
- C Assessing Residential Exposure
- C Aggregating Exposure from all Non-Occupational Sources
- C How to Conduct a Cumulative Risk Assessment for Organophosphate or Other Pesticides with a Common Mechanism of Toxicity
- C Selection of Appropriate Toxicity Endpoints for Risk Assessments of Organophosphates
- C Whether and How to Use Data Derived from Human Studies

The process developed by TRAC calls for EPA to provide one or more documents for public comment on each of the policy issues described above. Each of these issues is evolving and in a different stage of refinement. Some issue papers have already been published for comment in the *Federal Register* and others will be published shortly.

This document consists of six sections. Section I contains the regulatory framework for reregistration/tolerance reassessment as well as a description of the process developed by TRAC for public comment on science policy issues for the organophosphate pesticides. Section II provides a profile of the usage of this chemical. Section III gives an overview of the dietary risk assessment for fenitrothion, including a discussion of any revisions made to the preliminary assessment. Section IV presents the Agency's progress towards tolerance reassessment, its interim decision, and the regulatory position on this chemical. Section V discusses what the manufacturer's obligations are with respect to further actions required, and finally, Section VI provides information on how to access related documents. The entire revised risk assessment is not included in this document, but is available on the Agency's web page ([www.epa.gov/opp/op](http://www.epa.gov/opp/op)), and in the Public Docket.

## II. Chemical Overview

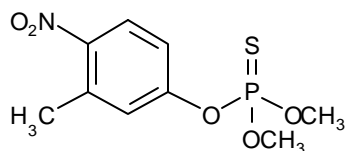
### A. Regulatory History

Fenitrothion, an organophosphate, is a cholinesterase inhibiting insecticide/acaricide registered for use in the U.S. in ant and roach baits. In the July 1995 RED a tolerance of 15 ppm was recommended for residues of fenitrothion in wheat gluten resulting from post-harvest application to stored wheat in Australia. The Agency has reassessed the tolerance for residues of fenitrothion in wheat gluten and is lowering it to 3 ppm, and will revise the tolerance expression to include only the parent compound.

In the July 1995 RED, greenhouse, outdoor ornamental, and containerized ant and roach baits in child resistant packaging were the only registered domestic uses assessed. The RED required an extensive amount of risk mitigation for the greenhouse and outdoor ornamental uses as well as a considerable amount of additional data. Subsequent to the issuance of the RED, these uses were voluntarily canceled, leaving ant and roach baits as the only registered domestic use.

### B. Chemical Identification

FENITROTHION:



|   |                             |   |
|---|-----------------------------|---|
| ! | <b>Common Name:</b>         | Fenitrothion                                      |
| ! | <b>Chemical Name:</b>       | O,O-dimethyl O-(4-nitro-m-tolyl) phosphorothioate |
| ! | <b>Chemical Family:</b>     | Organophosphate                                   |
| ! | <b>CAS Registry Number:</b> | 122-14-5  |
| ! | <b>OPP Chemical Code:</b>   | 105901  |
| ! | <b>Empirical Formula:</b>   | C <sub>9</sub> H <sub>12</sub> NO <sub>5</sub> PS |
| ! | <b>Molecular Weight:</b>    | 277.2   |

- ! **Trade and Other Names:** Tat Ant Trap X, Tat Roach Bait V, Sumithion
- ! **Basic Manufacturers:** Sumitomo Chemical Co.TDT., Osaka, Japan  
(Fenitrothion is not manufactured in the U.S.)

**C. Use Profile**

The following information is based on the current uses of fenitrothion both within and outside of the United States, and includes an overview of use sites and application methods.

**Type of Pesticide:** Insecticide/Acaricide

**Summary of Use Sites:**

**Food:** There are no registered food uses in the U.S.  
Fenitrothion is used in Australia on stored wheat and there is a U.S. tolerance for imported wheat gluten.

**Residential:** The only registered use in the U.S. is for containerized ant and roach baits in child resistant packaging.

**Target Pests:** Ants, roaches, palmetto bugs, waterbugs

**Formulation Types:** Emulsifiable concentrate (not registered in the U.S.), and as pellets and granular baits

**Method and Rates of Application:**

**Method and Rate** - Baits contain either 0.01563% or 1.0% active ingredient (a.i.). For stored wheat, fenitrothion emulsifiable concentrate is applied at 12 mg a.i./kg grain, prior to bin storage (not registered in the U.S.)

**D. Estimated Usage of Pesticide**

This section summarizes the best estimates available for the pesticide uses of fenitrothion. These estimates are derived from a variety of published and proprietary sources available to the Agency. The data, reported on an aggregate and site (crop) basis, reflect annual fluctuations in use patterns as well as the variability in using data from various sources.

Annual U.S. consumption of wheat gluten by the food industry is about 250 million pounds; currently approximately 26% (65 million pounds) is imported from Australia. Because no data are available on percent crop treated, for the purpose of this reassessment, EPA has assumed that all of the wheat gluten imported from Australia could be treated with fenitrothion. (Note: Wheat gluten is the natural protein derived from wheat. It is essentially wheat flour with the starch removed. It is used by the baking industry to improve consistency in bread products, and has other industrial uses.)

### **III. Summary of Fenitrothion Risk Assessment**

Following is a summary of EPA's revised human health risk findings and conclusions for the organophosphate pesticide fenitrothion, as fully presented in the revised risk assessment document, "Fenitrothion HED RED Chapter; Revised Risk Assessment (PC Code 105901)," dated May 19, 1999. The risk assessment presented here forms the basis of the Agency's interim risk management decision for fenitrothion only; the Agency must complete a cumulative assessment of the risks of all organophosphate pesticides before it can complete its reassessment of the fenitrothion tolerance.

The revised risk assessment for fenitrothion presents the individual dietary assessment for fenitrothion resulting from its use on wheat gluten imported from Australia. This assessment does not address residential, ecological, drinking water, or worker risks, because little or no exposure to residents, workers, or the environment is likely from the current limited domestic use of fenitrothion in ant and roach baits.

#### **A. Human Health Risk Assessment**

No comments affecting the risk assessment were received during the Phase 3 or Phase 5 public comment periods; therefore, the risk assessments were not revised.

##### **1. Dietary Risk from Food**

###### **a. Toxicity**

The Agency has reviewed all toxicity studies submitted and has determined that the toxicity database supports a dietary risk assessment for fenitrothion as well as a future FQPA tolerance reassessment for the import tolerance on wheat gluten. Further details on the toxicity of fenitrothion can be found in the May 19, 1999 HED Red Chapter; Revised Risk Assessment. A brief overview of the studies used for the dietary risk assessment is outlined in Table 1 of this document.

**b. FQPA Safety Factor**

The FQPA Safety Factor was removed based on a complete toxicity data base and adequate exposure information, which allowed reasonable understanding in predicting possible effects on infants and children, and the lack of increased susceptibility in the fetuses and/or pups in the developmental and reproduction studies. The Agency has granted a waiver for the developmental neurotoxicity (DNT) study for fenitrothion. The Agency has determined that exposure to any population group of concern under the FQPA is very low for the currently registered and labeled uses of fenitrothion, given the amount used, how it is used, and information available to the Agency regarding levels to which people are exposed.

**c. Population Adjusted Dose (PAD)**

The PAD is a relatively new term that characterizes the dietary risk of a chemical, and reflects the Reference Dose, either acute or chronic, that has been adjusted to account for the FQPA safety factor (i.e., RfD/FQPA safety factor). For the acute dietary assessment, risk is calculated considering what is eaten in one day (consumption) and maximum, high-end residue values in food. For chronic exposures, dietary risk is calculated by using the average consumption value for food and average residue value. In the case of fenitrothion, the FQPA Safety Factor Committee recommended removal of the 10X safety factor; therefore, the acute or chronic RfD is equal to the acute or chronic PAD. A risk estimate that is less than 100% of the acute or chronic PAD does not exceed the Agency's risk concern.

**d. Exposure Assumptions**

A tolerance level of 15 ppm was previously recommended to cover residues of fenitrothion in wheat gluten imported from Australia. However, the Agency has re-evaluated the magnitude of residue database for fenitrothion and concluded that the tolerance value for fenitrothion in wheat gluten can be lowered to 3 ppm. In four trials from four different states in Australia, residues ranged from 0.95 to 2.5 ppm in/on wheat gluten; the average residue was 1.84 ppm. Monitoring data from a commercial wheat gluten processing facility in Australia showed residues ranging from 0.09 to 0.9 ppm, with an average of 0.38 ppm. FDA has monitored just a few wheat gluten samples from Australia over the last several years. Most samples showed non-detectable residues of fenitrothion, although trace residues (residues less than the level which can be reliably quantified) were found in two samples.

The Agency estimates that approximately 65 million pounds of wheat gluten are imported from Australia each year, according to quotas that were created in 1998. Based on that figure, together with an annual U.S. consumption estimate for the U.S. food industry of 250 million pounds of wheat gluten, the maximum amount of all U.S. wheat gluten which could be treated with fenitrothion is 26%. This assumes that 100% of wheat gluten imported from Australia has been treated.

Dietary risk analyses for fenitrothion were conducted with the Dietary Exposure Evaluation Model (DEEM™). DEEM incorporates consumption data generated in USDA’s Continuing Surveys of Food Intake by Individuals (CSFII), 1989-1992. This model does not contain consumption values for wheat gluten. EPA used wheat flour consumption data and an adjustment factor (0.0062) to estimate the amount of wheat gluten consumed. [The adjustment factor represents the estimated amount of wheat gluten consumed annually as a proportion of the total wheat flour consumed annually]. Use of this factor assumes that the relative consumption of wheat gluten to wheat flour is the same for all population subgroups. Residues were estimated using the proposed revised tolerance level (3 ppm) and average per capita exposure.

**Table 1. Summary of Toxicological Endpoints and Other Factors Used in the Human Dietary Risk Assessment of Fenitrothion**

| Assessment      | Study                    | Dose (mg/kg/day)              | Endpoint  | UF  | FQPA Safety Factor | PAD              |
|-----------------|--------------------------|-------------------------------|---|-----|--------------------|------------------|
| Acute Dietary   | Acute Neurotoxicity- Rat | NOAEL = 12.5<br>LOAEL = 50    | Tremors and impaired motor coordination                             | 100 | 1X                 | 0.13 mg/kg/day   |
| Chronic Dietary | 1-year Feeding Study-Dog | NOAEL = 0.125<br>LOAEL = 0.25 | Plasma ChE inhibition and histopathology changes of the lymph nodes | 100 | 1X                 | 0.0013 mg/kg/day |

**e. Acute Food Risk**

The acute dietary (food) risk of fenitrothion is 0.02% of the aPAD for the general population, well below the Agency’s level of concern. An acute dietary risk assessment was not performed in the July 1995 RED because data to estimate single-day consumption of wheat gluten were not available. However, using the average U.S. population exposure estimate with the acute dietary NOAEL results in the above acute dietary risk estimate. Therefore, while there are uncertainties in the estimated risk due to uncertainties in the consumption estimate, this extremely low percent of the aPAD indicates that risks from this use will be insignificant. This analysis satisfies the FQPA requirement for the special consideration of pesticide risk to children.

**f. Chronic Food Risk**

Use of the average residues from field trials and limited FDA monitoring, together with percent of commodity treated data discussed above (26%) results in chronic dietary risk estimates of <1% of the cPAD for the general U.S. population and all population subgroups. The most highly exposed sub-population is children 1-6 at 0.7% of the cPAD. Note that this estimate is considered to be somewhat conservative, since 100% crop treatment is assumed for wheat gluten produced in Australia.

In summary, the potential acute and chronic dietary exposures on imported wheat gluten are well below the level of concern for all population sub-groups, including infants and children. Data on the actual percentage of stored Australian wheat treated with fenitrothion and the percent of imported Australian wheat gluten diverted for non-food purposes (e.g., the manufacture of bio-degradable plastic) would allow EPA to further refine the dietary risk estimates.

## **2. Residential Risk**

Exposure resulting from use of the containerized ant and roach baits in child resistant packaging is expected to be insignificant. The Agency did not quantitatively estimate risks for this type of use because of the expected low potential for exposure. Exposure is expected to be insignificant because the material is not available through the dermal and oral routes; and, due to the small amount of material which would be available through volatilization, inhalation exposure is expected to be minimal.

## **3. Aggregate Risk**

Because exposure from residential uses is expected to be insignificant, the aggregate exposure assessment for fenitrothion would include consideration of exposures only from food. Therefore, an aggregate assessment was not required.

# **IV. FQPA Tolerance Reassessment Progress & Interim Risk Management Decision**

## **A. Tolerance Reassessment Progress & Interim Risk Management Decision**

The Agency has completed its assessment of the dietary risk of fenitrothion but has not considered the cumulative effects of organophosphates as a class. Based on review of the generic and other data, EPA has sufficient information on the human health effects of fenitrothion to make an interim decision as part of the tolerance reassessment process under FQPA. Although the Agency has not yet completed its cumulative risk assessment for the organophosphates, the Agency has completed its assessment of risk from dietary exposure to fenitrothion alone in order to determine whether any risk reduction measures are necessary to allow the continued importation of wheat gluten containing fenitrothion, pending completion of the cumulative assessment.

As a result of its assessment, EPA has determined that dietary risk from exposure to fenitrothion does not exceed the Agency's level of concern. Therefore, no mitigation is necessary and no further actions are warranted at this time. The Agency may determine that further action is necessary after assessing the cumulative risk of the organophosphate class. At that time, the Agency will also address any other outstanding risk concerns that may arise. Such an incremental approach to the tolerance reassessment process is consistent with the Agency's goal of improving the transparency of the implementation of FQPA. By evaluating each organophosphate in turn and identifying

appropriate risk reduction measures, the Agency is addressing the risks from organophosphates in as timely a manner as possible.

Because the Agency has not yet completed the cumulative risk assessment for the organophosphates, this interim decision does not specifically address the reassessment of the existing fenitrothion food residue import tolerance as called for by the FQPA. When the Agency has completed the cumulative assessment, the fenitrothion tolerance will be reassessed in that light. At that time, the Agency will reassess fenitrothion along with the other organophosphate pesticides to complete the FQPA requirements. Nothing in this report will preclude the Agency from making further FQPA determinations and tolerance-related rulemaking that may be required on this pesticide or any other in the future.

If the Agency determines, before finalization of the FQPA assessment for fenitrothion, that any of the determinations described in this document are no longer appropriate, the Agency will pursue appropriate action, including but not limited to, reconsideration of any portion of this document.

## **B. Summary of Phase 5 Comments**

EPA released its revised risk assessment for fenitrothion to the public in September, 1999, and provided a 60 day comment period for interested parties to submit information, including risk mitigation suggestions or proposals. No comments were received. Sumitomo Chemical Company, the registrant, submitted a dietary toxicity study using human volunteers, on April 25, 2000. This study has not been reviewed.

## **C. Regulatory Position**

### **1. FQPA Assessment**

#### **a. “Risk Cup” Determination**

As part of the FQPA tolerance reassessment process, EPA assessed the risks associated with this individual organophosphate. FQPA also requires the Agency to consider available information on cumulative risk from substances sharing a common mechanism of toxicity, such as the toxicity expressed by the organophosphates through a common biochemical interaction with cholinesterase enzyme. The Agency will evaluate the cumulative risk posed by the entire class of organophosphates once the methodology is developed and the policy concerning cumulative assessments is resolved.

EPA has determined that risk from exposure to fenitrothion is within its own “risk cup.” In other words, if fenitrothion did not share a common mechanism of toxicity with other chemicals, EPA would be able to conclude today that the import tolerance for fenitrothion on wheat gluten meets the FQPA safety standards. In reaching this determination, EPA considered available information on the special sensitivity of infants and children, as well as chronic and acute food exposure. An aggregate

assessment was not conducted for fenitrothion, because little or no exposure is likely from the current limited domestic use of fenitrothion in containerized ant and roach baits in child resistant packaging. Exposure is expected to be insignificant because the material is not available through the dermal and oral routes; and, due to the small amount of material which would be available through volatilization, inhalation exposure is expected to be minimal. Results of the acute and chronic food assessments indicate that exposures are within acceptable levels; that is, risk from exposure to fenitrothion “fits” within the individual risk cup. Therefore, the import tolerance remains in effect until a full reassessment of the cumulative risk from all organophosphates is completed.

**b. Tolerance Summary**

A tolerance level of 30 ppm, of which no more than 15 ppm is O,O-dimethyl O-(4-nitro-m-tolyl) phosphorothioate or O,O-dimethyl O-(4-nitro-m-tolyl) phosphate, is established for combined residues of the insecticide O,O-dimethyl O-(4-nitro-m-tolyl) phosphorothioate and its metabolites O,O-dimethyl O-(4-nitro-m-tolyl) phosphate and 3-methyl-4-nitrophenol in wheat gluten resulting from postharvest application of the insecticide to stored wheat in Australia. However, the Agency has re-evaluated the magnitude of residue database for fenitrothion and concluded the tolerance can be lowered to 3 ppm, as shown in Table 2. Residues in four field trials from four different states in Australia resulted in residues ranging from 0.95 to 2.5 ppm in/on wheat gluten; the average residue was 1.84 ppm. The tolerance expression should be modified to include only the parent compound. Although 3-methyl-4-nitrophenol is of potential toxicological concern based on data relative to similar compounds, the risk assessment conducted for the cholinesterase-inhibiting metabolite(s) is expected to be more sensitive. Therefore, only cholinesterase-inhibiting metabolites need to be regulated and 3-methyl-4-nitrophenol should be deleted from the current tolerance expression. Although O,O-dimethyl O-(4-nitro-m-tolyl) phosphate is expected to be of greater toxicological concern than the parent, finite residues of O,O-dimethyl O-(4-nitro-m-tolyl) phosphate are not expected in/on wheat grain or in wheat gluten resulting from the postharvest use of fenitrothion on stored wheat in Australia; therefore, O,O-dimethyl O-(4-nitro-m-tolyl) phosphate should be deleted from the current tolerance expression. All other metabolites were determined not to be potential cholinesterase inhibitors and/or were present at such low levels compared to the parent that they were deemed insignificant and do not need to be regulated.

**Table 2. Tolerance Summary for Fenitrothion**

| Commodity    | Tolerance Currently Listed Under 40 CFR § 185.2200 | Reassessed Tolerance* | Comment  |
|--------------|--|-----------------------|--|
| Wheat Gluten | 30 ppm   | 3 ppm                 | Wheat Gluten, imported<br>The tolerance should be expressed as parent only and the tolerance will be listed in 180.540 |

\* The term “reassessed” is not meant to imply that the tolerance has been reassessed as required by FQPA, since this tolerance may be reassessed only upon completion of the cumulative risk assessment of all organophosphates, as required by this law. Rather, it provides a tolerance level for this single chemical, if no cumulative assessment were required, that is supported by all of the submitted residue data.

## **2. Endocrine Disruptor Effects**

EPA is required under the FFDCA, as amended by FQPA, to develop a screening program to determine whether certain substances (including all pesticide active and other ingredients) “may have an effect in humans that is similar to an effect produced by a naturally occurring estrogen, or other such endocrine effects as the Administrator may designate.” Following the recommendations of its Endocrine Disruptor Screening and Testing Advisory Committee (EDSTAC), EPA determined that there was scientific bases for including, as part of the program, the androgen and thyroid hormone systems, in addition to the estrogen hormone system. EPA also adopted EDSTAC’s recommendation that the Program include evaluations of potential effects in wildlife. For pesticide chemicals, EPA will use FIFRA and, to the extent that effects in wildlife may help determine whether a substance may have an effect in humans, FFDCA authority to require the wildlife evaluations. As the science develops and resources allow, screening of additional hormone systems may be added to the Endocrine Disruptor Screening Program (EDSP).

When the appropriate screening and/or testing protocols being considered under the Agency’s EDSP have been developed, fenitrothion may be subjected to additional screening an/or testing to better characterize effects related to endocrine disruption.

### **D. Regulatory Rationale**

Fenitrothion has only one import tolerance for wheat gluten, and little or no exposure is likely from the current limited domestic use of fenitrothion in containerized ant and roach baits in child resistant packaging. Exposure is expected to be insignificant because the material is not available through the dermal and oral routes; and, due to the small amount of material which would be available through volatilization, inhalation exposure is expected to be minimal. Therefore, only a dietary risk assessment for food was conducted. Based on analyses of both acute and chronic dietary risk, the Agency has determined that the risk estimates are below the Agency’s level of concern, therefore, no mitigation measures are necessary at this time.

## **V. What Manufacturers Must Do**

### **A. Additional Data Requirements**

EPA is requiring acute, subchronic, and developmental neurotoxicity studies for all organophosphates, including those with no domestic registrations (i.e., tolerances are established only to allow treated commodities to be imported into the U.S.). However, there are no additional data required for fenitrothion. The Agency has granted a waiver for the developmental neurotoxicity (DNT) study for fenitrothion. The Agency has concluded that exposure to any population group of concern

under the FQPA is very low for the currently registered and labeled uses of fenitrothion, given the amount used, how it is used, and information available to the Agency regarding levels to which people are exposed, as described in EPA's fenitrothion human health risk assessments.

## **B. Risk Mitigation Requirements**

As discussed in this document, the acute and chronic food risk from the use of fenitrothion on imported wheat gluten is not of concern to the Agency, therefore, no mitigation is necessary at this time. The Agency may need to pursue risk management measures for fenitrothion once the cumulative assessment is finalized.

## **VI. Related Documents and How to Access Them**

This report is supported by documents that are presently maintained in the OPP docket (#34197). The OPP docket is located in Room 119, Crystal Mall #2, 1921 Jefferson Davis Highway, Arlington, VA. It is open Monday through Friday, excluding legal holidays, from 8:30 am to 4 pm. All documents, in hard copy form, may be viewed in the OPP docket room or downloaded or viewed via the Internet at the following site: "<http://www.epa.gov/pesticides/op>."

## **Bibliography for Fenitrothion Docket**

1. Christine L. Olinger (USEPA/OPPTS/OPP/HED) Fenitrothion HED RED Chapter; Revised Risk Assessment, (PC 105901). 5/19/99.
2. John C. Redden (USEPA/OPPTS/OPP/HED) HED RED Chapter for Fenitrothion (PC 105901). 5/7/94.
3. Jess Rowland (USEPA/OPPTS/OPP/HED) Fenitrothion-Correction to the Report of HIARC Review Committee. 2/23/99.
4. Jess Rowland (USEPA/OPPTS/OPP/HED) Fenitrothion - FQPA Requirement-Report of the Hazard Identification Assessment review Committee. 10/8/97.
5. Christine Swartz (USEPA/OPPTS/OPP/HED) Chronic Dietary Exposure Analyses for the Revised HED Reregistration Eligibility Decision Document (RED). 5/28/99.
6. Christine L. Olinger (USEPA/OPPTS/OPP/HED) Anticipated Residue and Tolerance Reassessment Recommendations. 5/19/99.
7. Michael S. Metzger (USEPA/OPPTS/OPP/HED) Update to Consider FQPA Requirements. 2/24/98.
8. Frank Hernandez (USEPA/OPPTS/OPP/BEAD) Fenitrothion on Wheat Gluten. 6/29/99.
9. Robin G. Todd, Ph. D (Sumitomo Chemical Company, Limited) Letter to EPA, Fenitrothion Human Health Risk Assessment. 7/22/99.