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

OFFICE OF
PREVENTION, PESTICIDES AND TOXIC
SUBSTANCES

MEMORANDUM

DATE: July 31, 2006

SUBJECT: Finalization of Interim Reregistration Eligibility Decisions (IREDs) and Interim Tolerance Reassessment and Risk Management Decisions (TREDs) for the Organophosphate Pesticides, and Completion of the Tolerance Reassessment and Reregistration Eligibility Process for the Organophosphate Pesticides

FROM: Debra Edwards, Director
Special Review and Reregistration Division
Office of Pesticide Programs

TO: Jim Jones, Director
Office of Pesticide Programs

As you know, EPA has completed its assessment of the cumulative risks from the organophosphate (OP) class of pesticides as required by the Food Quality Protection Act of 1996. In addition, the individual OPs have also been subject to review through the individual-chemical review process. The Agency's review of individual OPs has resulted in the issuance of Interim Reregistration Eligibility Decisions (IREDs) for 22 OPs, interim Tolerance Reassessment and Risk Management Decisions (TREDs) for 8 OPs, and a Reregistration Eligibility Decision (RED) for one OP, malathion.[1] These 31 OPs are listed in Appendix A.

EPA has concluded, after completing its assessment of the cumulative risks associated with exposures to all of the OPs, that:

(1) the pesticides covered by the IREDs that were pending the results of the OP cumulative assessment (listed in Attachment A) are indeed eligible for reregistration; and

[1] Malathion is included in the OP cumulative assessment. However, the Agency has issued a RED for malathion, rather than an IRED, because the decision was signed on the same day as the completion of the OP cumulative assessment.

(2) the pesticide tolerances covered by the IREDs and TREDs that were pending the results of the OP cumulative assessment (listed in Attachment A) meet the safety standard under Section 408(b)(2) of the FFDCA.

Thus, with regard to the OPs, EPA has fulfilled its obligations as to FFDCA tolerance reassessment and FIFRA reregistration, other than product-specific reregistration.

The Special Review and Reregistration Division will be issuing data call-in notices for confirmatory data on two OPs, methidathion and phorate, for the reasons described in detail in the OP cumulative assessment. The specific studies that will be required are:

- 28-day repeated-dose toxicity study with methidathion oxon; and
- Drinking water monitoring study for phorate, phorate sulfoxide, and phorate sulfone in both source water (at the intake) and treated water for five community water systems in Palm Beach County, Florida and two near Lake Okechobee, Florida.

The cumulative risk assessment and supporting documents are available on the Agency's website at www.epa.gov/pesticides/cumulative and in the docket (EPA-HQ-OPP-2006-0618).

Attachment A:

Organophosphates included in the OP Cumulative Assessment

Chemical	Decision Document	Status
Acephate	IRED	IRED completed 9/2001
Azinphos-methyl (AZM)	IRED	IRED completed 10/2001
Bensulide	IRED	IRED completed 9/2000
Cadusafos	TRED	TRED completed 9/2000
Chlorethoxyphos	TRED	TRED completed 9/2000
Chlorpyrifos	IRED	IRED completed 9/2001
Coumaphos	TRED	TRED completed 2/2000
DDVP (Dichlorvos)	IRED	IRED completed 6/2006
Diazinon	IRED	IRED completed 7/2002
Dicrotophos	IRED	IRED completed 4/2002
Dimethoate	IRED	IRED completed 6/2006
Disulfoton	IRED	IRED completed 3/2002
Ethoprop	IRED	IRED completed 9/2001 IRED addendum completed 2/2006
Fenitrothion	TRED	TRED completed 10/2000
Malathion	RED	RED completed 8/2006
Methamidophos	IRED	IRED completed 4/2002
Methidathion	IRED	IRED completed 4/2002
Methyl Parathion	IRED	IRED completed 5/2003
Naled	IRED	IRED completed 1/2002
Oxydemeton-methyl	IRED	IRED completed 8/2002
Phorate	IRED	IRED completed 3/2001
Phosalone	TRED	TRED completed 1/2001
Phosmet	IRED	IRED completed 10/2001
Phostebupirim	TRED	TRED completed 12/2000
Pirimiphos-methyl	IRED	IRED completed 6/2001
Profenofos	IRED	IRED completed 9/2000
Propetamphos	IRED	IRED completed 12/2000
Terbufos	IRED	IRED completed 9/2001
Tetrachlorvinphos	TRED	TRED completed 12/2002
Tribufos	IRED	IRED completed 12/2000
Trichlorfon	TRED	TRED completed 9/2001

United States
Environmental Protection
Agency

Prevention, Pesticides
And Toxic Substances
(7508C)

EPA 738-R-00-005
June 2000

Report on FQPA Tolerance Reassessment Progress and Interim Risk Management Decision

Cadusafos

UNITED STATES ENVIRONMENTAL PROTECTION AGENCY

WASHINGTON, D.C. 20460

OFFICE OF
PREVENTION, PESTICIDES
AND TOXIC SUBSTANCES

CERTIFIED MAIL

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 related to the revised risk assessment for the organophosphate pesticide cadusafos. 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 the dietary risk from cadusafos as part of the tolerance reassessment process for this chemical, presents a summary of the related food tolerance for this single chemical, and provides the Agency's current risk management decision based on the risk assessment. Cadusafos has no U.S. registrations and only one import tolerance on bananas, 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 Cadusafos" is published in the *Federal Register*. This document and the technical documents supporting it 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/pesticides/op."

This document is based on the updated technical information found in the cadusafos public docket. The docket not only includes background information and comments on the Agency's preliminary risk assessments, but also now includes the revised risk assessment for cadusafos**,** and a document summarizing the Agency's Response to Comments. The Response to Comments document addresses corrections to the preliminary risk assessment submitted by the chemical manufacturer, FMC Corporation, as well as comments submitted by the general public and stakeholders during the comment period on the risk assessment.

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 Food Quality Protection Act of 1996 (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 cadusafos 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 cadusafos 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, Jacqueline McQueen at (703) 308-8164.

Sincerely yours,

Lois A. Rossi, Director
Special Review and
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Attachment

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

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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

GLOSSARY OF TERMS AND ABBREVIATIONS

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_{50}	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_{50}	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.
NA	Not Applicable
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

GLOSSARY OF TERMS AND ABBREVIATIONS

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_1*	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(c) 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

GLOSSARY OF TERMS AND ABBREVIATIONS

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

EXECUTIVE SUMMARY

EPA has completed its review of public comments on the revised risk assessment for cadusafos, and is, in this document, issuing its interim decision on the risk mitigation for this chemical. The revised risk assessment is based on review of the required target data base supporting the single cadusafos import tolerance and information received during the public comment periods in the open process developed through the Tolerance Reassessment Advisory Committee (TRAC). Cadusafos is not registered under FIFRA and may not be sold, distributed, or used in the U.S. One import tolerance for cadusafos in/on bananas was established through a petition submitted by FMC Corporation, the manufacturer of this chemical, in 1986. EPA's revised risk assessment for cadusafos indicates that the dietary risk does not exceed the Agency's level of concern; therefore, no risk mitigation is necessary at this time.

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

I. INTRODUCTION

This report on the progress toward tolerance reassessment of cadusafos is the result of the pilot process developed through the TRAC to facilitate greater public involvement in the ongoing FIFRA reregistration and FQPA tolerance reassessment initiatives on pesticides. Cadusafos is subject only to FQPA because it has only an import tolerance and is not registered for use in the U.S. 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 Federal Insecticide, Fungicide, and Rodenticide Act (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 U.S. Environmental Protection Agency (referred to as EPA or "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 the potential hazards arising from the currently registered uses of the pesticide; to determine the need for additional data on health and environmental effects; and to determine whether the pesticide meets the "no unreasonable adverse effects" criteria of FIFRA.

On August 3, 1996, the Food Quality Protection Act of 1996 (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 the 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. Although not subject to the reregistration process, the individual dietary assessment for the organophosphate cadusafos has been completed, and will be used in the cumulative assessment of all of the organophosphate chemicals, to satisfy the requirements of FQPA.

Cadusafos is not registered for use in the United States; however, there is one import tolerance on bananas for this chemical. Because it is not registered in the U.S., it is not subject to the reregistration process. It is subject to the requirements of FQPA; therefore, a dietary risk assessment was completed. This document presents the Agency's dietary risk assessment for cadusafos, 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 cadusafos 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*. The Phase 6 of the pilot process did not include a public comment period; however, for some chemicals, the Agency may provide for another comment period, depending on the content of the risk management decision.

The 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. The TRAC identified the following science policy issues it believed were key to the implementation of FQPA and tolerance reassessment:

- Applying the FQPA 10-Fold Safety Factor
- Whether and How to Use "Monte Carlo" Analyses in Dietary Exposure Assessments
- How to Interpret "No Detectable Residues" in Dietary Exposure Assessments
- Refining Dietary (Food) Exposure Estimates
- Refining Dietary (Drinking Water) Exposure Estimates
- Assessing Residential Exposure
- Aggregating Exposure from all Non-Occupational Sources

- How to Conduct a Cumulative Risk Assessment for Organophosphate or Other Pesticides with a Common Mechanism of Toxicity
- Selection of Appropriate Toxicity Endpoints for Risk Assessments of Organophosphates
- Whether and How to Use Data Derived from Human Studies

The process developed by the 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 the chemical. Section III gives an overview of the dietary risk assessment for cadusafos, including a discussion of any revisions that were 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/pesticides/op), and in the Public Docket.

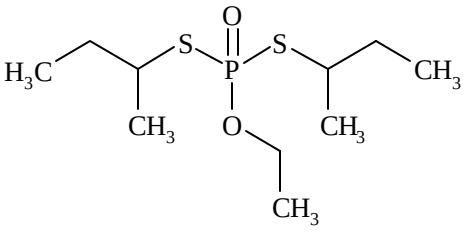
II. CHEMICAL OVERVIEW

A. Regulatory History

Cadusafos, a nematicide and soil insecticide, is not registered under FIFRA and may not be sold, distributed, or used in the United States. However, a permanent tolerance of 0.01 ppm has been established by the U.S. EPA under 40 CFR §180.461 for residues of cadusafos in/on bananas imported into this country.

B. Chemical Identification

CADUSAFOS:



- **Common Name:** Cadusafos
- **Chemical Name:** O-ethyl S,S-bis (1-methylpropyl) phosphorodithioate
- **Chemical Family:** Organophosphate
- **CAS Registry Number:** 95465-99-9
- **OPP Chemical Code:** 128864
- **Empirical Formula:** $C_{10}H_{23}O_2PS_2$
- **Molecular Weight:** 270.39
- **Trade and Other Names:** Rugby, Apache
- **Basic Manufacturers:** FMC Corporation

A detailed discussion on the physical properties of cadusafos can be found in the EPA document entitled "Cadusafos: HED Risk Assessment for the Risk Management Proposal," dated December 17, 1998.

C. Use Profile

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

Type of Pesticide:	Nematicide and soil insecticide.
Summary of Use Sites:	Cadusafos is registered in Ecuador, Costa Rica, Honduras, Guatemala, Columbia and Mexico for use in/on bananas. Cadusafos is not registered under FIFRA and may not be sold, distributed, or used in the U.S.
Target Pests:	Plant parasitic nematodes and soil insects.

Formulation Types: FMC Corporation produces a 10% granular formulation for use in banana-producing countries.

Method and Rates of Application:

Method and Rate - The established maximum seasonal rate is 6 grams of active ingredient (ai.) per mat per year, applied to the base of the plants.

Timing - Cadusafos is applied at the beginning of the banana planting season. It may also be applied a second time, as needed.

Use Classification: N/A -- Not registered for use in the U.S.

D. Estimated Usage of Pesticide

This section summarizes the best estimates available for the pesticide uses of cadusafos. 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.

In the current risk assessment, the Agency estimated that cadusafos is used on about 10-15% of the annual banana imports into the U.S. The principal countries exporting bananas treated with cadusafos to the U.S. are Guatemala, Costa Rica, Ecuador, Columbia, Mexico and Honduras. Since the risk assessment was completed, more current information on the percent of imported bananas treated with cadusafos was submitted by the International Banana Association (IBA). This organization worked with banana growers to more accurately estimate the amount of cadusafos-treated bananas imported into the U.S. The estimates provided by the IBA range from a typical or average of 5.1% imported, to a high-end estimate of 7% for the years 1997 to 1998. These estimates are consistent with new information received by EPA from outside economic sources. Although the risk assessment was not updated again to include these figures, they will be considered for use in both the acute and chronic risk assessments at the time the cumulative assessment is conducted for all of the organophosphates.

III. SUMMARY OF CADUSAFOS RISK ASSESSMENT

Following is a summary of EPA's revised human health risk findings and conclusions for the organophosphate pesticide cadusafos, as fully presented in the revised risk assessment document, "Cadusafos: Dietary Risk Assessment Update for FQPA Requirements," dated December 17, 1998. The risk assessment presented here forms the basis of the Agency's interim risk management decision for cadusafos only; the Agency must complete a cumulative assessment of the risks of all organophosphate pesticides before it can complete its reassessment of the cadusafos tolerance.

Because cadusafos is not currently registered for use in the U.S., only a human health dietary assessment from exposure to this chemical through food was necessary.

Human Health Risk Assessment

During the comment period on the cadusafos preliminary risk assessment, FMC Corporation, the manufacturer, submitted comments noting that the decision to retain the 10X FQPA safety factor was based on the assumption that there were data gaps for all required neurotoxicity studies, although the company had previously submitted an acute delayed neurotoxicity study. FMC Corporation re-submitted this study and requested that the Agency evaluate the data and consider reducing the FQPA Factor. The Agency reviewed the study, and it was found to be acceptable and to show no delayed neurotoxicity and no evidence of neuropathology. Based on this information, the FQPA safety factor was reduced from 10X to 3X; the 3X was retained due to continuing data gaps for acute and subchronic neurotoxicity studies in rats. This was the only major revision to the risk assessment.

Dietary Risk from Food

Toxicity

The Agency has reviewed all toxicity studies submitted and has determined that the toxicity database supports a dietary risk assessment for cadusafos as well as a future FQPA tolerance reassessment for the import tolerance on bananas. Further details on the toxicity of cadusafos can be found in the December 17, 1998 HED Risk Assessment. A brief overview of the studies used for the dietary risk assessment is outlined in Table 1 of this document.

FQPA Safety Factor

The FQPA Safety Factor was reduced to 3X. As stated earlier in this document, the safety factor was initially 10X because of data gaps for three neurotoxicity studies: an acute delayed neurotoxicity study in hens, and acute and subchronic studies in rats. The acute delayed neurotoxicity study in hens was received and reviewed by the Agency, found to be acceptable, and to show no neurotoxicity and no delayed neuropathology in the treated animals. It was determined that adequate

actual data, surrogate data, and/or modeling outputs were available to satisfactorily assess exposure through food, and that the assumptions and models used in the assessments do not underestimate the potential risk for infants and children. Results of the study allowed for a reduction in the safety factor; however, because data gaps for the acute and subchronic rat neurotoxicity studies remain; an FQPA safety factor of 3X was retained.

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 cadusafos, the FQPA safety factor is 3X; therefore, the acute or chronic RfD / 3 = 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.

Exposure Assumptions

Residues of cadusafos in banana pulp were not detected in field trials conducted in seven sites. Further, no detections have been reported by the Food and Drug Administration, based on analysis of hundreds of samples from approximately a dozen countries. For this assessment, the Limit of Detection (LOD) of 0.001 ppm was used for the acute dietary assessment. For the chronic dietary assessment, ½ of the LOD, or 0.0005, was used. The value of 0.001 ppm represents a probable upper-end estimate of cadusafos residues in banana pulp.

Dietary risk analyses for cadusafos were conducted with the Dietary Exposure Evaluation Model (DEEM™). DEEM incorporates consumption data generated in USDA's Continuing Surveys of Food Intakes by Individuals (CSFII), 1989-1992.

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

Assessment	Study	Dose	Endpoint	UF	FQPA Safety Factor	PAD
Acute Dietary	14-day (range finding) oral toxicity study in dogs (MRID 40017902)	NOAEL= 0.02 mg/kg/day	Plasma ChE inhibition	100	3X	0.00007 mg/kg/ day
Chronic Dietary	One-year feeding study in dogs (MRIDs 40017901/40017 902)	NOAEL= 0.001 mg/kg/day	Plasma ChE inhibition	100	3X	0.000003 mg/kg/ day

Acute Food Risk

An acute dietary assessment was conducted for cadusafos. The assessment used a residue estimate of 0.001 ppm, the LOD, and a distribution of consumption values. The acute risk estimates are considered upper-end estimates since the residue level assumed is a point estimate rather than a range, and because 100% of the crop treated is assumed. Based on the above parameters, DEEM estimates that the "Average U.S. Population" and the population subgroups of "All Infants (<1 year)" and “Children (1-6 years)” are exposed to cadusafos (per day) at a level less than the cadusafos acute PAD; that is, less than 100% of the aPAD is utilized. At the 99.9th percentile of exposure, the % acute PAD utilized is 21%, 31%, and 39%, respectively. Because these values are significantly lower than 100%, the acute dietary risk is not of concern to the Agency. The population group "All Infants" is noted since this group is typically estimated to be the most highly exposed group. This analysis satisfies the FQPA requirement for the special consideration of pesticide risk to children.

Chronic Food Risk

The chronic risk estimates are based on the residue level of ½ LOD (0.0005 ppm), the upper-end of the crop treated estimate (10-15%), and averaged food consumption estimates. The resultant risk estimate is not considered upper-end since the estimate is refined by the percent crop treated data. Based on these parameters, DEEM estimates that the "Average U.S. Population" and all population subgroups including "All Infants (<1 year)" are chronically exposed to cadusafos at a level less than the cadusafos chronic PAD. The percent of the chronic PAD utilized is less than 5% for all population groups; the % cPAD for infants less than 1 year and children 1-6 years were 4% and 2%,

respectively. Because these levels are significantly lower than 100%, the chronic dietary risk is not of concern.

In summary, the potential acute and chronic dietary exposures to cadusafos-treated bananas are below the level of concern for all U.S. citizens, including infants and children. As discussed in the "Chemical Overview" section of this document, the Agency has recently received updated information on the percent of bananas imported into the United States. This information indicates that 5-7% is imported, not 10-15%, as the Agency's previous information indicated. This updated information will be considered for the acute and chronic risk assessments at the time that the cumulative assessment for all of the organophosphates is conducted.

IV. FQPA TOLERANCE REASSESSMENT PROGRESS AND INTERIM RISK MANAGEMENT DECISION

A. Tolerance Reassessment Progress & Interim Risk Management Decision

The Agency has completed its assessment of the dietary risk of cadusafos but has not considered the cumulative effects of organophosphates as a class. Based on a review of these generic data and public comments on the Agency's revised risk assessment for the active ingredient cadusafos, EPA has sufficient information on the human health effects of cadusafos to make some interim decisions 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 cadusafos alone in order to determine whether any risk reduction measures are necessary to allow the continued importation of bananas containing this chemical, pending completion of the cumulative assessment.

As a result of its assessment, EPA has determined that dietary risk from exposure to cadusafos 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 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 the 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 cadusafos food residue import tolerance as called for by the FQPA. When the Agency has completed the cumulative assessment, the cadusafos tolerance will be reassessed in that light. At that time, the

Agency will reassess cadusafos 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 cadusafos, 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 cadusafos to the public in July, 1999 and provided a 60 day comment period for interested parties to submit information, including risk mitigation suggestions or proposals. No comments were received.

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 cadusafos is within its own "risk cup." In other words, if cadusafos did not share a common mechanism of toxicity with other chemicals, EPA would be able to conclude today that the import tolerance for cadusafos on bananas meets the FQPA safety standards. In reaching this determination, EPA has considered the 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 cadusafos, because there are no domestic uses. But, results of the acute and chronic food assessments indicate that exposures are within acceptable levels; that is, risk from exposure to cadusafos "fits" within the individual risk cup. Therefore, the import tolerance remains in effect and unchanged until a full reassessment of the cumulative risk from all organophosphates is completed.

b. Tolerance Summary

The established tolerance for residues of cadusafos in/on plant commodities is currently expressed in terms of residues of cadusafos per se (O-ethyl S,S-di-sec-butyl phosphorodithioate) [40 CFR § 180.461]. It should be noted, however, that the preferred chemical name for cadusafos is O-ethyl S,S-bis(1-methylpropyl) phosphorodithioate.

Sufficient residue field trial data are available to assess the established import tolerance on bananas. These trials were conducted in the Ivory Coast, Costa Rica, the Philippines, Guatemala, and Honduras using the granular formulation according to the maximum use patterns registered to foreign countries which export bananas to the United States. The tolerance for residues of cadusafos in/on imported bananas is 0.01 ppm, as shown in Table 2.

Table 2. Tolerance Summary for Cadusafos

Commodity	Tolerance Listed Under 40 CFR § 180.461	Reassessed Tolerance*	Comment
Bananas	0.01 ppm	0.01 ppm	Banana, whole fruit

* The term “reassessed” here 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 was 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, cadusafos may be subjected to additional screening and/or testing to better characterize effects related to endocrine disruption.

D. Regulatory Rationale

Cadusafos has only one import tolerance, and no U.S. registrations; 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.). These chemicals are not subject to Data Call-In (DCI) requirements under FIFRA. Although cadusafos has no U.S. registrations and therefore is not subject to a FIFRA DCI, it does have a tolerance for bananas that are imported into the U.S. EPA is currently working to require the submission of acute, subchronic, and developmental neurotoxicity studies under the authority of FFDCA. Results of these studies may further refine the risk assessments.

B. Risk Mitigation Requirements

As discussed in this document, the acute and chronic food risk from the use of cadusafos on imported bananas 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 cadusafos 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. 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.

The docket initially contained preliminary risk assessments and related documents as of September 10, 1998. Sixty days later the first public comment period closed. The EPA then considered comments, revised the risk assessment, and added the formal “Response to Comments” document and the revised risk assessment to the docket on July 7, 1999.

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

MRID **CITATION**

00146347 FMC Corp. (19??) Toxicology: For FMC 67825 20G. Unpublished summaries. 18 p.

00146348 Freeman, C. (1983) Acute Dermal Toxicity of FMC 67825 Technical in Rabbits: Study No. A83-916. Unpublished study prepared by FMC Toxicology Laboratories. 64 p.

00146349 Roberts, N.; Phillips, C.; Gopinath, C.; Fish, C. (1984) Acute Delayed Neuroroxicity Study With FMC 67825 Tecnical In The Domestic Hen: FMC Study No. A84-1246. Unpublished study prepared by Huntingdon Research Centre plc. 55 p.

00146350 Freeman, C. (1984) Acute Oral Toxicity Of FMC 67825 206 In Rats: Study No. A84-1233. Unpublished study prepared by FMC Toxicology Laboratory. 48 p.

00146351 Putman, D. (1984) Morphological Transformation Of BALB/3T3 Mouse Embryo Cells In The Presence And Absence Of Exogenous Metabolic Activation: Final Report: Study No. T2199.304. Unpublished study prepared by Microbiological Association, Inc. 19 p.

00147538 Freeman, C. (1983) Acute Oral Toxicity of FMC 67825 Technical in Mice: Study No. A83-915. Unpublished study prepared by FMC Toxicology Laboratory. 62 p.

00147539 Freeman, C. (1984) Acute Oral Toxicity of FMC 67825 Technical in Rats: Study No. A83-1164. Unpublished study prepared by FMC Toxicology Laboratory. 55 p.

00147540 Dudek, R. (1984) Four Hour Acute Aerosol Inhalation Toxicity Study in Rats of FMC 67825 Technical: Study No. A84-1231. Unpublished study prepared by Toxigenics, Inc. 67 p.

00147541 Freeman, C. (1984) Primary Eye Irritation of FMC 67825 Technical in Rabbits: Study No. A83-1154. Unpublished study prepared by FMC Toxicology Laboratory. 34 p.

00147542 Freeman, C. (1984) Primary Skin Irritation of FMC 67825 Technical in Rabbits: Study No. A84-1238. Unpublished study prepared by FMC Toxicology Laboratory. 32 p.

BIBLIOGRAPHY

MRID	CITATION
00147543	Freeman, C. (1984) Skin Sensitization of FMC 67825 Technical in Guinea Pigs: Study No. A84-1271. Unpublished study prepared by FMC Toxicology Laboratory. 37 p.
00147544	Freeman, C. (1984) Acute Dermal Toxicity of FMC 67825 20G in Rabbits: Study No. A84-1235. Unpublished study prepared by FMC Toxicology Laboratory. 50 p.
00147545	Freeman, C. (1984) Primary Eye Irritation of FMC 67825 20G in Rabbits: Study Number A84-1236. Unpublished study prepared by FMC Laboratory. 37 p.
00147546	Freeman, C. (1984) Primary Skin Irritation of FMC 67825 20G in Rabbits: Study No. A84-1234. Unpublished study prepared by FMC Toxicology Laboratory. 3 p.
00147547	Freeman, C. (1984) Skin Sensitization of FMC 67825 20G in Guinea pigs: Study No. A84-1237. Unpublished study prepared by FMC Toxicology Laboratory. 39 p.
00147548	Haworth, S. (1984) Salmonella/Mammalian-microsome Plate Incorporation Mutagenicity Assay (Ames Test): Study No. T2199.501. Unpublished study prepared by Microbiological Associates. 35 p.
00147549	Thilagar, A. (1984) Chromosome Aberrations in Chinese Hamster Ovary (CHO) Cells: Final Report: Study No. T2199.337. Unpublished study prepared by Microbiological Associates. 57 p.
00147550	Thilagar, A. (1984) Unscheduled DNA Synthesis in Rat Primary Hepatocytes: Final Report: Study No. T2199-380. Unpublished study prepared by Microbiological Associates. 26 p.
00255690	See MRIDs 146347, 146348, and 147538 to 147543
00255691	See MRIDs 146349 to 146351, and 147544 to 147550

BIBLIOGRAPHY

MRID	CITATION
00152019	Roberts, N.; Phillips, C.; Gopinath, C.; et al. (1984) Acute Delayed Neurotoxicity Study with FMC 67825 Technical in the Domestic Hen: Retp. No. FCC 59/84738/1: Study No. A84-1246. Unpublished study prepared by Huntingdon Research Centre, plc. 62 p.
40017901	Nolan, T.; Shellenberger, T.; Billups, L. (1986) One-year Oral Toxicity Study in the Dog with FMC 67825: Revised Final Report: Tegeris Report No. 8432: FMC Study No. A84-1538. Unpublished study prepared by Tegeris Laboratories, Inc. 640 p.
40017902	Mann, R.; Seely, J.; Shellenberger, T. (1985) 14-Day Range Finding Oral Toxicity Study in the Dog with FMC 67825: Tegeris Report No. 8406: FMC Study No. A84-1203. Unpublished study prepared by Tegeris Laboratories, Inc. 113 p.
41441803	De Prospo, J.; Seaman, L.; Van Ness, M.; et al. (1987) Multi-generation Reproduction Study with FMC 67825 Technical in Rats: Lab Project Number: A85-1731. Unpublished study prepared by FMC Corp. and Hazleton Laboratories, Inc. 1459 p.