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-00-017
September 2000

Report on FQPA Tolerance Reassessment Progress and Interim Risk Management Decision

Phostebupirim

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 preliminary and revised human health risk assessment for the organophosphate pesticide phostebupirim (also known as tebupirimphos). The enclosed "Report on FQPA Tolerance Reassessment and Interim Risk Management Decision for Phostebupirim," which was approved on September 29, 2000, summarizes the Agency's assessment of the dietary and occupational risk from phostebupirim. Based on its review, EPA has recommended risk mitigation measures to address the human health risks associated with the current use of phostebupirim. These risk mitigation measures can be found in the attached document.

The major means by which the Agency reassesses tolerances is through its reregistration process. Each pesticide registered prior to 1984 is subject to a comprehensive evaluation of its effects on human health and the environment. Such an evaluation includes a determination of whether the tolerances are safe. Since phostebupirim was registered after 1984, it is not subject to reregistration. However, phostebupirim tolerances are subject to reassessment in accordance with the Federal Food, Drug, and Cosmetic Act (FFDCA) as amended by the Food Quality Protection Act of 1996 (FQPA). The FQPA requires EPA to re-evaluate existing tolerances to ensure that children and other sensitive subpopulations are protected from pesticide risk.

When phostebupirim was registered in July 1995, it was granted a conditional registration contingent on the submission of additional data. All of the data and information requested as conditions of the registration have been received by the Agency. The Agency decided, in addition to reassessing phostebupirim tolerances, to also reassess occupational risks under the Federal Insecticide, Fungicide, and Rodenticide Act (FIFRA). The Agency has not conducted a new risk assessment for the effects of phostebupirim on non-target species (e.g., fish and birds) since it believes that the conclusions reached at the time of the initial decision to register phostebupirim in 1995 remain unchanged.

The "Report on FQPA Tolerance Reassessment Progress and Interim Risk Management Decision for Phostebupirim" is based on the revised human health assessment, updated technical information, and public comments received by the Agency, all of which are available in the phostebupirim public docket. The docket includes both the preliminary and revised risk assessment for phostebupirim as well as comments on the risk assessments submitted by the general public and

stakeholders. A Notice of Availability for this Report on FQPA Tolerance Reassessment Progress and Interim Risk Management Decision for Phostebupirim is being published in the *Federal Register*. To obtain a copy of this document, please contact the OPP Public Regulatory Docket (7502C), US EPA, Ariel Rios Building, 1200 Pennsylvania Avenue, N.W., Washington D.C., 20460, telephone (703) 305 - 5805. Electronic copies of this report and the documents supporting it are available on the internet and can be found on the Agency's web page, www.epa.gov/pesticides/op.

This document and the process used to develop it are the result of a pilot process to facilitate greater public involvement and participation in the reregistration and/or tolerance reassessment decisions for these 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. This open process follows the guidance 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 phostebupirim risk assessment concerns only this particular organophosphate. It does not address the cumulative effects of other organophosphates as a class. Because the FQPA directs the Agency to evaluate food tolerances on the basis of cumulative risk from substances sharing a common mechanism of toxicity, such as the toxicity expressed by the organophosphates through a common biochemical interaction with the cholinesterase enzyme, the Agency will evaluate the cumulative risk posed by the entire organophosphate class of chemicals after completing the risk assessments for individual organophosphates. The Agency is working towards completion of a methodology to assess cumulative risk and the individual risk assessments for 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 necessary to address those human health risks associated with the current uses of phostebupirim. The Agency will issue the final tolerance reassessment decision for phostebupirim and finalize any other decisions once the cumulative assessment for all organophosphates is complete.

Based on the phostebupirim risk assessment, the Agency believes that current uses of phostebupirim may pose unreasonable adverse effects to human health, and that such effects can be mitigated with the risk mitigation measures identified in this document. Accordingly, the Agency recommends that registrants implement these risk mitigation measures immediately. Section IV of this document describes labeling amendments for end-use products and data requirements necessary to implement these mitigation measures. Instructions for registrants on submitting revised labeling and the time frame established to do so can be found in Section V of this document.

Should a registrant fail to implement any of the recommended occupational risk mitigation measures, the Agency will continue to have concerns about the risks posed by phostebupirim. Where the Agency has identified any unreasonable adverse effect to human health, the Agency may at any time

initiate appropriate regulatory action to address this concern. At that time, any affected person (s) may challenge the Agency's action.

If you have questions on this document or the label changes, please contact the Special Review and Reregistration Division representative, Stacey Milan, at (703) 305-2505.

Sincerely yours,

Lois A. Rossi, Director
Special Review and
Reregistration Division

Attachment

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

Table of Contents

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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
TMRC	Theoretical Maximum Residue Contribution

Glossary of Terms and Abbreviations

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

EPA has completed its review of public comments on the revised risk assessment for phostebupirim, and is, in this document, setting forth its interim decision on the risk mitigation for this chemical. The revised dietary risk assessment includes the Agency's review of additional studies and a revision of the FQPA safety factor based on the study reviews. The Agency identified the risk management measures set forth in this report after inviting stakeholders to provide proposals and suggestions on appropriate mitigation measures. This report on FQPA Tolerance Reassessment Progress and Interim Risk Management Decision will not be considered final until the cumulative risk assessment of all organophosphate pesticides is complete. The cumulative assessment may result in further risk mitigation measures for phostebupirim.

Phostebupirim is an organophosphate insecticide registered for use on field corn, seed corn, sweet corn, and popcorn for the control of corn rootworms, wireworms, cutworms, seed corn maggots, seedcorn beetle and white grubs. It was first registered in the United States in 1995 and is registered as a 2.1% and 4.67% granular end-use product (Aztec® 2.1G and 4.67G), although only the Aztec® 2.1G product is currently being marketed. The Aztec® 2.1G product has two formulations: a new cellulose-based Biodac formulation along with a clay-based granular formulation. Phostebupirim is used on average once a season at planting, at a maximum rate of 0.15 lbs ai/acre. Annual domestic usage of phostebupirim is estimated to be approximately 270,000 pounds active ingredient. Between 3-6% of all corn acreage is treated.

Overall Risk Summary

EPA's dietary (food) risk assessment for phostebupirim indicates that neither the acute nor chronic risks exceed the Agency's level of concern, i.e., less than 100% of the acute or chronic Population Adjusted Dose (PAD) is utilized for the general U.S. population and all population subgroups, including infants and children using a Tier 1 screening level assessment (100% crop treated and tolerance levels).

Acute and chronic dietary risks from drinking water are also below the Agency's level of concern. Surface water and ground water estimated environmental concentrations (EECs) do not exceed the Agency's drinking water levels of comparison (DWLOC) for acute and chronic aggregate dietary exposure. Aggregate risk, based on food and water exposure, does not exceed the Agency's level of concern; therefore, no risk mitigation based on dietary risk estimates is necessary at this time.

The Agency has determined that there is potential exposure to handlers for use-patterns associated with phostebupirim. Occupational handler risk estimates are based on two separate studies for estimating short-term and intermediate-term exposure risks and PHED exposure studies. With the exception of intermediate-term risks for applicators, the risks in all exposure scenarios generally do not

exceed the Agency's level of concern when the appropriate PPE and engineering controls are utilized during the loading and application processes.

EPA did not quantitatively assess the risks to post application workers. Minimal post-application exposure is anticipated since phostebupirim is typically incorporated into the soil, is applied at planting and is not systemic in the plant and degrades readily.

Based on the phostebupirim risk assessment, the Agency believes that label changes requiring use of dust/mist respirators (or comparable mitigation) by loaders of the Aztec® 2.1G clay-based formulation would mitigate inhalation exposures. Loaders of the Aztec® 4.67G SmartBox® system must have a dust/mist respirator immediately available for use in case of an emergency. The Agency is not requiring the use of dust/mist respirators for handlers who use the cellulose-based formulation. EPA believes this formulation is sufficiently less dusty than the clay-based formulation that there will not be a risk concern for loaders.

The registrant will need to submit an exposure or dust comparison study to confirm that the Biodac formulation is sufficiently less dusty than the clay-based formulation. This study should be submitted to EPA by April 1, 2001.

Under current label restrictions, EPA does have risk concerns for the short and intermediate-term inhalation risk for applying granular phostebupirim with an open cab tractor drawn spreader (MOE=79). However, the risk was calculated using low confidence PHED data (one study with a small number of replicates using only a broadcast spreader). In actual use, phostebupirim will typically be applied in-furrow or T-Band. These methods of application should make the granular formula less available for exposure than in the broadcast spreader scenario. Therefore, the Agency believes the MOE of 79 is an overestimate of the risk for this specific phostebupirim use scenario and inhalation risks for applicators are likely to be acceptable. Therefore, no risk mitigation is required to address applicator risk.

Currently available data suggests that dermal occupational risk is also of concern. However, EPA believes the current risk assessment overestimates this risk to workers as well. The registrant will initiate a 21-day rat dermal toxicity study using the 4.67% granular formulation to better characterize dermal risk from occupational exposure to phostebupirim products. The Agency believes that this study will provide a more appropriate dermal endpoint for regulating both short and intermediate-term worker exposures and that worker risk under current label conditions does not exceed the Agency’s level of concern. This study should be submitted to EPA by April 1, 2001.

However, in the event that these studies do not adequately demonstrate that worker risk is not a concern, the Agency will recommend that the registrant implement additional label amendments to mitigate remaining worker risks that exceed the Agency's level of concern. The Agency will review the phostebupirim data prior to July 5, 2001, the date the conditional registration expires.

I. Introduction

This report on the progress toward tolerance reassessment for phostebupirim is the result of the pilot process developed through the Tolerance Reassessment Advisory Committee (TRAC) to facilitate greater public involvement in the ongoing FIFRA reregistration and/or FQPA tolerance reassessment initiatives on pesticides. Since phostebupirim was first registered in 1995, it is currently not subject to the reregistration process, only to the requirements of FQPA. However, some history and background on reregistration and 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 of all existing tolerances. The Agency has decided that, for those chemicals that have tolerances and are undergoing reregistration, the tolerance reassessment will be initiated primarily through this reregistration process. It also requires that by 2006, EPA must review all tolerances in effect on the day before the date of the enactment of the FQPA, which was August 3, 1996. FQPA also amends the FFDCA to require a safety finding in tolerance reassessment based on factors including an assessment of cumulative effects of chemicals with a common mechanism of toxicity. Phostebupirim belongs to a group of pesticides called organophosphates, which share a common mechanism of toxicity - they all affect the nervous system by inhibiting cholinesterase. Although FQPA significantly affects the Agency's reregistration process, it 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 phostebupirim has been completed, and will be used in the cumulative assessment of all of the organophosphate chemicals to satisfy the requirements of FQPA.

This document presents the Agency's revised dietary risk assessment for phostebupirim, as part of the tolerance reassessment process. The Agency has also revised occupational risk estimates for phostebupirim.

As part of the EPA's effort to involve the public in the implementation of 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 public process was discussed by 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 organophosphates are following this new process.

Phases 1 through 4 of the pilot process address the development and refinement of the risk assessments. Phases 5 and 6 are concerned with the development and implementation of risk management plans and provide opportunity for the registrants, user community, and general public to propose risk mitigation based on the revised risk assessments. During phase 6 of the process, the Agency prepares an Interim Reregistration Eligibility Decision (RED) Document or a Report on FQPA Tolerance Reassessment and Interim Risk Management Decision Document, from which risk management will be implemented. Prior to finalizing a risk management decision, the Agency typically arranges a conference call with USDA, growers, registrants, and other interested parties to assess the feasibility of proposed mitigation measures.

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 phosetebupirim has already been subject to numerous public comment periods and a further comment period was deemed unnecessary. A Notice of Availability for this document, however, has been published in the *Federal Register*.

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.

In addition to the policy issues that resulted from the TRAC process, the Agency published in the *Federal Register* on August 12, 1999, a draft Pesticide Registration Notice that presents EPA's proposed approach for managing risks from organophosphate pesticides to occupational users. This notice describes the Agency's baseline approach to managing risks to handlers and workers of organophosphate pesticides. Generally, basic protective measures such as closed mixing and loading systems, enclosed cab equipment, or protective clothing, as well as increased reentry intervals will be required for most uses where current risk assessments indicate a risk and such protective measures are feasible. The draft guidance policy also states that the Agency will assess each pesticide individually, and based upon the risk assessment, determine the need for specific measures tailored to the potential risks of the chemical. The measures included in this interim document are consistent with that draft Pesticide Registration Notice.

This document consists of six sections. Section I contains the regulatory framework for reregistration/tolerance reassessment as well as descriptions of the process developed by TRAC for public comment on science policy issues for the organophosphate pesticides and the worker risk management PR notice. Section II provides a profile of the use and usage of the chemical. Section III gives an overview of the revised human health risk assessment resulting from public comments and other information. Section IV presents the Agency's interim risk management decisions. Section V summarizes required label changes based on the risk mitigation measures outlined in Section IV. Section VI provides information on how to access related documents. Finally, the Appendices list Data Call-In (DCI) information. The revised risk assessments and related addenda are not included in this document, but are available on the Agency's web page, www.epa.gov/pesticides/op, and in the Public Docket.

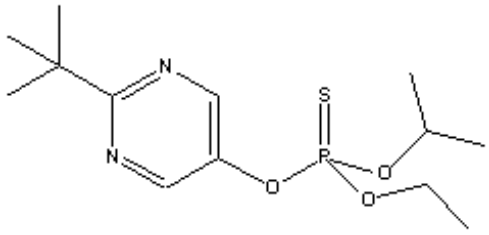
II. Chemical Overview

A. Regulatory History

Phostebupirim was first registered in the United States in July 1995 for at-plant control of a variety of soil-dwelling insect pests in or on corn.

B. Chemical Identification

PHOSTEBUPIRIM



- **Common Name:** Phostebupirim
- **Chemical Name:** O-[2-(1,1-dimethylethyl)-5-pyrimidinyl] O-ethyl O-(1-methylethyl) phosphorothioate
- **Chemical Family:** Organophosphate
- **CAS Registry Number:** 96182-53-5
- **OPP Chemical Code:** 129086
- **Empirical Formula:** $C_{13}H_{23}N_2O_3PS$
- **Molecular Weight:** 318.37 g/mol.
- **Vapor Pressure:** 3.75×10^{-4} mm Hg
- **Trade and Other Names:** Aztec 2.1% Granular Insecticide, Aztec 4.67% Granular Insecticide
- **Basic manufacturer:** Bayer Corporation (technical registrant)

Technical phostebupirim is a colorless liquid. Phostebupirim is soluble in water at 5.5 mg/mL and is completely miscible with all solvents tested at 20° C.

C. Use Profile

The following information is based on the currently registered uses of phostebupirim:

Type of pesticide:	Insecticide.
Summary of Use Sites and Target Pests:	Phostebupirim is only registered for use on corn. Phostebupirim is used for the control of corn rootworms, cutworms, and other soil insect pests in corn commodities (forage and fodder, pop, and sweet).
Formulation Types Registered:	In addition to the technical, there are three end-use formulations: two 2.1% granular formulations (clay-based and cellulose-based) and a 4.67% granular formulation for use only with a SmartBox® applicator system.

Method and Rates of Application:

Equipment -	Phostebupirim can be applied to corn only with tractor drawn spreader.
Method and Rate -	At-plant band and T-band application with soil incorporation, and in-furrow application. Application rates vary from 0.11 to 0.15 pounds active ingredient per acre.
Timing -	At-plant.
Use Classification:	Phostebupirim is a restricted use chemical, registered only for use on corn.

D. Estimated Usage of Pesticide

This section summarizes the best estimates available for phostebupirim use, based on available pesticide usage information for 1990 through 1997 as obtained by EPA and USDA - NASS. As discussed in the February 8, 1999, "Quantitative Usage Analysis," approximately 270,000 pounds of phostebupirim active ingredient are applied annually to corn. Approximately 3% of corn acreage receive applications of phostebupirim, with up to 6% crop treated as a maximum estimate. The

majority of phostebupirim use (85%) occurs in the states of Iowa, Nebraska, Illinois, Indiana, Ohio, and Minnesota. Phostebupirim use has been steadily increasing in the years for which data were available.

III. Summary of Phostebupirim Risk Assessments

Following is a summary of EPA's human health risk findings and conclusions for the organophosphate phostebupirim, as fully presented in the documents, "Phostebupirim: Dietary Risk Assessment Update," dated April 9, 1999, and "Occupational Exposure and Risk Assessment Regarding the Use of Phostebupirim," dated May 5, 1999. The purpose of this summary is to assist the reader by identifying the key features and findings of these risk assessments, and to better understand the conclusions reached in the assessments.

EPA's preliminary risk assessments for phostebupirim were made available for public comment on May 26, 1999 (Phase 3 of the TRAC process). Comments submitted during the Phase 3 comment period did not support any revisions to the Agency's risk assessments, as discussed in "Phostebupirim: HED's Response to Comments Submitted During Phase 3 (Public Comment Period)," dated September 22, 1999. Thus, the preliminary and final risk assessments for phostebupirim are the same. On March 27, 2000, the Agency requested public comment on risk management for phostebupirim.

The risk assessments presented here form the basis of the Agency's interim risk management decision for phostebupirim only; the Agency must complete a cumulative assessment of the dietary risks of all the organophosphate pesticides before any final tolerance decisions can be made for the organophosphate pesticides, including phostebupirim.

A. Dietary Risk from Food

1. Toxicity

The Agency has reviewed all toxicity studies submitted and has determined that the toxicity database is complete, and that it supports an interim human health risk determination for all currently registered uses. Further details on the toxicity of phostebupirim can be found in the April 9, 1999, "Phostebupirim: Dietary Risk Assessment Update." A brief overview of the studies used for the dietary risk assessment is outlined in Table 1 in this document.

2. FQPA Safety Factor

The FQPA safety factor is 1X. The toxicity database includes an acceptable two-generation reproduction study in rats, acceptable developmental toxicity studies in rats and rabbits, and acceptable acute and subchronic neurotoxicity studies in the rat. These studies show no increased susceptibility of rat or rabbit fetuses to *in utero* exposure to phostebupirim. There was no indication of increased

susceptibility in the offspring as compared to parental animals in the two generation reproduction study. In these studies, effects in the fetuses/offspring were observed only at or above treatment levels which resulted in evidence of parental toxicity. Therefore, the additional 10X factor for the protection of infants and children as required by FQPA was reduced to 1X as discussed in the March 30, 1999, "Phostebupirim - Report of the FQPA Safety Factor Committee." As the dietary assessments were based on water modeling, tolerance levels and a 100% crop treated assumption, the Agency also found that the exposure assessments will not underestimate the potential dietary (food and water) exposures for infants and children from the use of phostebupirim and no non-dietary (residential) exposures are expected.

3. Population Adjusted Dose (PAD)

The Reference Dose (RfD) is derived from an exposure level at which there are no statistically or biologically significant increases in the frequency or severity of adverse effects between the exposed population and its appropriate control, along with the application of uncertainty factors. 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). In the case of phostebupirim, the FQPA safety factor is 1; therefore, the acute or chronic RfD = 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 level of risk concern.

4. Exposure Assumptions

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

The Tier I acute dietary analysis used tolerance levels and assumed 100% of the registered commodities were treated. The chronic dietary analysis for phostebupirim was also a Tier 1 estimate with all residues at tolerance levels and 100% of the commodities assumed to be treated with phostebupirim. Further refinements to the dietary risk assessment were not conducted, given the low dietary risk estimates based on the tolerance-level residues and 100% crop treated screening assumptions.

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

Assessment	Dose	Endpoint	Study	Uncertainty Factor (UF)	FQPA Safety Factor	PAD[c]
Acute Dietary	LOAEL = 0.5 mg/kg/day[a]	Plasma and RBC ChEI[b]	Acute rat neurotoxicity (MRID 43473001)	UF = 300 100X inter- and intraspecies variation and 3X lack of NOAEL	1X	0.002 mg/kg (same as acute RfD)
Chronic Dietary	NOAEL = 0.02 mg/kg/day	Plasma, RBC and brain ChEI	1-year dog feeding study (MRID 42005452 and 42119301)	UF = 100 100X inter- and intraspecies variation	1X	0.0002 mg/kg/day (same as chronic RfD)

[a] NOAEL not achieved in males
[b] ChEI = Cholinesterase Inhibition
[c] PAD = Population Adjusted Dose = $\frac{\text{Acute or Chronic RfD}}{\text{FQPA Safety Factor}}$

5. Food Risk Characterization

Generally, a dietary risk estimate that is less than 100% of the acute or chronic Population Adjusted Dose does not exceed the Agency's risk concerns. The phostebupirim acute dietary risk from food is well below the Agency's level of concern – that is, less than 100% of the acute PAD is utilized. For example, the percent of the acute PAD utilized for the most exposed subpopulation group, children (1-6 years), is <5% at the 95th percentile. The 95th percentile is reported here because a Tier 1 deterministic assessment was conducted. A probabilistic assessment was not conducted at this time because the results of the Tier I assessment were so low.

Similarly, the chronic dietary risk from food alone is well below the Agency's level of concern. For the most exposed subpopulation group, children (1-6 years old), the percent of the chronic PAD utilized is 17.6%. In summary, both acute and chronic dietary exposure and risk associated with phostebupirim-treated foods are considered to be well below the Agency's level of concern, even when tolerance-level residue values are used along with a 100% crop treated assumption.

Refinements to the dietary analyses can be made using monitoring data and percent crop treated data for the chronic dietary analysis, and a probabilistic assessment for acute dietary analysis; however, given the low dietary risk estimates based on tolerance level residues and 100% crop treated assumptions, the Agency determined that further refinements are not warranted at this time. Refinements will be considered when the cumulative assessment for all of the organophosphates is conducted.

B. Dietary Risk from Drinking Water

Drinking water exposure to pesticides can occur through ground water and surface water contamination. EPA considers both acute (one day) and chronic (lifetime) drinking water risks and uses either modeling or actual monitoring data, if available, to estimate those risks. Modeling is considered to be an unrefined assessment and provides a high-end estimate of risk. In the case of phostebupirim, no monitoring data for either ground or surface water were available; therefore, modeling was used to estimate drinking water risks from these sources.

The GENEEC model was used to estimate surface water concentrations, and SCI-GROW was used to estimate groundwater concentrations of phostebupirim in drinking water. Both of these models are considered to be screening models which provide high end estimates of water concentrations. These drinking water assessments are described in greater detail in "Tier 1 Screen for Drinking Water Assessment for Phostebupirim," dated December 8, 1997.

Based on available environmental fate data regarding half-lives under environmental conditions, phostebupirim appears to be quite persistent in the environment. Based on relatively high K_{ad} values, phostebupirim also appears to be quite immobile in soil. Two phostebupirim metabolites have been identified: TBHP (2-[1,1-dimethyllethyl]-5-hydroxypyrimidine) and OMAT (2-[1,1-dimethylethyl]-5-pyrimidinyl ethyl 1-methylethyl phosphate). The OMAT metabolite is structurally very similar to phostebupirim; however it appears to be quite mobile in soil.

1. Surface water

EPA used a Tier 1 GENEEC model to estimate the upper-bound phostebupirim concentrations in drinking water derived from surface water based on phostebupirim use on corn. This model is the least refined model, based on the most conservative assumptions, which is used as an initial screening tool. The highest estimated concentrations of phostebupirim in surface water, based on this screening model, were a peak acute concentration of 1.89 ppb and a chronic concentration of 0.86 ppb.

2. Ground water

Drinking water concentrations from ground water were estimated with SCI-GROW, also a Tier 1 unrefined assessment tool. For ground water, the maximum acute and chronic estimated concentration of phostebupirim is 0.3 ppb. This screening model does not provide different values for acute and chronic estimated residue values.

3. Drinking Water Levels of Comparison (DWLOCs)

To determine the maximum allowable contribution of water containing pesticide residues permitted in the diet, EPA first looks at how much of the overall allowable risk is contributed by food (and if appropriate, residential uses) then determines a "drinking water level of comparison" (DWLOC) to determine whether modeled or monitored levels exceed this level. The Agency uses the DWLOC as a surrogate to capture risk associated with exposure from pesticides in drinking water. The DWLOC is the maximum concentration in drinking water which, when considered together with dietary exposure, does not exceed a level of concern.

OPP has calculated DWLOCs for acute exposure to phostebupirim in surface and ground water for the U.S. general population and children (ages 1-6). These DWLOCs are 68.36 ppb and 19.04 ppb, respectively. For chronic (non-cancer) exposure to phostebupirim in surface and ground water, the DWLOCs are 6.48 ppb for the U.S. general population, and 1.65 ppb for children (ages 1-6).

Estimated maximum concentrations of phostebupirim in surface and ground water are 1.89 ppb and 0.3 ppb, respectively. Estimated average concentrations of phostebupirim in surface and ground water are 0.86 ppb and 0.3 ppb, respectively.

The maximum and average drinking water estimated concentrations in surface and ground water are less than OPP's levels of comparison for phostebupirim in drinking water. As residues of phostebupirim in drinking water are less than calculated drinking water levels of comparison, the Agency concludes that drinking water risk from phostebupirim use is not of concern.

C. Aggregate Risk

Aggregate risk consists of the combined risk from exposure through food, drinking water, and non-occupational uses of a pesticide. For phostebupirim, acute and chronic aggregate risk is limited to food and water exposure because phostebupirim is not used in residential settings or other areas that are frequented by the general public. Generally, the combined risks from these different exposures must be less than 100% of the acute or chronic PAD, respectively. Since the ground and surface water estimated concentrations are substantially below the DWLOCs based on screening models, acute and chronic aggregate (food and water) exposure to phostebupirim is not of concern for any population sub-group. There are no residential uses of phostebupirim, and no residential exposures resulting from phostebupirim use on corn.

D. Occupational Risk

Occupational workers can be exposed to a pesticide through mixing, loading, and/or applying a pesticide, or re-entering treated sites. Risk to workers handling phostebupirim is measured by a

Margin of Exposure (MOE) which determines how close the occupational or residential exposure comes to a No Observed Adverse Effect Level (NOAEL). Generally, MOEs greater than 100 do not exceed the Agency's level of concern.

1. Toxicity

Table 2 presents the acute toxicity categories for phostebupirim.

Table 2. Toxicity Categories

Study Type	Toxicity Category (technical)	Toxicity Category (Aztec 4.67%)
Acute Oral Toxicity	I	II
Acute Dermal Toxicity	I	III
Acute Inhalation Toxicity	I	III
Primary Eye Irritation	Not Available	III
Primary Dermal Irritation	Not Available	IV
Dermal Sensitization	Not Available	slight

The phostebupirim endpoints were obtained from the Agency's "Risk Assessment for Use of Aztec 2.1% Granular on Corn Commodities," dated February 16, 1995, and they indicate that there are toxicological endpoints of concern for phostebupirim. Phostebupirim is not expected to be used on a continuous long-term basis (greater than 6 months a year) resulting in chronic exposure. Therefore, the risk assessments were conducted for short- (1-7 days) and intermediate- (one week- several months) term occupational exposure scenarios. Dermal and inhalation endpoints of concern have been identified for short-term and intermediate-term exposures.

Table 3 lists the toxicity endpoints selected for the phostebupirim risk assessment. These are based primarily on plasma, red blood cell, and brain cholinesterase inhibition. While a 21-day rabbit dermal toxicity study was submitted by the registrant, this could not be relied on for risk assessment since phostebupirim is a sulfur-containing organophosphate and detoxification can occur in rabbits when dermally exposed to sulfur-containing organophosphates. Phostebupirim is classified as a Group E chemical, indicating that it is "Not Likely" to be carcinogenic in humans via relevant routes of exposure. This classification is supported by adequate carcinogenicity studies in rats and mice.

Table 3. Phostebupirim Hazard Endpoints and Uncertainty Factors

Route / Duration	NOAEL (mg/kg/day)	Effect	Study	Uncertainty Factors	Absorption Factor
Dermal short term	0.1	Increased Number of Fetal Resorptions	developmental toxicity in rabbits.	Interspecies: 10x Intraspecies: 10x	100 percent dermal assumed.
Dermal intermediate term	0.02	Red Blood Cell Cholinesterase Inhibition	1-year chronic dog study	Interspecies: 10x Intraspecies: 10x	100 percent dermal assumed.
Inhalation (short and intermediate term)	0.043 (0.16 mg/m^3)[a]	Red Blood Cell Cholinesterase Inhibition	28 day inhalation study in rats.	Interspecies: 10x Intraspecies: 10x	Wistar Rats, 6 hrs/day exposure, 100 percent lung absorption assumed.

a 0.16 mg/m^3 was converted to 0.043 mg/kg/day by the following formula: NOAEL (mg/kg/day) = NOAEL (mg/m^3) * Conversion Factor (1m^3 / 1000 L) * Wistar Rat Respiratory Volume for Males and Females (8.46 L/hr) * Body Weight of Wistar Rats for Males and Females (1/0.187 kg) * Exposure Duration per day (6 hrs/day).[4]

2. Exposure

Chemical-specific exposure data were not available for phostebupirim; therefore, risks to pesticide handlers were assessed using data from the *Pesticide Handlers Exposure Database (PHED)*, and standard assumptions about average body weight, work day, daily areas treated, volume of pesticide used, etc. to calculate risk estimates. The quality of the data and exposure factors represents the best sources of data currently available to the Agency for completing these kinds of assessments; the application rates are derived directly from phostebupirim labels. The exposure factors (e.g., body weight, amount treated per day, protection factors, etc.) are all standard values that have been used by the Agency over several years, and the PHED unit exposure values are the best available estimates of exposure. Some PHED unit exposure values are high quality while others represent low quality, but are the best available data. The quality of the data used for each scenario assessed is discussed in "Occupational Exposure and Risk Assessment Regarding the Use of Phostebupirim," dated May 5, 1999, which is available in the public docket.

The following general assumptions are made:

- Average body weight of an adult handler is 70 kg. An average body weight of 60 kg was used for an adult female for short-term dermal exposure since the NOAEL is based on a reproductive study. Since the dermal and inhalation NOAELs for the short-term were not based on identical effects, the doses were not combined in this risk assessment to identify a total MOE. However, the MOEs were combined for the intermediate-term since the effect was the same.

- Average work day interval represents an 8 hour workday (e.g., the acres treated or volume of spray solution prepared in a typical day).

- Calculations of handler scenarios are completed using the application rates recommended by the available phostebupirim labels.

- PHED Version 1.1 data were used to estimate exposures for all scenarios.

- Due to a lack of scenario-specific data, the Agency calculated unit exposure values using generic data from the Pesticide Handler Exposure Database (PHED) and, in lieu of PHED data for a scenario, using protection factors that are applied to represent various risk mitigation options (i.e., the use of PPE and engineering controls).

- Exposures were estimated for handlers using 213 acres per day maximum acreage (20 row planter) and 69 acres per day typical acreage (8 row planter) for a tractor drawn spreader at the minimum and maximum application rates, since these data were available from the "Corn Insecticide Cluster Risk Assessment for Occupational Exposure," dated November, 1993.

3. Risk Assessment

Occupational exposure scenarios identified for phostebupirim were (1) loading phostebupirim granulars and (2) applying phostebupirim granulars with a tractor drawn spreader. Within each of these occupational categories, further analyses were conducted to determine the MOE at minimum and maximum application rates, and at maximum and typical acreage. The Agency assessed the exposure and risks for the two scenarios considering both inhalation and dermal exposure. Phostebupirim is not expected to be used on a continuous long-term basis (greater than 6 months a year) resulting in chronic exposure. Therefore, the risk assessments were conducted for short- (1-7 days) and intermediate- (one week - several months) term occupational exposure scenarios.

Based on the available toxicity data, it is not appropriate to combine short-term dermal and inhalation MOEs because the effects observed at the LOAELs are different. However, it is necessary to combine the intermediate-term dermal and inhalation MOEs, since the effects observed at the LOAELs were identical. The short-term and intermediate-term MOE for dermal exposure were calculated using a NOAEL of 0.1 mg/kg/day and a NOAEL of 0.02 mg/kg/day, respectively. Both the short-term and intermediate-term MOE for inhalation exposure were calculated using a NOAEL of 0.16 mg/m^3 which translates to 0.043 mg/kg/day. Since a developmental study was used to determine the short-term dermal NOAEL, the body weight used to calculate short-term dermal dose was 60 kg, the average weight of an adult female. No chronic scenarios were identified. All of the risk calculations for handlers completed in this assessment are described in the document entitled, “Occupational Exposure and Risk Assessment

Regarding the Use of Phostebupirim," dated May 5, 1999, available in the public docket. The results are summarized in Tables 5-6 of this document. Table 4 summarizes the PPE requirements on current phostebupirim labels.

Table 4: PPE on Current Phostebupirim Labels

Formulation	Loaders	Applicators
Aztec 2.1% Granular Insecticide	Long pants, long sleeved shirt, waterproof gloves and shoes plus socks.	Long pants, long sleeved shirt, waterproof gloves and shoes plus socks.
Aztec 4.67% Granular Insecticide	Long pants, long sleeved shirt, waterproof gloves and shoes plus socks. Smart Box® required.	Long pants, long sleeved shirt, waterproof gloves and shoes plus socks.

a. Short-Term Risks

Table 5 presents the MOEs for short-term worker exposures. Under current phostebupirim labels, short-term dermal MOEs exceed the Agency's level of concern for all worker handler scenarios, with the exception of loading granules with the Smart Box formulation and at the minimum application rate and typical acreage for the 2.1G formulation. Additional personal protective equipment (double layer of clothing for loaders and respirators for applicators) partially addresses these MOEs, while engineering controls (closed loading systems and enclosed cabs) result in MOEs greater than 100 for all use scenarios with the exception of application at maximum rates and for the maximum acreage.

Table 5: Short-Term Dermal and Inhalation Exposure to Phostebupirim*

Scenario	Acres[a]	Rate[b] (pounds ai/acre)	Short-Term Dermal MOEs			Short-Term Inhalation MOEs		
			Current Label[c]	Current label + additional PPE[d]	Engineering controls[e]	Current Label[c]	Current Label + addn PPE[d]	Engineering Controls[e]
Loading granules	69	0.11	110	230	4700	230	1200	12000
		0.15	84	170	3400	170	860	8600
Loading granules	213	0.11	37	75	1500	76	380	3800
		0.15	27	55	1100	55	280	2800
Applying granules with tractor drawn spreader	69	0.11	110	190	380	330	1700	1800
		0.15	81	140	280	240	1200	1300
Applying granules with tractor drawn spreader	213	0.11	36	61	120	110	540	580
		0.15	26	45	89	79	390	430

* Dermal and inhalation exposures were not combined due to the difference in effects observed at the LOAELs.

[a] Typical acreage = 69 acres; Maximum acreage = 213 acres.

[b] Minimum application rate = 0.11 lbs ai/Acre; Maximum application rate = 0.15 lbs ai/Acre.

[c] Current labels reflect risks for loaders, and applicators of the 2.1%G products, but only applicators for the 4.67%G product (risks for loaders of the 4.67%G are reflected under engineering controls due to the Smart Box®). Current label specified PPE for dermal unit exposure are long pants, long sleeved shirt, water-proof gloves, open mixing/loading, open cab tractor. Inhalation exposure represents no respirator.

[d] Additional PPE for all dermal scenarios includes double layer of clothing (50% Protection Factor for clothing). Additional PPE for all inhalation scenarios includes a dust/mist respirator (80% Protection Factor).

[e] Engineering controls for dermal scenarios include closed mixing/loading (e.g., Lock and Load® or Smart Boxes® 98% protection factor), single layer clothing, chemical resistant gloves. Engineering controls for inhalation scenarios include enclosed cab, single layer clothing, no gloves (98% protection factor).

b. Intermediate-Term Risk

Table 6 presents MOEs for intermediate-term worker exposures. There are intermediate-term risks of concern for all use scenarios under current labels and with additional PPE, except for the Smart Box formulation which has MOEs greater than 100 for loaders. Use of closed loading systems brings all MOEs to greater than 100 for loaders, while use of enclosed cabs results in MOEs for applicators ranging from 20 to 84, which exceed the Agency's level of concern.

Table 6: Intermediate-Term Dermal and Inhalation Exposure to Phostebupirim*

Scenario	Acres[a]	Rate[b] (pounds ai/acre)	Intermediate-Term Dermal MOEs			Intermediate-Term Inhalation MOEs			Intermediate-Term Combined MOEs		
			Current Label[c]	Current label + additional PPE[d]	Engineering controls[e]	Current Label[c]	Current label + additional PPE[d]	Engineering controls[e]	Current Label[c]	Current label + additional PPE[d]	Engineering controls[e]
Loading granules	69	0.11	27	54	1100	230	1200	1200	24	52	990
		0.15	20	40	800	170	860	8600	18	38	730
Loading granules	213	0.11	9	18	350	76	380	3800	8	17	320
		0.15	6	13	260	55	280	2800	6	12	240
Applying granules with tractor drawn spreader	69	0.11	26	44	88	330	1700	1800	24	43	84
		0.15	18	32	64	240	1200	1300	17	31	61
Applying granules with tractor drawn spreader	213	0.11	8	14	28	110	540	580	8	14	27
		0.15	6	10	21	79	390	430	6	10	20

* Dermal and inhalation exposures were combined since the effects observed at the LOAELs were identical.

[a] Typical acreage = 69 acres; Maximum acreage = 213 acres.

[b] Minimum application rate = 0.11 lbs ai/Acre; Maximum application rate = 0.15 lbs ai/Acre.

[c] Current labels reflect risks for loaders, and applicators of the 2.1%G products, but only applicators for the 4.67%G product (risks for loaders of the 4.67%G are reflected under engineering controls due to the Smart Box®). Current label specified PPE for dermal unit exposure are long pants, long sleeved shirt, water-proof gloves, open mixing/loading, open cab tractor. Inhalation exposure represents no respirator.

[d] Additional PPE for all dermal scenarios includes double layer of clothing (50% Protection Factor for clothing). Additional PPE for all inhalation scenarios includes a dust/mist respirator (80% Protection Factor).

[e] Engineering controls for dermal scenarios include closed mixing/loading (e.g., Lock and Load® or Smart Boxes® 98% protection factor), single layer clothing, chemical resistant gloves. Engineering controls for inhalation scenarios include enclosed cab, single layer clothing, no gloves (98% protection factor).

4. Post-Application Risk

The present labels for phostebupirim establish a re-entry interval (REI) of 0 hours. The Agency's decision to establish the REI at this level is reflected in the memorandum entitled "Requested Waiver of WPS Label Statements for Aztec 2.1% Granular Insecticide," dated September 13, 1994. This decision was based on the belief that soil incorporated insecticides, such as phostebupirim, would not result in any dermal exposure after incorporation.

Since the phostebupirim REI of zero hours was established in 1994, the Agency has clarified implementation of the Worker Protection Standards and when an REI must be established. As part of its reassessment of occupational risks for phostebupirim, EPA has reevaluated potential postapplication exposures and risks following soil-incorporated applications during planting of corn. The Agency has determined that the Worker Protection Standard and current Agency policy indicate that a restricted-entry interval must be established for this use pattern. The Agency notes that phostebupirim does not qualify as a low risk pesticide, because of its high acute toxicity and because it is classified as an organophosphate. Therefore, the restricted-entry interval will be established based on available data on its dermal toxicity and its skin and eye irritation potential.

Under the Worker Protection Standard (WPS), restricted entry intervals for all uses within the scope of the WPS are based on the acute toxicity of the active ingredient. The toxicity categories of the active ingredient for acute dermal toxicity, eye irritation, and skin irritation are used to determine the WPS REI. If one or more of the three acute toxic affects are in toxicity category I, the WPS REI is established at 48 hours (72 hours in areas that receive less than 25 inches of rainfall per year). Since phostebupirim has a toxicity category of 1 for acute dermal, the REI should be 48 hours (72 hours in areas that receive less than 25 inches of rainfall per year) to comply with the Worker Protection Standard.

IV. FQPA Tolerance Reassessment Progress and Interim Risk Management Decision

A. Determination of Tolerance Reassessment & Interim Risk Management Decision

This interim evaluation presents the Agency's current position on products containing the active ingredient phostebupirim. The Agency has sufficient information on the human health effects of phostebupirim to make interim decisions as part of the tolerance reassessment process under FQPA and to reassess occupational risks under FIFRA. Should a registrant fail to implement any of the recommended risk mitigation measures outlined in this document, the Agency will continue to have concerns about the risks posed by phostebupirim. Where the Agency has identified any unreasonable adverse effect to human health, the Agency may at any time initiate appropriate regulatory action to address this concern. At that time, any affected person(s) may challenge the Agency's action.

Based on its current evaluation of phostebupirim alone, the Agency has determined that phostebupirim products, labeled and used as specified in this document, will not present unreasonable dietary and occupational risks. Occupational risks can be brought above the Agency's level of concern with additional personal protective equipment. In addition, data from both an exposure or dust comparison study and a new dermal toxicity study will allow the Agency to refine its occupational risk assessment.

The Agency will finalize the decision for phostebupirim after evaluating the cumulative risk of the organophosphate class. Because the Agency has not yet completed the cumulative risk assessment for the organophosphates, this interim decision does not fully address the reassessment of the existing phostebupirim food residue tolerances as required by section 408(q) of the FQPA. When the Agency has completed the cumulative assessment, phostebupirim tolerances will be reassessed along with the other organophosphate pesticides and a final determination will be made. 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.

This interim evaluation does not limit the Agency from making further FQPA determinations and tolerance-related rulemakings that may be required on this pesticide or any other in the future. If the Agency determines, as a result of this later implementation process, that any of the determinations described in this Report on FQPA Tolerance Reassessment Progress and Interim Risk Management document are no longer appropriate, the Agency will pursue appropriate action, including but not limited to, reconsideration of any portion of this interim document.

B. Summary of Phase 3 Comments and Revisions to Preliminary Assessment

The Agency solicited comments on the preliminary human health assessment for phostebupirim. In response to the May 26, 1999, Federal Register Notice (64 FR 28469) announcing the availability of the preliminary risk assessment and supporting documents, comments on the risk assessment were submitted by the phostebupirim registrant, Bayer Corporation. The registrant disagreed with the selection of a developmental toxicity study in rabbits for establishing the acute RfD and with the selection of a developmental toxicity study for evaluating dermal exposure to workers. The Agency acknowledged that it was more appropriate to use an acute neurotoxicity study for the acute dietary endpoint and noted that the 3X FQPA safety factor had been reduced to 1X by the Hazard Identification Assessment Review Committee as a result of its March 25, 1999, meeting based on the Agency’s review of that data. However, the Agency noted that it was not appropriate to use the 21-day dermal toxicity study in rabbits submitted by the registrant instead of the developmental toxicity study to determine the endpoint for short-term dermal exposure. This is because the use of rabbits to evaluate the dermal toxicity of sulfur-containing organophosphates is not appropriate because detoxification can occur in rabbits when dermally exposed to sulfur-containing organophosphates. The

registrant also disagreed with the use of technical phostebupirim to measure inhalation exposure, rather than use of a formulated product. The Agency determined that comments received during Phase 3 did not warrant further revisions to the risk assessment. A fuller discussion of the registrant comments and the Agency's response can be found in "Phostebupirim: HED's Response to Comments Submitted During Phase 3 (Public Comment Period), dated September 22, 1999.

C. Summary of Phase 5 Comments and Responses

The availability of the revised risk assessment and supporting documents was announced on March 27, 2000, in Federal Register Notice (65 FR 16197). Interested parties were provided a 60-day period to submit comments, including risk mitigation proposals. Only two submissions were received during this public comment period, one from the President of the Illinois Corn Growers Association and the other from the phostebupirim registrant, Bayer Corporation. These comments are available in their entirety in the docket. A brief summary of the comments and the Agency response is noted here.

1) *Comment*. The President of the Illinois Corn Growers Association noted that Aztec plays an important role in managing corn pests and objected to EPA's use of maximum rates and worst-case scenarios in conducting risk assessments as unrealistic. He also expressed the opinion that EPA's use of exposure data derived from a broadcast study was inappropriate because phostebupirim is applied through in-furrow or banded application methods which are more targeted than broadcast application.

Response. This comment provided no specific mitigation suggestions. However, the Agency's policy is to use the maximum labeled application rates and maximum daily treated acreage for calculating short and intermediate-term occupational risks. Since the endpoint of concern for phostebupirim results from a short and intermediate-term exposure, it is appropriate to protect workers who use the maximum recommended application rates and who are applying it to larger corn fields. The Agency has reviewed acreage information for corn and believes that the 213 acres used is a realistic estimate of the maximum number of acres of corn which may be treated with phostebupirim in a given day (based on the Corn Cluster analysis and follow-up information).

While the Agency does not agree that it was inappropriate to use exposure data derived from a broadcast study in the risk assessment, EPA does agree that this has likely resulted in an overestimate of exposure. This likely overestimate of exposure has been factored into the risk mitigation recommended in this document.

2) *Comment*. Bayer Corporation did not provide any risk mitigation suggestions; instead Bayer reiterated many of the same comments on the risk assessment raised in its Phase 3 comments. Specifically, (1) Bayer alleged that the Agency had chosen different toxicological endpoints in 1999 than in 1995 to assess occupational risk despite the submission of no new studies, (2) Bayer suggested that the use of in-furrow and T-Band application data could reduce calculated exposure values, (3)

Bayer reiterated its objection to the Agency's rejection of the 21-day dermal toxicity study in rabbits for regulating occupational dermal exposure, (4) Bayer objected to the Agency's assumption of 100% dermal absorption, suggesting sufficient information was available to estimate a lower dermal absorption value, (5) Bayer suggested that the Agency amortize intermediate-term exposure from the 1-year chronic dog study to more accurately represent the shorter-term intermediate-term exposure, and (6) Bayer proposed that 150 acres should be used for maximum daily acres treated rather than the 213 used by the Agency.

Response. As discussed more fully in the Agency's June 23, 2000, Response to Bayer's Comments found in the docket and on the internet, (1) the Agency used the exact same toxicological endpoints in both its 1995 and 1999 occupational risk assessment, (2) the Agency's exposure data included the use of in-furrow and T-Band application studies, (3) it is inappropriate to use dermal toxicity studies in rabbits for sulfur-containing organophosphates such as phostebupirim, (4) the Agency does not have sufficient information to estimate an appropriate dermal absorption value and therefore assumes 100% dermal absorption in the absence of additional data, (5) the Agency agrees that a 1-year chronic dog study is not the ideal study for estimating intermediate-term worker risk; however, the Agency does not have sufficient information to amortize intermediate-term exposure from the 1-year chronic dog study and in the absence of a more appropriate study, the 1-year chronic dog study is a more appropriate duration study than the other available studies, and (6) the data available to the Agency indicates that 213 acres is an appropriate maximum daily acres treated value for corn and does not result in an overly conservative estimate of risk.

D. Regulatory Position

1. FQPA and Occupational Risk 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 the 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 phostebupirim is within its own “risk cup.” In other words, if phostebupirim did not share a common mechanism of toxicity with other chemicals, EPA would be able to conclude today that the proposed tolerances for phostebupirim on corn meet 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 conducted for exposures through food and drinking water (there are no

residential uses). Results of this aggregate assessment indicate that the human health risks from these combined exposures are considered to be within acceptable levels; that is, combined risks from all exposures to phostebupirim "fit" within the individual risk cup. Therefore, unless phostebupirim can be shown to meet the Agency's Threshold of Regulation policy such that no tolerances are required, the Agency will consider establishing phostebupirim tolerances after EPA has completed a full assessment of the cumulative risk from all organophosphates.

b. Tolerance Summary

Time-limited tolerances of 0.01 parts per million (ppm) were established July 5, 1995, in 60 FR 34871 for phostebupirim residues in or on field corn, sweet corn, pop corn and corn forage and fodder. The tolerances were set at the Limit of Detection (LOD). There have been no detected residues of phostebupirim at the LOD in food monitoring programs or field trials where phostebupirim was applied at the label rate.

The time-limited tolerances for phostebupirim expired July 6, 1999, while the conditional registration for phostebupirim was extended through July 5, 2001. The Agency was not able to establish or extend tolerances for phostebupirim at the time the time-limited tolerance expired due to the requirements under the FQPA to establish a reasonable certainty of no harm from the cumulative effects of the residues of all organophosphates that show a common mechanism of toxicity, a level of assessment which the Agency has not yet completed. However, the Agency believed it was appropriate to allow for the continued conditional registration of phostebupirim for pre-plant applications on corn since there is no reasonable expectation of finite residues of phostebupirim. This determination was made before the Agency issued its Threshold of Regulation (TOR) policy for deciding whether a pesticide food use pattern needs a tolerance. The Agency believes that phostebupirim complies with the spirit of the policy because no phostebupirim residues in corn commodities have been detected in either corn metabolism studies, crop field trials, or in sampling programs.

Under the TOR policy, a tolerance or an exemption from the tolerance requirement is not necessary for a pesticide use that results in no detected residues in food and for which the degree of potential risk posed by any theoretically possible residues is so minimal that tolerance setting serves no purpose. While phostebupirim does not meet the TOR policy based on currently available data, Bayer may be able to generate data which would support a finding under the policy that no tolerances are required. In order to allow the EPA to make such a determination, it would be necessary to conduct additional field trial studies using a more sensitive, validated, analytical method, along with exaggerated application rates. For phostebupirim to be considered under the policy, the registrant should submit a request in writing, along with any supplemental data to support its request, asking the Agency to determine whether phostebupirim uses need a tolerance under the TOR policy.

The time-limited tolerances for residues of phostebupirim in/on plant commodities were expressed in terms of residues of phostebupirim *per se*. Based upon the lack of phostebupirim residues measured in field corn, popcorn, and sweet corn commodities (<0.01 ppm), there is no reasonable expectation of finite residues of phostebupirim in meat, milk, poultry or eggs and no tolerances would be needed for these commodities if the tolerances for the raw agricultural commodities were established. If the Agency is able to establish phostebupirim tolerances after it completes its cumulative dietary risk assessment from all organophosphates, Table 7 provides the appropriate tolerance levels for phostebupirim [O-[2-(1,1-dimethylethyl)-5-pyrimidinyl] O-ethyl O-(1-methylethyl) phosphorothioate], as supported by submitted residue data. Sufficient data are available to ascertain the adequacy of these tolerances for the following commodities, as defined in 40 CFR § 180.486. Note that these tolerances cannot be established, or considered "reassessed" as required by FQPA, until the cumulative risk assessment of all organophosphates is completed.

Table 7: Tolerance Summary for Phostebupirim

Commodity	Parts per million
Corn, field, forage	0.01
Corn, field, stover	0.01
Corn, pop, forage	0.01
Corn, pop, stover	0.01
Corn, sweet, forage	0.01
Corn, sweet, stover	0.01
Corn, field, grain	0.01
Corn, pop, grain	0.01
Corn, sweet, kernel plus cob with husks removed	0.01

2. Endocrine Disruptor Effects

EPA is required to develop a screening program to determine whether certain substances (including all pesticides and inerts) "may have an effect in humans that is similar to an effect produced by a naturally occurring estrogen, or such other endocrine effect...". The Agency is currently working with interested stakeholders, including government agencies, public interest groups, industry and research scientists in developing a screening and testing program and a priority setting scheme to implement this program. The EPA may require further testing of phostebupirim for endocrine disruptor effects when this program is in place.

3. Recommended Label Modifications

The Agency recommends the following measures, in addition to the existing label requirements, to clarify and strengthen the existing label language to help minimize worker risks. These measures are expected to result in minimal impact on grower costs and ability to effectively use phostebupirim products.

- Labels should state that for granular products packaged in the SmartBox® closed loading system (or any other closed loading system that meets the requirements of the WPS), loaders, applicators and other handlers must wear long-sleeved shirt, long pants, shoes plus socks, and chemical resistant gloves such as or made out of any waterproof material. In addition, loaders must be provided with and have immediately available for use in case of an emergency, a NIOSH approved dust/mist respirator.

- Labels should state that for clay-based products not packaged in the SmartBox® closed loading system (or any other closed loading system that meets the requirements of the WPS), loaders, applicators and other handlers must wear long-sleeved shirt, long pants, shoes plus socks and chemical resistant gloves such as or made out of any waterproof material. In addition, loaders must wear a dust/mist respirator.

- Labels should state that for cellulose-based products not packaged in the SmartBox® closed loading system (or any other closed loading system that meets the requirements of the WPS), loaders, applicators and other handlers must wear long-sleeved shirt, long pants, shoes plus socks and chemical resistant gloves such as or made out of any waterproof material.

- The REI should be 48 hours or 72 hours where there is less than 25 inches of rainfall.

- Labels should state that PPE during early re-entry consists of coveralls, chemical resistant gloves such as or made out of any waterproof material, socks plus shoes, and protective eye wear.

- Labels should include a "double notification" statement. Double notification requires that workers are advised about the application both orally and by posting warning signs at entrances to treated areas during the REI.

The Agency is not recommending any further label modifications, beyond the above listed measures, to mitigate occupational risks from phostebupirim use at this time. Bayer has agreed to implement the above label modifications for the 2001 use season and the Agency believes that remaining worker risk concerns will be adequately addressed as a result of confirmatory data, which will be submitted by April 1, 2001, to refine the occupational risk assessment. The Agency will review the phostebupirim data prior to July 5, 2000, the date the conditional registration expires.

E. Regulatory Rationale

The following is a summary of the rationale for managing risks associated with the use of phostebupirim. Where labeling revisions are recommended, specific language is set forth in the summary tables of Section V of this document.

1. Dietary Mitigation

a. Dietary (Food) Risk Mitigation

Acute and chronic dietary risk from food is well below the Agency's level of concern -- a Tier 1 DEEM^{TM} analysis yielded percent acute and chronic PAD values that are only 4.79% and 17.6% respectively at the 95th percentile of exposure for the most exposed population subgroup (children 1-6 years old). Therefore, no mitigation measures are recommended at this time to address acute or chronic dietary risk from food.

b. Dietary (Water) Risk Mitigation

Acute and chronic dietary risk from water is not of concern based on the comparison of the DWLOC against the estimated concentrations from surface and ground water modeling, based on Tier 1 screening models which provide an upper-bound unrefined estimate of drinking water concentrations. Therefore, no mitigation measures are recommended at this time to address acute or chronic drinking water risks.

c. Aggregate (Food + Water) Risk Mitigation

For phostebupirim, the aggregate risk is limited to food and water. No risk mitigation for aggregate risk is necessary at this time because food and drinking water estimates indicate that the Agency's level of concern is not exceeded for any subgroup.

2. Occupational Risk Mitigation

Under the current label, the Agency's risk assessment shows a risk concern for short and intermediate-term exposures for both granular loaders and applicators. Adding a dust/mist respirator requirement to the 2.1G clay-based formulation product labels for loaders would address inhalation risk concerns. The Agency believes the inhalation risks for applicators are overstated because the MOEs were calculated with low confidence PHED data based on a broadcast spreader study. Phostebupirim is applied in-furrow or T-Band, which will have lower exposures. Therefore, no risk mitigation is necessary to address applicator inhalation risk.

Although dermal risks are of concern, the registrant has agreed to initiate a 21-day rat dermal toxicity study which the Agency believes will confirm that its current dermal risk assessment overestimates the potential for worker exposure for the following reasons:

(1) In the absence of an acceptable dermal toxicity study, the Agency is regulating worker dermal exposures based on an oral developmental study. The Agency's preference is to use route-specific studies when possible, and thus a dermal toxicity study would be preferred over an oral study especially when coupled with the more conservative 100% dermal absorption assumption. While it is not appropriate to use a rabbit dermal toxicity study for sulphur-containing organophosphates like phostebupirim, it would be appropriate to use a rat dermal toxicity study.

(2) The registrant is conducting its dermal toxicity study using the granular (4.67% a.i.) rather than the technical (98% a.i.) formulation. The Agency believes this is appropriate since only a 2.1% and 4.67% a.i. granular formulation are registered. This will provide a more realistic picture of the impacts of the granular product, which has a much lower percent active ingredient than the liquid technical product.

(3) Since short-term worker exposures are 1-7 days while intermediate-term exposures are 7 days to several months, the Agency had to use two different studies to approximate these different exposure durations. One, the oral rabbit developmental study, provided an acute (short-term) exposure, while the other, the 1-year chronic dog study, provided a longer-term exposure duration, although the Agency believes intermediate-term exposures to phostebupirim do not exceed 30 days. By conducting a 21-day rat dermal toxicity study, the registrant will provide a study which better represents both the short-term and intermediate-term worker exposure durations. Thus, the Agency will be able to use a single, more appropriate, study to establish a NOAEL for both short-term and intermediate-term exposure durations.

Thus, for the above-mentioned reasons, the Agency believes that a 21-day rat dermal toxicity study will provide a more appropriate endpoint for regulating both short-term and intermediate-term occupational dermal exposures and will provide a more refined occupational risk assessment.

In conclusion, to mitigate inhalation risks to loaders, the Agency is recommending label amendments to require the use of a dust/mist respirator when loading the Aztec® 2.1G granular clay-based formulation. The Agency believes that handlers of Aztec® 2.1G cellulose-based products are exposed to comparatively lower levels via inhalation. As a result, no mitigation is recommended at this time for the Biodac cellulose-based formulation. However, to confirm the Agency's belief that cellulose-based formulations pose less inhalation risk than the clay-based formulation, the registrant has agreed to submit an exposure or dust comparison study by April 1, 2001.

The Agency is not requiring further risk mitigation to address applicator inhalation risk. Although the risk assessment shows a risk concern for this exposure (MOE=79), the Agency believes this risk is overstated. This is because the risk was calculated using low confidence PHED data (one study with a small number of replicates using only a broadcast spreader). In actual use, phostebupirim will typically be applied in-furrow or T-Band. These methods of application should make the granular formula less available for exposure.

With regard to dermal risks, the Agency believes that the 21-day rat dermal toxicity study using the 4.67G formulation, which the registrant will submit by April 1, 2001, will demonstrate that the NOAEL is substantially higher and that worker dermal MOEs no longer exceed the Agency's level of concern. As a result, the Agency is not recommending any additional measures at this time to address worker risks from dermal exposure. However, in the event that there are risk concerns after results of the new studies are reviewed, the Agency will recommend additional mitigation measures to the registrant.

3. Post Application Risk Mitigation

Since the phostebupirim REI of 0 hours was established in 1995, the Agency has clarified implementation of the Worker Protection Standards and when an REI must be established. For phostebupirim, EPA has reevaluated potential postapplication exposures and risks following soil-incorporated applications during planting of corn. The Agency has determined that the Worker Protection Standard and current Agency policy indicate that a restricted-entry interval should be established for this use pattern. The Agency notes that phostebupirim does not qualify as a low risk pesticide, because of its high acute toxicity and because it is classified as an organophosphate. Therefore, the restricted-entry interval will be established based on available data on its dermal toxicity and its skin and eye irritation potential. The restricted-entry interval (REI) is the time immediately after a pesticide application when entry into the treated area is limited. The current REI on phostebupirim end-use products of 0 hours must be replaced by 48 hours or 72 hours where average rainfall is less than 25 inches per year in order to comply with the Worker Protection Standard (WPS). Early re-entry PPE, as required by WPS, must also be specified on labels and include coveralls over long-sleeved shirt, long pants, chemical resistant gloves such as or made out of any waterproof material, chemical resistant footwear plus socks and protective eye wear. Protective eye wear is being required because the active ingredient (a.i.) is assumed to be Toxicity Category I for Acute Eye Irritation in the absence of available data. A double notification requirement for re-entry is required because the a.i. is assumed to be Toxicity Category I for Dermal Irritation in the absence of available data.

V. Recommended Mitigation Measures

A. Manufacturing Use Products

The generic database supporting the registration of phostebupirim for use on corn has been reviewed and determined to be substantially complete. However, the registrant is conducting a 21-day rat dermal toxicity study and an exposure or dust comparison study which will provide further refinement of the current risk assessment. Theses studies are to be submitted to the Agency by April 1, 2001.

B. End-Use Products

1. Labeling Changes for End-Use Products

The Agency recommends the following label language and modifications detailed in Table 8 to mitigate occupational risks.

Table 8: Summary of Recommended Occupational Labeling for Phostebupirim

Description	Recommended Labeling	Placement on Label
End Use Products Intended for Use on Corn		
PPE Requirements[1] for granular products contained in a SmartBox® system	"Personal Protective Equipment (PPE)" "Some materials that are chemical-resistant to this product are any water proof materials. "If you want more options, follow the instructions for category *A* on an EPA chemical-resistance category selection chart." "Loaders, applicators and other handlers must wear: -- Long-sleeved shirt and long pants, -- Chemical resistant gloves such as or made out of any waterproof material, -- Shoes plus socks "See Engineering Controls for additional requirements."	Precautionary Statements: Hazards to Humans and Domestic Animals
PPE Requirements* for the granular clay-based product (not in a SmartBox® system)	"Personal Protective Equipment (PPE)" "Some materials that are chemical-resistant to this product are any water proof materials. If you want more options, follow the instructions for category *A* on an EPA chemical-resistance category selection chart." "Loaders, applicators and other handlers must wear: -- Long-sleeved shirt and long pants -- Chemical resistant gloves such as or made out of any waterproof material, -- Shoes plus socks In addition, loaders must wear: -- A NIOSH-approved dust mist filtering respirator with MSHA/NIOSH approval number prefix TC-21C *or* a NIOSH-approved respirator with any N[2] R, P, or HE filter."	Precautionary Statements: Hazards to Humans and Domestic Animals

Description	Recommended Labeling	Placement on Label
PPE Requirements[1] for the granular cellulose-based product (not in a SmartBox® system)	"Personal Protective Equipment (PPE)" "Some materials that are chemical-resistant to this product are any water proof materials. "If you want more options, follow the instructions for category *A* on an EPA chemical-resistance category selection chart." "Loaders, applicators and other handlers must wear: -- Long-sleeved shirt and long pants -- Chemical resistant gloves such as or made out of any waterproof material -- Shoes plus socks	Precautionary Statements: Hazards to Humans and Domestic Animals
User Safety Requirements	"Follow manufacturer's instructions for cleaning/maintaining PPE. If no such instructions for washables, use detergent and hot water. Keep and wash PPE separately from other laundry."	Precautionary Statements: Hazards to Humans and Domestic Animals (immediately following the PPE requirements)
Engineering Controls for Product packaged in the SmartBox® system.	"Engineering Controls This product is formulated into a "Smart Box" system that meets the definition of a closed loading system as defined by the Worker Protection Standard for Agricultural Pesticides. IMPORTANT: In addition to wearing the required PPE specified above, loaders must be provided and must have immediately available for use in case of an accident or spill: A NIOSH-approved dust mist filtering respirator with MSHA/NIOSH approval number prefix TC-21C *or* a NIOSH-approved respirator with any N* R, P, or HE filter." "When applicators use enclosed cabs, in a manner that meets the requirements listed in the Worker Protection Standard (WPS) for agricultural pesticides (40 CFR 170.240(d)(4-6), the handler PPE requirements may be reduced or modified as specified in the WPS."	Precautionary Statements: Hazards to Humans and Domestic Animals (immediately following PPE and User Safety Requirements.)
Engineering Controls (not in SmartBox® system or in any other closed system)	"When applicators use enclosed cabs, in a manner that meets the requirements listed in the Worker Protection Standard (WPS) for agricultural pesticides (40 CFR 170.240(d)(4-6), the handler PPE requirements may be reduced or modified as specified in the WPS."	

Description	Recommended Labeling	Placement on Label
User Safety Recommendations	"User Safety Recommendations: • Wash hands before eating, drinking, chewing gum, using tobacco, or using the toilet. • Remove clothing/PPE immediately if pesticide gets inside. Then wash thoroughly and put on clean clothing. • Remove PPE immediately after handling this product. Wash the outside of the gloves before removing. As soon as possible, wash thoroughly and change into clean clothing."	Precautionary Statements under: Hazards to Humans and Domestic Animals immediately following Engineering Controls
Restricted-Entry Interval	"Do not enter or allow worker entry into treated areas during the restricted entry interval (REI) of 48 hours. The REI is 72 hours where average rainfall is less than 25 inches per year." "Exception: if the product is soil-injected or soil-incorporated, the Worker Protection Standard, under certain circumstances, allows workers to enter the treated area without restrictions if there will be no contact with anything that has been treated."	
Early Entry Personal Protective Equipment	"PPE required for early entry to treated areas that is permitted under the Worker Protection Standard and that involves contact with anything that has been treated, such as plants, soil, or water, is: -- coveralls over long-sleeved shirt and long pants, -- chemical resistant gloves such as or made out of any waterproof material, -- chemical resistant footwear plus socks, -- protective eye wear	Directions for Use, Agricultural Use Requirements Box
Double Notification Statement	"Notify workers of the application by warning them orally and by posting warning signs at entrances to treated areas."	Directions for Use, Agricultural Use Requirements Box
General Application Restrictions	"Do not apply this product in a way that will contact workers or other persons, either directly or through drift. Only protected handlers may be in the area during application."	Directions for Use directly above the Agricultural Use Box.

[1] PPE that is established on the basis of Acute Toxicity of the end-use product must be compared to the active ingredient PPE in this document. The more protective PPE must be placed in the product labeling. For guidance on which PPE is considered more protective, see PR Notice 93-7.

[2] *The registrant must drop the N type filter from the respirator statement if the pesticide product contains or is used with oil.*

Instructions in the Labeling Required section appearing in quotations represent the exact language that must appear on the label.
Instructions in the Labeling Required section not in quotes represent actions that the registrant must take to amend their labels or product registrations.

2. Procedure and Timing for Label Amendment

Registrants should submit applications for amended registration. This application should include the following items: EPA application form 8570-1 (filled in), five copies of each revised label, and a description on the application, such as, "Responding to Interim Tolerance Reassessment Evaluation and Risk Management Document." Registrants should send applications for amendment to the appropriate following address within 90 days after receipt of this document.

Document Processing Desk (APPL)
Office of Pesticide Programs
Room 266A, Crystal Mall 2
1921 Jefferson Davis Highway
Arlington, VA 22202

Attn: Marilyn Mautz
Insecticide-Rodenticide Branch (7504C)

C. Existing Stocks

Registrants may generally distribute and sell products bearing old labels/labeling for 12 months from the date of the issuance of this Report on FQPA Tolerance Reassessment and Interim Risk Management Decision. Persons other than the registrant may generally distribute or sell such products for 24 months from the date of the issuance of this Report on FQPA Tolerance Reassessment Progress and risk management decision. However, existing stocks time frames will be established case-by-case, depending on the number of products involved, the number of label changes, and other factors. Refer to "Existing Stocks of Pesticide Products; Statement of Policy"; Federal Register, Volume 56, No. 123, June 26, 1991.

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 4:00 PM.

The docket initially contained the preliminary risk assessment and related documents as of January 15, 1999. On March 15, the first public comment period closed. EPA then considered comments, revised the risk assessment, and placed the revised risk assessment in the docket on August 18, 1999. All documents, in hard copy form, may be viewed in the OPP docket room or viewed or downloaded via the Internet (http://www.epa.gov/oppsrrd1/op/).

VII. APPENDICES

Appendix A: Citations Supporting the FQPA Tolerance Reassessment and Interim Occupational Risk Management Decision (Bibliography)

GUIDE TO APPENDIX A

1. CONTENTS OF BIBLIOGRAPHY. This bibliography contains citations of all studies considered relevant by EPA in arriving at the positions and conclusions stated elsewhere in the Reregistration Eligibility Document. Primary sources for studies in this bibliography have been the body of data submitted to EPA and its predecessor agencies in support of past regulatory decisions. Selections from other sources including the published literature, in those instances where they have been considered, are included.

2. UNITS OF ENTRY. The unit of entry in this bibliography is called a "study." In the case of published materials, this corresponds closely to an article. In the case of unpublished materials submitted to the Agency, the Agency has sought to identify documents at a level parallel to the published article from within the typically larger volumes in which they were submitted. The resulting "studies" generally have a distinct title (or at least a single subject), can stand alone for purposes of review and can be described with a conventional bibliographic citation. The Agency has also attempted to unite basic documents and commentaries upon them, treating them as a single study.

3. IDENTIFICATION OF ENTRIES. The entries in this bibliography are sorted numerically by Master Record Identifier, or "MRID" number. This number is unique to the citation, and should be used whenever a specific reference is required. It is not related to the six-digit "Accession Number" which has been used to identify volumes of submitted studies (see paragraph 4(d)(4) below for further explanation). In a few cases, entries added to the bibliography late in the review may be preceded by a nine character temporary identifier. These entries are listed after all MRID entries. This temporary identifying number is also to be used whenever specific reference is needed.

4. FORM OF ENTRY. In addition to the Master Record Identifier (MRID), each entry consists of a citation containing standard elements followed, in the case of material submitted to EPA, by a description of the earliest known submission. Bibliographic conventions used reflect the standard of the American National Standards Institute (ANSI), expanded to provide for certain special needs.

    a. Author. Whenever the author could confidently be identified, the Agency has chosen to show a personal author. When no individual was identified, the Agency has shown an identifiable laboratory or testing facility as the author. When no author or laboratory could be identified, the Agency has shown the first submitter as the author.

b. Document date. The date of the study is taken directly from the document. When the date is followed by a question mark, the bibliographer has deduced the date from the evidence contained in the document. When the date appears as (1999), the Agency was unable to determine or estimate the date of the document.

c. Title. In some cases, it has been necessary for the Agency bibliographers to create or enhance a document title. Any such editorial insertions are contained between square brackets.

d. Trailing parentheses. For studies submitted to the Agency in the past, the trailing parentheses include (in addition to any self-explanatory text) the following elements describing the earliest known submission:

(1) Submission date. The date of the earliest known submission appears immediately following the word "received."

(2) Administrative number. The next element immediately following the word "under" is the registration number, experimental use permit number, petition number, or other administrative number associated with the earliest known submission.

(3) Submitter. The third element is the submitter. When authorship is defaulted to the submitter, this element is omitted.

(4) Volume Identification (Accession Numbers). The final element in the trailing parentheses identifies the EPA accession number of the volume in which the original submission of the study appears. The six-digit accession number follows the symbol "CDL," which stands for "Company Data Library." This accession number is in turn followed by an alphabetic suffix which shows the relative position of the study within the volume.

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Appendix B: EPA's Batching of Phostebupirim Products for Meeting Acute Toxicity Data Requirements for Reregistration

In an effort to reduce the time, resources and number of animals needed to fulfill the acute toxicity data requirements for reregistration of products containing ***Phostebupirim*** as the primary active ingredient, the Agency has batched products which can be considered similar for purposes of acute toxicity. Factors considered in the sorting process include each product's active and inert ingredients (identity, percent composition and biological activity), type of formulation (e.g., emulsifiable concentrate, aerosol, wettable powder, granular, etc.), and labeling (e.g., signal word, use classification, precautionary labeling, etc.). Note the Agency is not describing batched products as "substantially similar" since some products with in a batch may not be considered chemically similar or have identical use patterns.

Using available information, batching has been accomplished by the process described in the preceding paragraph. Notwithstanding the batching process, the Agency reserves the right to require, at any time, acute toxicity data for an individual product should need arise.

Registrants of products within a batch may choose to cooperatively generate, submit or cite a single battery of six acute toxicological studies to represent all the products within that batch. It is the registrants' option to participate in the process with all other registrants, only some of the other registrants, or only their own products within in a batch, or to generate all the required acute toxicological studies for each of their own products. If the registrant chooses to generate the data for a batch, he/she must use one of the products within the batch as the test material. If the registrant chooses to rely upon previously submitted acute toxicity data, he/she may do so provided that the data base is complete and valid by to-days standards (see acceptance criteria attached), the formulation tested is considered by EPA to be similar for acute toxicity, and the formulation has not been significantly altered since submission and acceptance of the acute toxicity data. Regardless of whether new data is generated or existing data is referenced, the registrants must clearly identify the test material by EPA Registration Number. If more than one confidential statement of formula (CSF) exists for a product, the registrant must indicate the formulation actually tested by identifying the corresponding CSF.

In deciding how to meet the product specific data requirements, registrants must follow the directions given in the Data Call-In Notice and its attachments appended to the RED. The DCI Notice contains two response forms which are to be completed and submitted to the Agency within 90 days of receipt. The first form, "Data Call-in Response, " asks whether the registrant will meet the data requirements for each product. The second form, "Requirements Status and Registrant's Response," lists the product specific data required for each product, including the standard six acute toxicity tests. A registrant who wishes to participate in a batch must decide whether he/she will provide the data or depend on someone else to do so. If the registrant supplies the data to support a batch of products, he/she must select the one of the following options: Developing data (Option 1), Submitting an existing Study (Option 4), Upgrading an existing Study (Option 5), or Citing an Existing Study (Option 6). If a

registrant depends on another's data, he/she must choose among: Cost sharing (Option 2), Offers to Cost Share (Option 3) or Citing an Existing Study (Option 6). If a registrant does not want to participate in a batch, the choices are Options 1, 4, 5 or 6. However, a registrant should know that choosing not to participate in a batch does not preclude other registrants in the batch from citing his/her studies and offering to cost share (Option 3) those studies.

Four products were found which contain ***Phostebupirim*** as the active ingredient. These products have been placed into ***one*** batch and a ***"No Batch"*** category in accordance with the active and inert ingredients and type of formulation.

Batch 1	EPA Reg. No.	Percent active ingredient	Formulation Type
	3125-412	2.0	Solid
	3125-539	2.0	Solid

No Batch	EPA Reg. No.	Percent active ingredient	Formulation Type
	3125-411	93.0	Liquid
	3125-513	4.45	Solid

Appendix C: List of Available Related Documents

These documents are available from the Public Docket Office or at the following web site: www.epa.gov/pesticides/op/phostebupirim.htm

1. Hazard Assessment of the Organophosphates
2. FQPA Safety Factor Recommendations for the Organophosphates
3. Frequently Asked Questions
4. *Federal Register* Notice Vol. 65, Number 59, Pages 16197-16199 (Comment period ending May 26, 2000)
5. *Federal Register* Notice Vol. 64, Number 101, Pages 28469-28471 (Comment period ending July 26, 1999)
6. Health Effects Preliminary Assessment
7. Occupational Exposure and Risk Assessment Regarding the Use of Phostebupirim
8. Dietary Risk Assessment Update
9. HIARC Reevaluation of Acute Dietary RfD
10. Acute and Chronic Dietary Exposure and Risk Analysis
11. Reassessment of Acute and Chronic RfDs
12. Report of the FQPA Safety Factor Committee
13. Tier 1 Screen for Drinking Water Assessment
14. Transmittal Letter to Bayer Corporation Regarding the Preliminary Risk Assessment
15. Phostebupirim Summary
16. Overview of Phostebupirim Revised Risk Assessments
17. Quantitative Usage Analysis
18. HED's Response to Comments on the Preliminary Risk Assessment
19. Letter to Bayer Regarding the Revised Risk Assessment
20. Registrant's Confidential Business Certification Statement
21. Bayer's Initial Response to "Risk Assessment Update for FQPA Requirements"