United States Environmental Protection Agency

Prevention, Pesticides and Toxic Substances (7508C)

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August 2005

Reregistration Eligibility Decision (RED) for

Metiram

Reregistration Eligibility Decision

for

Metiram

List A
Case No. 0644

Approved By:

_____/s/_____
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Director, Special Review and
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_____August 29, 2005_____
Date

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GLOSSARY OF TERMS AND ABBREVIATIONS

AGDCI	Agricultural Data Call-In
ai	Active Ingredient
aPAD	Acute Population Adjusted Dose
AR	Anticipated Residue
ARTF	Agricultural Re-entry Task Force
BCF	Bioconcentration Factor
CCA	Comparative Cholinesterase Assay
CFR	Code of Federal Regulations
cPAD	Chronic Population Adjusted Dose
CSF	Confidential Statement of Formula
CSFII	USDA Continuing Surveys for Food Intake by Individuals
DCI	Data Call-In
DEEM	Dietary Exposure Evaluation Model
DFR	Dislodgeable Foliar Residue
DNT	Developmental Neurotoxicity
DWLOC	Drinking Water Level of Comparison.
EC	Emulsifiable Concentrate Formulation
EC	Engineering Control
EDWC	Estimated Drinking Water Concentration
EEC	Estimated Environmental Concentration
EPA	Environmental Protection Agency
EUP	End-Use Product
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
GLN	Guideline Number
HAFT	Highest Average Field Trial
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.
LOC	Level of Concern
LOD	Limit of Detection
LOAEL	Lowest Observed Adverse Effect Level
MATC	Maximum Acceptable Toxicant Concentration
µg/g	Micrograms Per Gram
µg/L	Micrograms Per Liter
mg/kg/day	Milligram Per Kilogram Per Day
mg/L	Milligrams Per Liter
MOE	Margin of Exposure
MRID	Master Record Identification (number). EPA's system of recording and tracking studies submitted.
MUP	Manufacturing-Use Product
NA	Not Applicable

NAWQA	USGS National Water Quality Assessment
NPDES	National Pollutant Discharge Elimination System
NR	Not Required
NOAEL	No Observed Adverse Effect Level
OP	Organophosphate
OPP	EPA Office of Pesticide Programs
OPPTS	EPA Office of Prevention, Pesticides and Toxic Substances
PAD	Population Adjusted Dose
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
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
RED	Reregistration Eligibility Decision
REI	Restricted Entry Interval
RfD	Reference Dose
RQ	Risk Quotient
SCI-GROW	Tier I Ground Water Computer Model
SAP	Science Advisory Panel
SF	Safety Factor
SLC	Single Layer Clothing
SLN	Special Local Need (Registrations Under Section 24©) of FIFRA)
TGAI	Technical Grade Active Ingredient
TRR	Total Radioactive Residue
USDA	United States Department of Agriculture
USGS	United States Geological Survey
UF	Uncertainty Factor
UF_{db}	Database Uncertainty Factor
UV	Ultraviolet
WPS	Worker Protection Standard

EXECUTIVE SUMMARY

EPA has completed its review of public comments on the revised metiram risk assessments and is issuing its risk management decision for metiram. There are currently two tolerances being reassessed for metiram. The revised risk assessments are based on review of the required target data base supporting the use patterns of currently registered products and additional information received. After considering the risks identified in the revised risk assessment, comments, and mitigation suggestions from interested parties, EPA developed its risk management decision for uses of metiram that pose risks of concern. As a result, the Agency has determined that metiram containing products are eligible for reregistration provided that data needs are addressed, risk mitigation measures are adopted, and labels are amended accordingly. The decision is discussed fully in this document.

Metiram was first registered in the United States in 1948 as a broad spectrum fungicide. Metiram is used on apples, potatoes, and ornamental plants (leatherleaf ferns) in nurseries and greenhouses. Metiram was previously registered for use on tobacco seedlings and roses, but these uses have since been voluntarily cancelled. There are no residential labels, and no agricultural uses that could result in exposure to metiram in residential settings. Approximately 900,000 pounds of metiram are used for about 125,000 acres treated on an annual basis. Metiram's largest markets in terms of total pounds of active ingredient (lbs ai) are allocated to apples (55%) and potatoes (45%).

Metiram is a member of the ethylene bisdithiocarbamate (EBDC) group of fungicides, which includes the related active ingredients mancozeb and maneb. This document summarizes risk estimates for both metiram and its metabolite and environmental degradate ethylene thiourea (ETU). Metiram and two other EBDC fungicides, maneb and mancozeb, are all metabolized to ETU in the body and all degrade to ETU in the environment. Therefore, EPA has considered the aggregate or combined risks from food, water and non-occupational exposure resulting from metiram alone, ETU resulting from metiram use, and ETU from all sources (i.e., the other EBDC fungicides: maneb and mancozeb). The aggregate risk from ETU from all sources must be considered to reassess the tolerances for metiram, maneb and mancozeb.

Overall Risk Summary

Metiram dietary risks from food and drinking water sources are low and not of concern. Since there are no registered residential uses of metiram, no residential risks were assessed. There are some risk concerns for some occupational handlers, which will be mitigated with additional personal protective equipment (PPE). In addition, some application restrictions are to be added to product labels in order to maintain a 24 hour restricted entry interval (REI). For ecological risks, metiram poses some chronic risk to birds and mammals, which will be reduced with various application reductions.

Dietary Risk

Acute, chronic, and cancer dietary (food only) risk from metiram, metiram-derived ETU, and ETU from all sources are low and below Agency's level of concern. The drinking water exposure assessment for metiram addresses concentrations of ETU only, since metiram is not expected to remain in drinking water long enough to reach a location that would supply water for human consumption, whether from surface or groundwater sources. Estimated concentrations of ETU, for both surface and ground water sources of drinking water, are low and not of concern.

Residential Risk

The Agency is not considering residential exposures from metiram, since there are no existing or proposed residential or other non-occupational sources of exposure, and metiram is not used in or around public buildings, schools or recreational areas where children or others might be exposed.

Aggregate Risk/ETU

Aggregate risk refers to the combined risk from food, drinking water, and residential (as a result of residential exposures to ETU from mancozeb uses) exposures. In addition, aggregate risk can result from one-time (acute), short-term and/or chronic (non-cancer and cancer) exposures, and considers exposures from metiram-derived ETU and ETU from all sources, depending upon the scenario assessed. Acute, short-term, and chronic (non-cancer) aggregate risks are low and not of concern. Aggregate cancer risk estimates are within a negligible risk range, and therefore no mitigation measures are needed.

For short-term aggregate risks, EPA's original analysis indicated risks above levels of concern for toddler exposure to transplanted turf for maneb and mancozeb. Recognizing that potential risk, the maneb and mancozeb registrants voluntarily agreed to reduce the maximum application rate and/or extend the time between treatment and harvesting of sod from one to three days (i.e., a 3 day PHI for transplanted turf). The reduced application rate and/or extended PHI, combined with the logistics of transplanting turf and installation restrictions, effectively reduced the potential contribution from this use pattern to a level not of concern to the Agency.

Occupational Risk

Workers can be exposed to metiram and metiram-derived ETU through mixing, loading, and/or applying (handlers) the pesticide to apples, potatoes (foliar and seed piece) and ornamentals (ferns), or re-entering treated sites. There are some risks of concern to handlers, in particular to mixer/loaders of dry flowable formulations for aerial/chemigation to apples and potatoes; airblast applicators; flaggers; and loaders of dust for potato seed treatment. To mitigate these risk concerns, additional personal protective equipment (PPE) are required on the product labels (i.e., PF5 respirator).

At the current restricted entry interval (REI) of 24 hours and use patterns on current labels, predicted metiram and ETU exposures exceed levels of concern for post-application high-end exposure scenarios for apples and leatherleaf ferns. For leatherleaf ferns, by requiring that use be restricted to a maximum of 1 application per week and 10 applications per year, the Agency has concluded that the existing 24 hour REI may be retained. For apples, high exposure activities (pruning, tying, and training) result in predicted exposures that exceed standard levels of concern (MOE of 54) at the current REI of 24 hours. However, based on information that indicates very low usage in western states where the short re-entry period is observed and the clear integrated pest management (IPM) and resistance management advantages from use of metiram, the Agency plans to maintain the current 24 hour REI for apples.

Ecological Risk

For terrestrial species, short-term or acute metiram risks are low to mammals, birds, and non-target insects. However, the screening-level ecological risk assessment for terrestrial species indicates some risk quotient (RQ) exceedance of the chronic levels of concern (LOCs), especially from metiram applications to apples and potatoes. Aquatic species (freshwater fish, freshwater invertebrates, and non-vascular plants) result in low acute risk. Currently, there is no data on estuarine/marine species and no toxicity data to assess aquatic chronic risk. The Agency is requiring additional acute and chronic toxicity data as part of this RED to address these data gaps. Therefore, to be more protective of these species that may be exposed on a chronic basis, the technical registrant has agreed to additional label changes to reduce potential risk, including reducing the maximum application rate to apples and the maximum number of applications to apples and potatoes.

Endangered Species

Based on available screening-level information, there is a potential concern for acute effects on listed birds and freshwater fish species, and chronic effects on listed birds and mammals should exposure actually occur. Even though metiram is only slightly acutely toxic to birds, RQs exceed the endangered species LOC (RQ range from 0.11 to 1.02) at maximum EEC levels. The Agency does not currently have data to quantify risks for metiram at the screening-level and can not preclude potential direct effects to the following taxonomic groups; listed non-target terrestrial plants, freshwater invertebrates, estuarine/marine fish, or vascular aquatic plants. These findings are based solely on EPA's screening-level assessment and do not constitute "may affect" findings under the Endangered Species Act (ESA) for any specific listed species. If the Agency determines use of metiram "may affect" listed species or their designated critical habitat, EPA will employ the provisions in the Services regulations (50 CFR Part 402).

Mitigation Summary

To address assessed risks of concern, the following mitigation measures will be implemented:

- Add a PF5 respirator to label PPE for some worker scenarios: mixer/loaders of dry flowables for aerial/chemigation applications; airblast applicators to apples; and flaggers,
- Add the use of engineering controls to labels for aerial applicators (enclosed cockpits),
- Reduce apple pre-bloom maximum application rate from 4.8 to 3.6 lbs ai/A,
- Reduce maximum number of applications for apples from 4 to 3 per year,
- Reduce maximum number of applications for potatoes from 7 to 6 per year,
- Limit the number of applications to leatherleaf ferns to 1 per week and 10 per year, and
- Metiram use on roses and dust and wettable powder formulations have been voluntarily cancelled prior to completion of the RED. Further, as a result of the voluntary cancellation of the dust formulation by the technical registrant and risks associated with this formulation, the end-use registrant has requested voluntary cancellation of their active potato seed treatment fungicide product registration (EPA Registration No. 2935-540).

Next Steps

Numerous opportunities for public comment were offered as this decision was being developed. Therefore, the Agency is issuing this RED document for metiram without a formal public comment period, as announced in a Notice of Availability published in the ***Federal Register***. However, the docket remains open, and any comments submitted in the future will be placed in this public docket and addressed by the Agency, as appropriate.

EPA will issue a generic DCI for additional data necessary to confirm the conclusions of this RED for the active ingredient metiram EPA will also issue a product-specific DCI for data necessary to complete product reregistration for products containing metiram.

I. INTRODUCTION

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 risks 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 or not 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 and the Federal Food Drug and Cosmetic Act (FFDCA) to require reassessment of all existing tolerances for pesticides in food. FQPA also requires EPA to review all tolerances in effect on August 3, 1996 by August 3, 2006. In reassessing these tolerances, the Agency must consider, among other things, aggregate risks from non-occupational sources of pesticide exposure, whether there is increased susceptibility to infants and children, and the cumulative effects of pesticides with a common mechanism of toxicity. When a safety finding has been made that aggregate risks are not of concern and the Agency concludes that there is a reasonable certainty of no harm from aggregate exposure, the tolerances are considered reassessed. EPA decided that, for those chemicals that have tolerances and are undergoing reregistration, tolerance reassessment will be accomplished through the reregistration process.

As mentioned above, FQPA requires EPA to consider "available information" concerning the cumulative effects of a particular pesticide's residues and "other substances that have a common mechanism of toxicity" when considering whether to establish, modify, or revoke a tolerance. Potential cumulative effects of chemicals with a common mechanism of toxicity are considered because low-level exposures to multiple chemicals causing a common toxic effect by a common mechanism could lead to the same adverse health effect as would a higher level of exposure to any one of these individual chemicals. Metiram belongs to a group of pesticides called dithiocarbamates, which also includes the ethylene bis-dithiocarbamate (EBDC) fungicides maneb and mancozeb. For the purposes of this reregistration eligibility decision (RED), EPA has concluded that metiram does not share a common mechanism of toxicity with other substances. The Agency reached this conclusion after a thorough internal review and external peer review of the data on a potential common mechanism of toxicity. For more information, please see the December 19, 2001 memorandum, "*The Determination of Whether Dithiocarbamate Pesticides Share a Common Mechanism of Toxicity*," which is available on the internet at http://www.epa.gov/oppsrrd1/cumulative/dithiocarb.pdf. However, the EBDCs share a common metabolite and degradate, ethylene thiourea (ETU), which is considered in this RED.

This document presents EPA's revised human health and ecological risk assessments, its progress toward tolerance reassessment, and the RED for metiram. The document consists of six sections. Section I contains the regulatory framework for reregistration/tolerance reassessment. Section II provides a profile of the use and usage of the chemical. Section III gives an overview of the revised human health and environmental effects risk assessments based on data, public comments, and other information received in response to the preliminary risk assessments. Section IV presents the Agency's reregistration eligibility and risk management decisions. Section V summarizes label changes necessary to implement the risk mitigation measures outlined in Section IV. Section VI contains the Appendices, which list related information, supporting documents, and studies evaluated for the reregistration decision. The preliminary and revised risk assessments for metiram are available in the Office of Pesticide Programs (OPP) Public Docket, under docket numbers OPP-2004-0078 and OPP-2005-0177, respectively, on the Agency's web page, http://www.epa.gov/edockets.

II. CHEMICAL OVERVIEW

A. Regulatory History

Metiram was first registered in the United States in 1948 for use on food and ornamental crops to prevent crop damage in the field and to protect harvested crops from deterioration in storage or transport. Metiram is a member of the ethylene bisdithiocarbamate (EBDC) group of fungicides, which includes the related active ingredients mancozeb and maneb. Moreover, it has been determined that the EBDCs share the common degradate ethylenethiourea (ETU). The EBDCs have been the subject of two Special Reviews. In 1977, the Agency initiated a Special Review and Continued Registration of Pesticide Products containing EBDCs based on evidence suggesting that the EBDCs and ETU, a contaminant, metabolite and degradation product of these pesticides, posed potential risks to human health and the environment. In 1982, the Agency concluded this Special Review by issuing a Final Determination (PD 4), which required risk reduction measures to prevent unreasonable adverse effects pending development and submission of additional data needed for improved risk assessment.

The Agency issued several comprehensive documents summarizing the reregistration status of metiram. The Metiram Registration Standard Document was issued on 9/8/86, an Addendum to the Registration Standard on 1/13/87, and an Update to the Metiram Registration Standard on 8/11/92. In 1987, EPA issued a second Notice of Initiation of Special Review of the EBDC pesticides because of health concerns caused by ETU, including potential carcinogenic, developmental and thyroid effects. Subsequent Data Call-Ins (DCIs) were issued in 1988 and 1995 which included standard and worker exposure data requests, respectively. The Special Review's Preliminary Determination (PD 2/3) was published on December 20, 1989 (54 FR 52158) and the Final Determination (PD 4) on March 2, 1992 (57 FR 7484). The Agency concluded that the dietary risks of EBDCs exceeded the benefits for the following food/feed uses for which one or more of the EBDC pesticides were registered: apricots, carrots, celery, collards, mustard greens, nectarines, peaches, rhubarb, spinach, succulent beans, and turnips. Accordingly, EPA canceled all metiram and other EBDC products registered for use on the

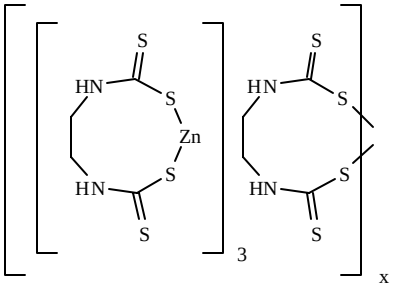
above-listed food/feed crops. Currently, the only food/feed uses of metiram eligible for continued registration are apples and potatoes, provided the label revisions are submitted.

The 1992 Special Review initially set the pre-harvest interval (PHI) for use on potatoes at fourteen (14) days for most states. The only exceptions to the 14 day PHI were Connecticut, Florida, Maine, Massachusetts, New Hampshire, New York, Pennsylvania, Vermont, and Wisconsin, where EPA determined that disease pressures caused by late blight justified a 3 day PHI. Subsequently, presented with evidence of late blight in additional states, EPA extended the 3 day PHI to Delaware, Michigan, Rhode Island and Ohio. Recently, EPA received requests for amendments to several EBDC product registrations and a petition to amend the 1992 cancellation order to allow for a three day PHI in all states, due to an alleged increase in the occurrence of late blight nationwide. EPA has not determined whether the petition warrants a hearing under 40 C.F.R. § 164 nor has it determined whether it will grant the attendant registration amendment requests. Although EPA has not reached any conclusions on the merits of the petition or the amendment requests, potential risks that would result from a nationwide reduction in the PHI for potatoes to 3 days have been considered in this RED. That consideration is for informational purposes only and cannot be interpreted as an indication of the Agency's position on the petition or amendment requests.

B. Chemical Identification

1. Metiram

Chemical Structure:



Common Name: A mixture of 5.2 parts by weight of ammoniates of {ethylenebis(dithiocarbamato)} zinc with 1 part by weight ethylenebis {dithiocarbamic acid} bimolecular and tri molecular cyclic anhydrosulfides and disulfides

Chemical Name: Metiram

Trade Name: Polygram

Chemical Family: Dithiocarbamate

Case Number: 0644

CAS Registry No.: 9006-42-2

OPP Chemical Code: 014601

Moleculer weight: $(1088.6)_x$

Empirical Formula: $(C_{16}H_{33}N_{11}S_{16}Zn_3)_x$

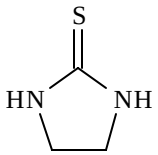
Basic Manufacturers: BASF Corporation

Metiram is a light yellow solid which decomposes at - 140 °C, and has a bulk density of 0.33-0.49 kg/L, an octanol/water partition coefficient of 1.76-2.48 at pH 7 and 21°C, and vapor pressure of <1 x 10^{-7} mbar at 20 °C. Metiram is practically insoluble in water (2 mg/L) and organic solvents, and decomposes under strong acid and alkaline conditions.

2. Ethylene thiourea (ETU)

Ethylenethiourea (ETU) is a metabolite, environmental degradate, and cooking byproduct of metiram and the other EBDC fungicides, maneb and mancozeb. Chemical information is provided for ETU because many of the risk concerns for metiram and the other EBDCs are driven by risk from ETU.

Chemical Structure:



Chemical Name: Ethylene thiourea

CAS Registry Number: 96-45-7

OPP Chemical Code: 600016

Molecular Weight: 102.2

Empirical Formula: $C_3H_6N_2S$

Technical ethylene thiourea (ETU) is a crystalline solid with a white to pale green color, and a faint amine odor. It has a melting point of 203-204˚C. ETU has an octanol/water partition coefficient of 0.22. ETU is considered soluble in water, with a water solubility of 20,000 ppm at 30˚C, but it is also slightly soluble in methanol, ethanol, ethylene glycol, pyridine, acetic acid and naphtha. When ETU is heated to decomposition, nitrogen and sulfur oxides are emitted.

C. Use Profile

The following is information on the currently registered uses including an overview of use sites and application methods. A detailed table of the uses of metiram eligible for reregistration is contained in Appendix A.

Type of Pesticide: Fungicide

Target organism(s): Downy mildews, anthracnose, rusts, leaf spots and blight.

Mode of action: Contact poison (non-systemic)

Use Sites:

- Food/Feed Uses: Metiram is registered for foliar applications to apples and potatoes. Although not currently registered, exposure from a proposed import use of metiram on grapes has been assessed. It has also been included in this RED document to assist the Agency in making a determination of whether to establish an import tolerance for metiram use on wine grapes. A determination regarding establishment of this import tolerance is outside the scope of this RED and will be made separately by the Agency.

- Non-Food & Residential Uses: Horticultural use is permitted on ornamental plants (leatherleaf ferns) in nurseries and greenhouses as a 24(c) registration in Florida only. Metiram was previously registered for use on tobacco seedlings and roses, but these uses have since been voluntarily cancelled. There are no residential labels, and no agricultural uses that could result in exposure to metiram in residential settings.

- Public Health Uses: None.

Use Classification: General Use.

Formulation Types: Metiram is formulated as 80 percent active ingredient dry flowable (water soluble granules). Metiram was previously formulated into wettable powders and dust, but these formulations have since been voluntarily cancelled.

Application Methods: Metiram application methods are aerial, groundboom, chemigation, high- and low-pressure handheld equipment, backpack sprayers, as well as seed and seed-piece treatment equipment. The application methods for seed and seed-piece treatment are commercial stationary equipment, on-farm stationary equipment, and tractor drawn planter boxes.

Application Rates: Metiram application rates vary depending on the crop. There are currently 4 active metiram labels and one FIFRA Section 24(c) Special Local Need (SLN) registration. The maximum rate per application is 1.6 pounds of active ingredient per acre (lbs ai/A) for potatoes and 4.8 lbs ai/A for apples. The allowable number of applications per season ranges from 4 for apples to 7 for potatoes, and the minimum application intervals range from 5 to 14 days. The application rate in horticulture is 1.6 lbs ai/A for leatherleaf ferns. Horticultural applications are allowed as much as twice weekly with no limit on the total number of applications per season. The application rate for potato seed-piece treatments is 0.105 lbs ai per 100 pounds of seed-pieces.

Application Timing: Metiram is applied at foliar, pre-bloom, and pre-bloom through foliar stages and also as a seed-piece treatment.

EBDCs Maximum Application Rates: As a result of Special Review, the Agency set usage limitations on the EBDC fungicides (mancozeb, maneb, and metiram) to establish consistency between the EBDCs registrations and Market Basket Survey data. The total poundage of all of the EBDCs used on each crop must not exceed the maximum seasonal application rate for any one of these fungicides. The maximum season rate for all of EBDCs used is the same for most of the crops regardless of which EBDC is used, with the exception of cucurbits (cucumbers, melons, and summer and winter squash), for which the maximum rate per season depends upon which EBDC is used. The current maximum seasonal application rates for the EBDCs, by crop, are summarized in Table 1.

Table 1. Maximum Label Application Rates for the EBDC Fungicides

Crop Group	Crop(s)	EBDC Used MZ = Mancozeb MN = Maneb MT = Metiram	Maximum Label Application Rates (lb ai/acre)	
			Per Application	Total EBDC Per Season
Field Crops	Barley, Oats, Rye, Triticale, Wheat	MZ	1.6	4.8
Field Crops	Beans, Dry	MN	1.6	9.6
Field Crops	Corn: hybrid seedcorn	MZ, MN	1.2	12
Field Crops	Corn: field	MZ	1.2	12
Field Crops	Cotton	MZ	1.6	6.4
Field Crops	Peanuts	MZ	1.6	12.8
Field Crops	Sugar Beets	MZ, MN	1.6	11.2
Fruits	Bananas	MZ, MN	2.4	24
Fruits	Cranberries	MZ, MN	4.8	14.4

Table 1. Maximum Label Application Rates for the EBDC Fungicides

Crop Group	Crop(s)	EBDC Used MZ = Mancozeb MN = Maneb MT = Metiram	Maximum Label Application Rates (lb ai/acre)	
			Per Application	Total EBDC Per Season
Fruits	Figs, Kodota	MN	2.4	2.4
Fruits	Grapes - West	MZ, MN	2	6
Fruits	Grapes- East	MZ, MN	3.2	19.2
Fruits	Papayas	MZ, MN	2	28
Fruits	Plantains	MZ	2.4	24
Miscellaneous	Christmas Trees, Douglas Fir	MZ	3.2	NA
Non-Food	Tobacco fields	MZ	1.5	6
Non-Food	Tobacco seedlings	MZ	2	No Max
Nut Crops	Almonds	MN	6.4	25.6
Ornamentals	Ornamentals, Pachysandra	MZ	13 -14	NA
Ornamentals	Ornamentals, Variety	MZ, MN	1.2 - 1.6	NA
Pome Fruits	Apples	MZ, MN, MT	2.4 or 4.8	16.8 or 19.2
Pome Fruits	Pears, Crabapples, Quince	MZ	2.4 or 4.8	16.8 or 19.2
Turf	Sod Farm	MZ, MN	16.3 - 19	NA
Turf	Golf Course, Athletic Fields	MZ	16.3 - 19	NA
Vegetables	Asparagus	MZ	1.6	6.4
Vegetables	Brassica	MN	1.6	9.6
Vegetables	Corn: sweet/pop/seed: East of Miss.	MZ, MN	1.2	18
Vegetables	Corn: sweet/ pop/seed: West of Miss.	MZ, MN	1.2	6
Vegetables	**Cucumbers**	**MZ, MN**	**MZ = 2.4 MN = 1.6**	**MZ = 19.2 MN = 12.8**
Vegetables	Fennel	MZ	1.6	12.8
Vegetables	Gourds: Edible	MZ	2.4	19.2
Vegetables	Lettuce	MN	1.6	6.4 (CA), 9.6 (US)
Vegetables	**Melons**	**MZ, MN**	**MZ = 2.4 MN = 1.6**	**MZ = 19.2 MN = 12.8**
Vegetables	Onions: Dry Bulb, Garlic	MZ, MN	2.4	24
Vegetables	Onions: Green	MN	2.4	11.2
Vegetables	Peppers	MN	1.6 (w), 2.4 (e)	9.6 (w), 14.4 (e)
Vegetables	Potatoes	MZ, MN, MT	1.6	11.2
Vegetables	Pumpkins	MN	1.6	12.8
Vegetables	Shallots	MZ, MN	2.4	24
Vegetables	**Squash (winter) Squash (summer)**	**MN MZ, MN**	**MZ = 2.4 MN = 1.6**	**MZ = 19.2 MN = 12.8**

Table 1. Maximum Label Application Rates for the EBDC Fungicides				
Crop Group	**Crop(s)**	**EBDC Used MZ = Mancozeb MN = Maneb MT = Metiram**	**Maximum Label Application Rates (lb ai/acre)**	
			Per Application	**Total EBDC Per Season**
Vegetables	Tomatoes	MZ, MN	2.4 (w), 1.6 (e)	6.4 (w), 16.8 (e)
Vegetables	Watermelons	MZ, MN	2.4	19.2
Note - Crops in bold have different rates depending upon which EBDC is used. Also, the not applicable (NA) reference is because the use was not a part of Special Review. (w) - West of the Mississippi (e) - East of the Mississippi				

D. Estimated Usage of Metiram

Table 2 below summarizes the best available estimates for the pesticide usage of metiram. Based on Agency data, approximately 900,000 pounds of metiram are used for about 125,000 acres treated on an annual basis. Metiram's largest markets in terms of total pounds of active ingredient (lbs ai) are allocated to apples (55%) and potatoes (45%). Agricultural uses are concentrated in (but not limited to) the following states: ID, MI, MN, NY, NC, SC, PA, and WA.

Table 2. Metiram Crop Usage Summary			
Crop	**Pounds of Active Ingredient (lbs a.i.)**	**% Crop Treated**	
		Average	**Maximum**
Apples	500,000	15	25
Potatoes	400,000	10	10

III. SUMMARY OF METIRAM RISK ASSESSMENTS

The following is a summary of EPA's human health and ecological effects risk findings and conclusions for the non-systemic fungicide metiram, as presented fully in the documents: *Metiram. Health Effects Division (HED) Human Health Risk Assessment to Support Reregistration*, dated June 13, 2005; *ETU from EBDCs: Health Effects Division (HED) Human Health Risk Assessment of the Common Metabolite/Degradate ETU to Support Reregistration*, dated June 8, 2005; and *Environmental Fate and Ecological Risk Assessment for Metiram, Section 3 Reregistration for Control of Fungal Diseases on Apples, Potatoes, Potato Seed, Certain Ornamental Plants and Tobacco Seedling Plants (Phase 3 Response)*, dated June 21, 2005; hereafter referred to as the Environmental Fate and Effects Risk Assessment.

The purpose of this section is to summarize the key features and findings of the risk assessments in order to help the reader better understand the conclusions reached in the assessments. Risks summarized in this RED document are those that result only from the use of metiram. While the risk assessments and related addenda are not included in this RED document, they are available from the Office of Pesticide Programs (OPP) Public Docket: OPP-2005-0177 and may also be accessed on the Agency's website at http://www.epa.gov/edockets. Hard copies of these documents may be found in the OPP public docket under this same docket number. The OPP public docket is located in Room 119, Crystal Mall II, 1801 South Bell Street, Arlington, VA, and is open Monday through Friday, excluding Federal holidays, from 8:30 a.m. to 4:00 p.m.

A. Human Health Risk Assessment

EPA released its preliminary risk assessments for metiram for public comment on November 24, 2004 for a 90 day public comment period (Phase 3 of the public participation process). The preliminary risk assessments may be found in the OPP public docket at the address given above and in EPA's electronic docket under docket number OPP-2004-0078. In response to comments received and new studies submitted during Phase 3, the risk assessments were updated and refined. The risk assessments were revised again in June 2005 to incorporate comments and additional studies submitted by the registrant. Revised risk assessments may be found in the OPP dockets under docket number OPP-2500-0177. Major revisions to the metiram human health risk assessment include the following:

- Deletion of the rose use as a result of the voluntary cancellation of the use.
- Selection of a new NOAEL (No Observed Adverse Effect Level) for short-term dermal exposures.
- New dietary results for a pending import tolerance for use on wine grapes are included; however, a tolerance has not yet been established and a determination of whether to establish a tolerance will be made by the Agency separately from this RED.

This document summarizes risk estimates for both metiram and its metabolite and environmental degradate ethylene thiourea (ETU). Metiram and two other EBDC fungicides, maneb and mancozeb, are all metabolized to ETU in the body and all degrade to ETU in the environment. Therefore, EPA has considered the aggregate or combined risks from food, water and non-occupational exposure resulting from metiram alone, ETU resulting from metiram use, and ETU from all sources (i.e., the other EBDC fungicides: maneb and mancozeb). The aggregate risk from ETU from all sources must be considered to reassess the tolerances for metiram, maneb and mancozeb, in accordance with FQPA.

1. Toxicity Assessment of Metiram

Toxicity assessments are designed to predict if a pesticide could cause adverse health effects in humans (including short-term or acute effects such as skin or eye damage, and lifetime or chronic effects such as cancer, development and reproduction deficiencies, etc.) and the level or dose

at which such effects might occur. The Agency has reviewed all toxicity studies submitted for metiram and has determined that the toxicological database is sufficient for reregistration.

For more details on the toxicity and carcinogenicity of metiram see the *Metiram: HED Toxicology Chapter for the Reregistration Eligibility Decision Document (RED)*, dated December 23, 1999 and the *Metiram-Revised Report of the Hazard Identification Assessment Review Committee*, dated April 2, 2003, which are available at http://www.epa.gov/edockets under docket number OPP-2004-0078.

a. Acute Toxicity Profile for Metiram

Metiram demonstrates low acute toxicity via the oral (Toxicity Category IV), dermal (Toxicity Category III) and inhalation (Toxicity Category IV) routes of exposure. Because metiram is not irritating to the eyes or the skin, it is in Toxicity Categories III and IV, respectively. However, metiram is a strong-to-severe skin sensitizer. The acute toxicity profile for metiram is summarized in Table 3.

Table 3. Acute Toxicity Profile for Metiram

Guideline No.	Study Type	MRID	Results	Toxicity Category
870.1100	Acute Oral	40497002 40497005	LD_{50} * = >5000 mg/kg	IV
870.1200	Acute Dermal	40497007 40497008	LD_{50} = >2000 mg/kg	III
870.1300	Acute Inhalation	40497010	LC_{50} * = 5.7 mg/L	IV
870.2400	Eye Irritation	40497012	not an eye irritant	III
870.2500	Skin Irritation	40497004	not a skin irritant	IV
870.2600	Dermal Sensitization	40497006	strong-to-severe dermal sensitizer	N/A

* LD_{50} or LC_{50} = Median Lethal Dose or Concentration. A statistically derived single dose or concentration that can be expected to cause death in 50% of the test animals when administered by the route indicated (oral, dermal, inhalation).

b. FQPA Safety Factor Considerations for Metiram

The Federal Food Drug and Cosmetic Act (FFDCA) as amended by the Food Quality Protection Act (FQPA) directs the Agency to use an additional tenfold (10X) safety factor to take into account potential pre- and post-natal toxicity and completeness of the data with respect to exposure and toxicity to infants and children. FFDCA authorizes the Agency to modify the tenfold safety factor only if reliable data demonstrate that the resulting level of exposure would be safe for infants and children.

Special FQPA Safety Factor. The Agency concluded that there is qualitative indication of increased sensitivity to infants and children based on the results of the rat developmental toxicity study in which pre- and post-implantation loss were observed at a dose level that produced less severe maternal toxicity [decreased body-weight gain]. An adequate developmental toxicity study in rabbits and an adequate 2-generation reproduction study in rats are not available with which to assess susceptibility. The Agency considered the degree of concern for susceptibility within the context of all available toxicity data, and concluded there is low concern for the observed qualitative susceptibility based on the following:

- The doses selected for overall risk assessment address concerns seen in the prenatal developmental toxicity study;
- The dose-response in the rat developmental study was well-characterized;
- There was a clear NOAEL/LOAEL (No/Lowest Observed Adverse Effect Level) for maternal and developmental toxicity; and
- The doses selected for the risk assessment also address concerns for thyroid toxicity.

Since there are no residual uncertainties for pre- and/or post-natal toxicity, the Special FQPA Safety Factor was removed (reduced to 1X) for metiram.

FQPA Database Uncertainty Factor. The Agency concluded there is a concern for developmental neurotoxicity following exposure to metiram. Evidence of neurotoxicity and neuropathology has been seen in rats following oral exposure to metiram in both subchronic and chronic studies. The metiram metabolite/degradate ETU has been shown to be a teratogen in rats, with effects seen in the central nervous system, urogenital and skeletal systems. In addition, neurotoxic effects have been observed in studies with another EBDC, maneb. Therefore, the Agency will be requiring a developmental neurotoxicity study (DNT) for metiram.

In addition to the required DNT study, the Agency noted data gaps for an acute neurotoxicity study, a developmental toxicity study in the rabbit, and a 2-generation reproduction study in the rat. The comparative thyroid assay has been waived for metiram. The requirement for the rabbit developmental toxicity study is reserved for metiram, contingent on the performance of a rabbit developmental toxicity on ETU because the developmental effects are expected to be attributable to ETU. However, a waiver is not granted for the 2-generation reproduction and acute neurotoxicity studies. The Agency determined that a 10X database uncertainty factor (FQPA UF_{DB}) is needed to account for the lack of these studies, since the available data provide no basis to support reduction or removal of the 10X UF_{DB}.

c. Toxicological Endpoints for Metiram

The toxicological endpoints used in the human health risk assessment for metiram are listed in Table 4. The safety factors used to account for interspecies extrapolation, intraspecies variability, the potential for special susceptibility to infants and children (FQPA 10X), and database uncertainties

related to FQPA Safety Factor considerations are also described in Table 4 below.

Table 4. Toxicological Endpoints for Metiram

Exposure Scenario	Dose, Uncertainty Factors (UFs), and Safety Factors (SFs)	Population Adjusted Dose (PAD) or Target Margin of Exposure (MOE)	Study and Toxicological Effects
Metiram Dietary Exposures			
Acute Dietary Females 13 - 50	NOAEL = 10 mg/kg/day UF = 100X (inter and intraspecies) FQPA SF = 1X FQPA UF = $10X_{database}$ Total UF = 1000X Acute RfD = 0.01 mg/kg/day	aPAD = $\frac{\text{Acute RfD}}{\text{FQPA SF}}$ aPAD = 0.01 mg/kg/day	Developmental Toxicity (Rabbit) LOAEL = 40 mg/kg/day, based on abortions.
Acute Dietary General Population	N/A	No appropriate endpoint attributable to a single exposure (dose) was identified.	
Chronic Dietary	NOAEL = 0.4 mg/kg/day UF = 100X (inter and intraspecies) FQPA SF = 1X FQPA UF = $10X_{database}$ Total UF = 1000X Chronic RfD=0.0004 mg/kg/day	cPAD = $\frac{\text{Chronic RfD}}{\text{FQPA SF}}$ cPAD = 0.0004 mg/kg/day	Subchronic Oral Toxicity (Rat, bridging study) LOAEL= 6.7 mg/kg/day based on decreased forelimb grip strength
Metiram Dermal Exposures			
Short-Term [1-30 days]	NOAEL = 6.7 mg/kg/day UF = 100X (inter and intraspecies) Total UF = 100X Dermal Absorption: 1%	Occupational MOE = 100	Subchronic Oral Toxicity (Rat, bridging study) LOAEL= 27.3 mg/kg/day based on decreased forelimb grip strength at early time point
Intermediate-Term, Long-Term [>30 days - 6 months, > 6 months]	NOAEL = 0.4 mg/kg/day UF = 100X (inter and intraspecies) Total UF = 100X Dermal Absorption: 1%	Occupational MOE = 100	Subchronic Oral Toxicity (Rat, bridging study) LOAEL= 6.7 mg/kg/day based on decreased forelimb grip strength
Metiram Inhalation Exposures			
Inhalation (Any Duration, i.e., 1 day to more than 180 days)	NOAEL = 0.5 mg/kg/day UF = 100X (inter and intraspecies) Total UF = 100X	Occupational MOE = 100	13-week Inhal. Toxicity, Rat LOAEL = 5.1 mg/kg/day based on lung lesions (alveolitis).

NOAEL- No Observable Adverse Effect Level, the highest dose at which no adverse health effect is observed.
LOAEL - Lowest Observable Adverse Effect Level, the lowest dose at which an adverse health effect is observed.
aPAD/cPAD - acute and chronic, respectively, population adjusted dose (PAD), a reference dose which has been adjusted to account for the FQPA safety factor.

2. Toxicity Assessment for ETU

As previously mentioned, some of the toxicity of the parent EBDCs is attributed to their common metabolite, ETU. The toxicology database for ETU contains a limited number of FIFRA guideline studies; therefore, the Agency has relied on a combination of literature studies and unpublished studies conducted according to the OPPTS testing guidelines. The thyroid is a target organ for ETU, and thyroid toxicity as a result of ETU exposure has been noted in subchronic and chronic rat, mouse, and dog studies. Overt liver toxicity was observed in one chronic dog study. Developmental defects in the rat developmental study included hydrocephaly and related lesions, skeletal system defects, and other gross defects. These defects showed increased susceptibility to fetuses because they occurred at a dose that only caused decreased maternal food consumption and body weight gain.

For more details on the toxicity and carcinogenicity of ETU see the *ETU- 3rd Report of the Hazard Identification Assessment Review Committee,* dated May 28, 2003, which is available on the internet and in the public docket.

a. Acute Toxicity Profile for ETU

ETU demonstrates low acute toxicity via dermal (Toxicity Category III) and inhalation (Toxicity Category IV) routes of exposure. Because ETU is not irritating to the eyes or the skin, it is classified as a Toxicity Category IV for both. However, acute oral and dermal sensitization studies with ETU were not available to determine acute toxicity. The acute toxicity profile for ETU is summarized below in Table 5.

Table 5. Acute Toxicity of ETU

Guideline No.	Study Type	MRID Nos.	Results	Toxicity Category
870.1100	Acute Oral - rat	None	N/A	N/A
870.1200	Acute Dermal - rabbit	458881-01	LD_{50} > 2000 mg/kg	III
870.1300	Acute Inhalation - rat	458881-02	LC_{50} > 10.4 mg/L	IV
870.2400	Primary Eye Irritation	458881-04	No irritation	IV
870.2500	Primary Skin Irritation	458881-03	No irritation	IV
870.2600	Dermal Sensitization	None	N/A	N/A

b. FQPA Safety Factor Considerations for ETU

Special FQPA Safety Factor. Since there is evidence of increased susceptibility of fetuses following exposure to ETU in the rat developmental studies, the Agency evaluated the level of concern for the effects observed when considered in the context of all available toxicity data. In addition, the Agency evaluated the database to determine if there were residual uncertainties after establishing

toxicity endpoints and traditional uncertainty factors to be used in the ETU risk assessment. The Agency determined that the degree of concern for the susceptibility seen in ETU developmental studies was low because:

- The teratogenic effects have been well-characterized in numerous studies in the published literature, as well as in a guideline study submitted by the registrant;
- There is a clear NOAEL for these effects and the dose-response relationship, although steep, is well characterized in the numerous developmental studies in rats;
- The developmental endpoint with the lowest NOAEL was selected for deriving the acute RfD; and
- The target organ toxicity (thyroid toxicity) was selected for deriving the chronic RfD as well as endpoints for non-dietary exposures (incidental oral, dermal, and inhalation).

Since the ETU doses selected for overall risk assessments will address the concern for developmental and thyroid toxicity, there are no residual uncertainties with regard to pre- and/or post-natal toxicity. The Agency concluded that the Special FQPA Safety Factor could be reduced to 1X for ETU.

FQPA Database Uncertainty Factor. The Agency concluded that a developmental neurotoxicity study for ETU is required, based on severe central nervous system defects observed in the developmental toxicity study in rats. In addition to the developmental neurotoxicity study, the following data gaps were identified:

- Developmental toxicity study in rabbits
- 2-Generation reproduction study in rats
- A study evaluating the comparative thyroid toxicity in adults and offspring

The Agency determined that a 10x database uncertainty factor (FQPA UF_{DB}) is needed to account for the lack of these studies since the available data provide no basis to support reduction or removal of the 10X UF_{DB}.

c. Toxicological Endpoints for ETU

The toxicological endpoints used in the human health risk assessment for ETU are listed in Table 6. The safety factors used to account for interspecies extrapolation, intraspecies variability, the potential for special susceptibility to infants and children (FQPA 10X), and database uncertainties related to FQPA safety factor considerations are also described in Table 6 below.

Table 6. ETU Toxicological Endpoints for Use in Human Health Risk Assessment			
Exposure Scenario	**Dose, Uncertainty Factors (UFs), and Safety Factors (SFs)**	**Population Adjusted Dose (PAD) or Target Margin of Exposure (MOE)**	**Study and Toxicological Effects**
ETU Dietary Exposures			
Acute Dietary Females 13 - 50	NOAEL = 5 mg/kg/day UF = 100X (inter and intraspecies) FQPA SF = 1X FQPA UF = $10X_{database}$ Total UF = 1000X Acute RfD = 0.005 mg/kg/day	aPAD = Acute RfD / FQPA SF aPAD = 0.005 mg/kg/day	Developmental Rat Toxicity (Khera Study, MRID 45937601) LOAEL = 10 mg/kg/day, based on developmental defects of brain.
Acute Dietary General Population	Not Applicable	No appropriate endpoint attributable to a single exposure (dose) was identified.	
Chronic Dietary	NOAEL = 0.18 mg/kg/day UF=100X (inter and intraspecies) FQPA SF = 1X FQPA UF = $10X_{database}$ Total UF = 1000X Chronic RfD=0.0002 mg/kg/day	cPAD = Chronic RfD / FQPA SF cPAD = 0.0002 mg/kg/day	Dog Chronic Oral Toxicity (MRID No. 42338101) LOAEL= 1.99 mg/kg/day based on thyroid toxicity
ETU Incidental Oral Exposures [Residential/Postapplication]			
Short-Term [1-30 days] Intermediate-Term [>30 days to 6 months]	NOAEL = 7 mg/kg/day UF = 100X (inter and intraspecies) FQPA UF = $10X_{database}$ FQPA SF = 1X	Residential MOE = 1000 Occupational MOE = N/A	4-week range-finding dog study LOAEL= 34 mg/kg/day based thyroid toxicity
ETU Dermal Exposures			
Short-Term [1-30 days] Females 13-49 Intermediate-Term [30 days - 6 months]	NOAEL = 5 mg/kg/day UF = 100X (inter and intraspecies) FQPA UF = $10X_{database}$ FQPA SF = 1X Dermal Absorption = 26%	Residential MOE = 1000 Occupational MOE = 100	Same as above for acute dietary exposures.
Long-Term [> 6 months]	NOAEL = 0.18 mg/kg/day UF = 100X (inter and intraspecies) FQPA UF = $10X_{database}$ FQPA SF = 1X Dermal Absorption = 26%	Residential MOE = 1000 Occupational MOE = 100	Same as above for chronic dietary exposures.
ETU Inhalation Exposures			

Table 6. ETU Toxicological Endpoints for Use in Human Health Risk Assessment			
Exposure Scenario	**Dose, Uncertainty Factors (UFs), and Safety Factors (SFs)**	**Population Adjusted Dose (PAD) or Target Margin of Exposure (MOE)**	**Study and Toxicological Effects**
Short-Term [1-30 days] Females 13-49 Intermediate-Term [30 days - 6 months]	NOAEL = 5 mg/kg/day UF = 100X (inter and intraspecies) FQPA UF = $10X_{database}$ FQPA SF = 1X Inhalation Absorption = 100%	Residential MOE = 1000 Occupational MOE = 100	Same as above for acute dietary exposures.
Long-Term [>6 months]	NOAEL = 0.18 mg/kg/day UF = 100X (inter and intraspecies) FQPA UF = $10X_{database}$ FQPA SF = 1X Inhalation Absorption = 100%	Residential MOE = 1000 Occupational MOE = 100	Same as above for chronic dietary exposures.
NOAEL- No Observable Adverse Effect Level, the highest dose at which no adverse health effect is observed. **LOAEL** - Lowest Observable Adverse Effect Level, the lowest dose at which an adverse health effect is observed. **aPAD/cPAD** - acute and chronic, respectively, population adjusted dose (PAD), a reference dose which has been adjusted to account for the FQPA safety factor.			

3. Metiram and ETU Carcinogenicity

In assessing the carcinogenicity of pesticides, the Agency first evaluates evidence that the pesticide is a carcinogen. If there is evidence, such as tumor formation and the pesticide is classified as a carcinogen, a quantitative assessment is conducted using either a Q_1* (non-threshold) or a Margin of Exposure (threshold) approach. The mechanism of the tumor formation determines whether or not a threshold or non-threshold assessment is conducted. Table 7 below provides a comparison of tumor data for ETU, mancozeb, maneb, and metiram.

Table 7. Tumor Incidence in EBDC/ETU Carcinogenicity Studies in Rats and Mice

Species	ETU	Mancozeb	Maneb	Metiram
Rats	Thyroid follicular cell adenomas and carcinomas at 83 & 250 ppm	Thyroid follicular cell adenomas and carcinomas at 750 ppm (HDT) [56 ppm ETU]	No increase in tumor of any type at 1000 ppm (HDT) [75 ppm ETU]	No increase in tumor of any type at 320 ppm (HDT) [24 ppm ETU]

Table 7. Tumor Incidence in EBDC/ETU Carcinogenicity Studies in Rats and Mice				
Species	**ETU**	**Mancozeb**	**Maneb**	**Metiram**
Mice	Thyroid follicular cell adenomas and carcinomas, pituitary adenomas, hepatocellular adenomas and carcinomas at 1000 ppm	No increase in tumor of any type at 1000 ppm (HDT) [75 ppm ETU]	Increase incidence of hepatocellular adenomas and alveogenic adenomas in the lungs at 2400 ppm [180 ppm ETU]	No increase in tumor of any type at 1000 ppm [75 ppm ETU]
HDT - Highest Dose Tested [Numbers in brackets represent ETU "dose" levels based on a 7.5% conversion of parent EBDC to ETU]				

Historically, it has been assumed that metiram's potential for carcinogenicity (as well as that of the other EBDCs, maneb and mancozeb) is due to the formation of the metabolite ETU, which is classified as a probable human carcinogen (B2), with a cancer potency factor (Q_1^*) of 0.0601 $(mg/kg/day)^{-1}$ for risk assessment. On this basis, metiram cancer risk has been calculated by estimating exposure to metiram-derived ETU (including that converted from metiram into ETU in the body) and using the ETU cancer potency factor to provide a quantitative estimate of risk. In a 1999 review, the Agency concluded that cancer risk for metiram and the other EBDCs should continue to be evaluated in this way.

4. Metiram and ETU Endocrine Effects

The available human health and ecological effects data for metiram suggest possible thyroid effects, which may indicate potential endocrine disruption. EPA has considered these effects in the human health risk assessment by selecting endpoints based on thyroid effects. To further address these effects, EPA is requiring a confirmatory comparative thyroid toxicity study for ETU. Data on ecological effects suggest possible hormonal effects to birds and mammals. These effects will be addressed when the Agency's Endocrine Disruptor Screening and Testing Advisory Committee develops appropriate screening and/or testing protocols. At that time, metiram may be subjected to additional screening and/or testing to better characterize effects related to endocrine disruption.

5. Dietary Risk from Food

a. Exposure Assumptions

EPA conducted acute, chronic, and cancer dietary (food) risk assessments for metiram and its metabolite ETU using the Dietary Exposure Evaluation Model software with the Food Commodity Intake Database (DEEM-FCID™, Version 1.3), which incorporates consumption data from USDA's Continuing Survey of Food Intakes by Individuals (CSFII), 1994-1996 and 1998. Because ETU is

both a metabolite and environmental degradate of maneb and the other two EBDC fungicides, it was considered in the dietary risk assessment. The Agency conducted a dietary risk assessment for ETU from all sources, because ETU can be derived from mancozeb, maneb, or metiram.

The acute and chronic dietary (food) risk analyses were conducted using anticipated residue values from field trial and market basket survey data. The 1989-1990 market basket survey for EBDCs and ETU was the largest of its kind with 6000 samples (300 samples for each of 10 crops and food forms). Processing factors, cooking factors, and estimated percent crop treated information were also incorporated into the dietary risk assessment. EPA derived anticipated residues for ETU from market basket survey data, ETU formed from metiram during processing, ETU formed by metiram and ETU from all sources.

b. Population Adjusted Dose

Dietary risk assessment incorporates both exposure and toxicity of a given pesticide. For acute and chronic dietary assessments, the risk is expressed as a percentage of a level of concern (i.e., the dose predicted to result in no unreasonable adverse health effects to any human sub-population, including sensitive members of such sub-populations). This level of concern is referred to as the Population Adjusted Dose (PAD). Dietary risk is characterized in terms of the PAD, which reflects the Reference Dose (RfD), either acute or chronic, that has been adjusted to account for the FQPA Safety Factor.

Estimated dietary (food) risks less than 100% of the Population Adjusted Dose (PAD), either acute (aPAD) or chronic (cPAD), are not of concern to the Agency. The aPAD is the dose at which a person could be exposed at any given day with no adverse health effects expected. The cPAD is the dose at which an individual could be exposed over the course of a lifetime with no adverse health effects expected.

1) Acute Dietary Risk from Food

As previously mentioned, the acute dietary (food) risk assessment was conducted using the DEEM-FCID™ computer model, anticipated residues, processing and cooking factors, and estimates of percent crop treated. A highly refined, probabilistic acute dietary assessment was conducted using a distribution of residue data for nonblended and partially blended commodities. Acute dietary risk values for metiram, metiram derived ETU, and ETU from all sources (that is, ETU resulting from the application of all three EBDC compounds, mancozeb, metiram, and maneb) are presented in Table 8. *(For the acute dietary endpoints see Table 4 for the metiram and Table 6 for the ETU)*

Table 8. Summary of Acute Dietary Exposure Analysis						
Population Subgroup	**Metiram[a]**		**Metiram-derived ETU[b]**		**ETU from All Sources[b]**	
	99.9th Percentile Exposure (mg/kg/day)	% aPAD	99.9th Percentile Exposure (mg/kg/day)	% aPAD	99.9th Percentile Exposure (mg/kg/day)	% aPAD
Females 13-49 years	**Apples, Potatoes**				0.002725[c]	55
	0.000786	7.9	0.000108	2.2		
	Apples, Potatoes, Import Wine Grapes (Proposed)					
	0.000874	8.7	0.002218	44		

[a] aPAD is 0.01 mg/kg/day [b] aPAD is 0.005 mg/kg/day [c] excluding grapes (metiram treated import proposal)

For metiram, the estimated acute dietary risk is below the Agency's level of concern. Dietary exposure comprises 7.9% (without exposure from imported wine grapes) and 8.7% (including potential exposure from imported wine grapes) of the aPAD for females 13-49 years old. Even with the proposed use on imported wine grapes, metiram acute dietary (food) risk estimates are below the Agency's level of concern. Note that a tolerance on imported wine grapes has not yet been established because the determination of establishing this import tolerance is outside the scope of this RED. The determination of whether to establish an import tolerance will be made separately by the Agency.

For metiram-derived ETU, the estimated acute dietary risk for ETU is below the Agency's level of concern when the existing uses and residues from the proposed import tolerance on grapes, based on field trial and processing studies are included in the assessment. Both metiram and ETU residues were detected in grapes harvested from the day of treatment (day 0) to 57 days after treatment. In processing studies with both red and white wine, ETU residues concentrate up to 14X, while metiram *per se* residues are reduced by as much as 0.025X. As a result, dietary exposure comprises 2.2% of the aPAD (without potential exposure from imported wine grapes) and 44% (including potential exposure from imported wine grapes) of the aPAD for females 13-49 years of age.

For ETU from all sources, the estimated acute dietary risk for total ETU is also below the Agency's level of concern. Dietary exposure comprises 55% (excluding proposed import wine grapes) of the aPAD for females 13-49 years old.

2) Chronic Dietary Risk from Food

Chronic (non-cancer) dietary risk from food is calculated by using the average consumption value for foods and average residue values on those foods over a 70-year lifetime. The chronic dietary (food) risk assessment was conducted using the DEEM-FCID™ computer model, anticipated residues, processing and cooking factors, and estimates of percent crop treated. The chronic assessment used deterministic methodology to provide point estimates of risk. Chronic dietary risk

values for metiram, metiram-derived ETU, and ETU from all sources are presented in Table 9. *(For the chronic dietary endpoints see Table 4 for the metiram and Table 6 for the ETU)*

Table 9. Summary of Chronic (Noncancer) Dietary Exposure Analysis

Population Subgroup	Metiram[a]*		Metiram-derived ETU[b]*		ETU from All Sources[b]	
	Exposure (mg/kg/day)	%cPAD	Exposure (mg/kg/day)	%cPAD	Exposure (mg/kg/day)	%cPAD
Children (1-2)	0.000025	6.2	0.000007	2.5	0.000108	54
Adults (50+)	0.000005	1.3	0.000010	5.0	0.000026	13

[a] cPAD is 0.0004 mg/kg/day [b] cPAD is 0.0002 mg/kg/day * Includes proposed imported wine grape exposure

For metiram, the estimated chronic dietary risk is below the Agency's level of concern. Dietary exposure from metiram comprises 6.2% of the cPAD for children 1-2 years old, the most highly exposed population subgroup.

For metiram-derived ETU, the estimated chronic dietary risk is below the Agency's level of concern. The dietary exposure from metiram-derived ETU comprises 5% of the cPAD for adults 50+ years old, the most highly exposed population subgroup.

For ETU from all sources, the estimated chronic dietary risk is also below the Agency's level of concern. The dietary exposure from ETU from all sources comprises 54% (excluding proposed import wine grapes) of the cPAD for children 1-2 years old, the most highly exposed population subgroup.

3) Cancer Dietary Risk from Food

Cancer dietary risk from food is calculated by using the average consumption values for food and average residue values for those foods over a 70-year lifetime. The chronic exposure value is multiplied by a linear low-dose, or Q_1*, based on animal studies, to determine the lifetime cancer risk estimate. For cancer dietary exposure, risk estimates within the range of an increased cancer risk of 1 x 10^{-6} (one in a million) are generally not of concern to the Agency.

As mentioned above, metiram's potential for carcinogenicity has been based on its metabolite ETU. The ETU cancer potency factor has been used for assessing cancer risk associated with metiram uses.

The Agency evaluated the carcinogenicity potential of ETU and classified ETU as a "probable human carcinogen" (group B2). Based upon female mouse liver tumors in a National Toxicology Program (NTP) study, the Q_1* for ETU, using a 3/4 scaling factor to account for body weight ratio from animal to human, was determined to be 6.01 x 10^{-2} mg/kg/day^{-1}. On this basis, metiram estimated cancer risk has been calculated by estimating exposure to metiram-derived ETU (including the

metabolic conversion of 0.075) and using the ETU cancer potency factor. Cancer dietary risk values are listed in Table 10.

The cancer risk for metiram-derived ETU is approximately 7.6 x 10^{-8} (based on existing uses on apples and potatoes) and 4 x 10^{-7} (based on existing uses and a proposed import wine grape exposure), which both are below the Agency's level of concern for cancer risk. The cancer risk for ETU from all sources is approximately 1.86 x 10^{-6}, which is within the negligible risk range of 10^{-6} and not considered to be of concern.

Table 10. Cancer Dietary Exposure and Risk Summary for Metiram-Derived ETU and ETU from All Sources

Population	Metiram-Derived ETU		ETU from All Sources	
	Chronic Dietary Exposure (mg/kg/day)	Cancer Risk Estimate	Chronic Dietary Exposure (mg/kg/day)	Cancer Risk Estimate
Existing Uses				
General U.S. Population	0.000005	7.6 x 10^{-8}	0.000031	1.86 x 10^{-6}
Existing and Proposed Uses				
General U.S. Population	0.000007	4.0 x 10^{-7}	Not estimated	

6. Dietary Exposure from Drinking Water

Drinking water exposure to pesticides can occur through surface and ground water contamination. EPA considers acute (one day) and chronic (lifetime) drinking water risks and uses either modeling and/or monitoring data, if the latter is available and of sufficient quality, to estimate those exposures. Risks from exposure to ETU in drinking water are further discussed in the section titled "Aggregate Exposure and Risk."

The Agency prepared a drinking water exposure assessment for ETU only. The parent EBDC fungicides were not assessed because they are very short-lived in soil and water, and are not expected to reach water used for human consumption, whether from surface water or groundwater sources. ETU, however, is highly water soluble, and moderately mobile, and may reach both surface and groundwater under some conditions. ETU has an aerobic soil half-life of about 3 days; in the absence of data, the aerobic aquatic metabolism half-life was assumed to be about 6 days, or double the soil half-life. The measured anaerobic aquatic metabolism half-life, however, is substantially longer (149 days), which may lead to the periodic detections in groundwater. The ETU estimated drinking water concentrations (EDWCs) were generated using data from both monitoring and modeling. Table 11 shows the EDWCs used to assess exposure to ETU in drinking water from surface water and groundwater.

Table 11. Estimated Drinking Water Concentrations (EDWCs) for ETU			
Drinking water source	**Duration**	**EDWC (ppb)**	**Data Source**
Surface Water	Acute (Peak)	25.2	Modeling
	Chronic/Cancer	0.1	Monitoring
Groundwater	All Durations	0.21	Monitoring

a. Surface Water

Monitoring data for ETU from a targeted surface water monitoring study conducted in several states by the ETU Task Force were available for use in the risk assessment. In the study, none of the tested surface water samples had concentrations above the limit of detection of 0.1 ppb. Therefore, the chronic/cancer EDWC was assigned the value of 0.1 ppb of ETU. The monitoring value of 0.1 ppb of ETU was also assigned to be the lower limit of the acute EDWC. In addition, the Agency decided that a higher limit for the acute EDWC value is necessary because monitoring samples were taken every 14 days during the application season in the monitoring study and peak values may have been missed with this sampling frequency. To obtain the higher limit value, the Agency performed PRZM/EXAMS simulation modeling for 22 crop scenarios, considering the use patterns for all of the EBDCs and choosing to model the highest application rate and lowest application intervals. Modeling results showed the highest one-in-ten year acute surface water EDWC to be 25.2 ppb based on application of EBDCs to peppers in Florida. Therefore, a range of acute EDWCs was established with a lower limit, based on monitoring, and an upper limit, based on the PRZM/EXAMS modeling described above. The established range of acute EDWC values for surface water, at the national level, is expected to be between the detection limit of 0.1 ppb (from monitoring) and the highest peak value 25.2 ppb (from modeling after adjustment by the 0.87 national percent crop area factor or PCA). In summary, the Agency used a combined approach to assess drinking water exposure using both targeted surface water monitoring and simulation modeling to bracket the expected acute concentrations of ETU in drinking water between 0.1 and 25.2 ppb. Chronic surface water values were set conservatively at 0.1 ppb, the detection limit for the monitoring data.

b. Groundwater

A groundwater EDWC was selected from a targeted monitoring study conducted in 2001 to 2003 for seven states chosen to represent the high historic EBDC use areas in the US. Based on the monitoring results, the highest measured value in a public drinking water well was 0.210 ppb in Lee County, Florida. Therefore, the groundwater EDWC is assigned the value of 0.21 ppb of ETU. In this study, ETU was not detected in any of the treated community drinking water sampled from the monitored 84 sites even when it was detected in the raw water. The absence of ETU in potable water from community water supplies may be related to its rapid degradation resulting from aeration and chemical treatment.

7. Residential Exposure and Risk

Metiram has no labeled residential uses. In addition, no residential post-application exposure to metiram is expected following its use in agricultural or other commercial settings. Therefore, a residential risk assessment for metiram (and for ETU derived from metiram uses) was not prepared. However, some residential exposure to ETU may occur from use of the other EBDCs. Therefore, these exposures have been considered in the ETU (from all sources) aggregate assessment, in accordance with FQPA.

8. Aggregate Risks from Food, Drinking Water and Residential Uses

The FQPA amendments to the Federal Food, Drug, and Cosmetic Act (FFDCA, Section 408(b)(2)(A)(ii)) require "that there is a reasonable certainty that no harm will result from aggregate exposure to the pesticide chemical residue," including all anticipated dietary exposures and other exposures for which there are reliable information. Aggregate exposure will typically include exposures from food, drinking water, residential uses of a pesticide, and other non-occupational sources of exposure.

In accordance with the FQPA, the Agency must consider and aggregate pesticide exposures and risks from three major sources or pathways: food, drinking water and, if applicable, residential or other non-occupational exposures. For aggregate risk, EPA typically combines exposures from food and residential sources and calculates a drinking water level of comparison (DWLOC), which represents the maximum allowable exposure through drinking water after considering food and residential exposures. If the EDWCs are less than the DWLOCs, EPA does not have concern for aggregate exposure. If EDWCs are greater than DWLOCs, EPA will conduct further analysis to characterize the potential for aggregate risk of concern.

Short-term residential and other non-occupational exposure assessment considers all potential pesticide exposure, other than exposure due to residues in food and/or in drinking water. Each route of exposure (oral, dermal, inhalation) is assessed, where appropriate, and risk is expressed as a Margin of Exposure (MOE), which is the ratio of estimated exposure to an appropriate NOAEL dose. A MOE greater than or equal to the target MOE is considered adequately protective and not a risk of concern.

Note that there is no potential for exposure to metiram or metiram-derived ETU in residential settings, so metiram aggregate exposure and risk assessments include only dietary food and drinking water sources of exposure, and are limited to chronic and acute durations. However, there is potential exposure to ETU from all sources as result of the residential exposures from uses of mancozeb, which are included in the short-term aggregate risk assessment.

Exposure to metiram *per se* in drinking water is not expected, and metiram is not registered for residential uses, so the only exposure and risk for metiram *per se* is food alone. Therefore, an aggregate risk assessment for metiram *per se* was not conducted. Acute and chronic dietary exposures

to metiram *per se* are not of concern to the Agency, as presented in the dietary food section above.

For ETU resulting from metiram use, the Agency assessed the following aggregate exposure scenarios:

- acute aggregate (food + water)
- chronic (non-cancer) aggregate (food + water)
- cancer aggregate (food + water)

For ETU from all sources, the Agency assessed the following aggregate exposure scenarios:

- acute aggregate (food + water)
- short-term aggregate (food + water + residential [as a result of the residential exposures from mancozeb uses])
- chronic (non-cancer) aggregate (food + water)
- cancer aggregate (food + water + residential [as a result of residential exposures from mancozeb uses])

a. Acute Aggregate

Potential exposure to metiram-derived ETU from both groundwater and surface water sources of drinking water, when combined with exposure through food, is below the Agency's level of concern. EDWCs are significantly less than the DWLOC, as shown in Table 12 below.

Table 12. Acute DWLOC Calculations for Metiram-derived ETU

Population Subgroup	Acute DWLOC (ug/L)	Surface Water EDWC (ppb)	Groundwater EDWC (ppb)
Existing Uses Only (Apples and Potatoes)			
Females 13 - 49	147	25.2	0.21
Existing and Proposed Uses (Apples, Potatoes, and Grapes)			
Females 13 - 49	83	25.2	0.21

Unlike for metiram-derived ETU, aggregate (food + drinking water) acute risk to ETU from all sources was calculated using a more refined assessment on a semi-probabilistic basis using the full range of food residue data and the acute EDWC estimate of 25.2 ppb for the drinking water concentration. The acute aggregate risk of 87% of the aPAD at the 99.9th percentile for ETU from all sources is less than 100% of the aPAD and also below the Agency's level of concern.

b. Short-Term Aggregate

Short-term aggregate (food + drinking water + residential [as a result of residential exposures from mancozeb uses]) risk for ETU from all sources is below the Agency's level of concern for residential handlers, and children and adults exposed to ETU from re-entry activities. Short-term aggregate risks were calculated for adults by aggregating chronic food exposure, chronic drinking water exposure and golfing or gardening exposures. Short-term aggregate MOEs are significantly greater than the target MOE of 1000 (see Table 13).

EPA's original ETU analysis indicated risks above levels of concern for toddler exposure to transplanted turf treated with maneb and mancozeb. Recognizing that potential risk, the maneb and mancozeb registrants agreed to reduce the maximum application rate and/or extend the time between treatment and harvesting of sod from one to three days (i.e., 3 day pre-harvest interval [PHI]). Additionally, given the typical one to three day installation window following harvesting, the minimum time that would elapse between treatment and installation of sod in a residential setting would be within the range of four to six days. Further, the frequent and long duration of watering of newly installed sod and the need to restrict foot traffic for several weeks after planting should also minimize children's exposure to residues on transplanted turf. The reduced application rate and/or extended PHI, combined with the logistics of transplanting turf and installation restrictions, effectively reduced the potential contribution from this use pattern to a level not of concern to the Agency.

Table 13. Short-Term Aggregate Post-Application Risk Estimates for ETU from All Sources.

Exposure Scenario	Short-Term MOEs
Golfing	6200
Home Garden Handler (Handwand)	62000
Home Garden Post-Application	14450

c. Chronic (Non-Cancer) Aggregate

Chronic aggregate (food + drinking water) risk to metiram-derived ETU is below the Agency's level of concern. The aggregate chronic risk to metiram-derived ETU was calculated using food and drinking water only, because metiram does not have residential uses. The chronic aggregate risk estimate of 7.0% (groundwater) and 6.0% (surface water) of the cPAD (with wine grapes) for the most highly exposed population subgroup, adults 50+ years, is less than 100% of the cPAD.

Aggregate (food + drinking water) chronic risk to ETU from all sources is also below the Agency's level of concern. The aggregate chronic risks were calculated using food and drinking water exposure only, because golfing, athletic field and toddler transplanted turf exposure scenarios were considered to occur only on a short-term basis. The chronic aggregate risk estimate of 56% (surface water) and 58% (groundwater) of the cPAD for the most highly exposed population subgroup, children 1 to 2 years old, is less than 100% of the cPAD. Note that the ETU chronic exposure estimate from all sources does not include potential exposure from imported wine grapes.

d. Cancer Aggregate

Cancer aggregate (food + drinking water) risk to metiram-derived ETU for the general U.S. population is below the Agency's level of concern. Aggregate cancer risk estimates of 3×10^{-7} (groundwater) and 2×10^{-7} (surface water) are considered to be negligible.

If the proposed import tolerance on wine grapes is included, aggregate cancer risks for metiram-derived ETU are also below the Agency's level of concern; for groundwater the aggregate cancer risk is 7×10^{-7} and for surface water the aggregate cancer risk is 5×10^{-7}.

Aggregate cancer risk estimates for exposure to ETU from all sources are in the range of 2×10^{-6}, and food is the largest contributor. The Agency considers cancer risks as high as 3 in 1 million to be within the negligible risk range. The aggregate cancer risk estimates are within this range of risk, and therefore are considered negligible. The cancer risks were aggregated using the food and drinking water exposure estimates for the general population and the food, water and recreational doses for golfers, home gardeners and athletes. Note that the residential contribution to this risk estimate is a result of the application of mancozeb. Metiram does not have residential uses.

9. Occupational Risks

Workers can be exposed to metiram and metiram-derived ETU through mixing, loading, and/or applying the pesticide to apples, potatoes (foliar and seed piece) and ornamentals (ferns), or re-entering treated sites. Note that rose and tobacco uses have been voluntarily cancelled as a result of risk concerns, and are no longer included in the risk assessment. Occupational non-cancer risk to workers is measured by a Margin of Exposure (MOE), which determines how close the occupational exposure comes to a NOAEL. However, the occupational assessment does not consider an FQPA SF for sensitive populations (infants or children), nor is it affected by the FQPA database uncertainty factor being applied to dietary exposures for metiram. Thus, the target MOE for occupational risk is 100, and MOEs greater than 100 do not exceed the Agency's level of concern. For occupational cancer risks, as for dietary cancer risk and as described above in Section III.A.5., risk estimates within the range of an increased cancer risk of 1×10^{-6} (one in a million) generally do not exceed the Agency's level of concern. When occupational MOE are less than 100 or occupational cancer risks exceed the range of an increased risk of 1×10^{-6}, EPA strives to reduce worker cancer risks through the use of personal protective equipment and engineering controls or other mitigation measures. The Agency generally considers occupational cancer risks within the range of an increased cancer risk of 1×10^{-6} or less to be negligible, but will consider risks as high as 1×10^{-4} (1 in 10,000 persons) when all mitigation measures that are feasible have been applied, and when evaluating the advantages associated with the use of the pesticide. The cancer risks for application of metiram to agricultural crops are as a result of exposure to ETU, and calculated by estimating 30 days of exposure per year.

References to ETU in the occupational risk section of this document refer to metiram-derived ETU from three sources, ETU formed in tank mixes, ETU formed in the body by metabolic conversion,

and ETU formed in the environment through degradation. For both handler and post-application assessments, the metiram dose considered ETU from metabolic conversion of metiram to ETU and from metiram converted to ETU in tank mixes. Handler assessments addressed combined dermal and inhalation exposures, but post-application risks were derived solely from dermal exposure.

Occupational risk is assessed based on exposures at the time of application (termed "handler" exposure) and following application, or post-application exposure. Application parameters are generally defined by the physical nature of the formulation (e.g., formula and packaging), by the equipment required to deliver the chemical to the use site, and by the application rate required to achieve an efficacious dose. Post-application risk is assessed for activities such as scouting, irrigating, pruning, and harvesting and is based primarily on dermal exposure estimates. Note that occupational risk estimates are intended to represent pesticide workers, and on this basis assumptions are made concerning acres treated per day and the seasonal duration of exposure.

For more information on the assumptions and calculations of potential risks to workers handling metiram or working in metiram treated areas, see the *Metiram: Occupational and Residential Exposure Assessment and Recommendations for the Reregistration Eligibility Decision Document* dated June 8, 2005, which is available in the public docket OPP-2005-0177.

a. Occupational Handler Exposure

For handlers, most exposures were considered to be short-term (1-30 days) or intermediate-term (1-6 months) in duration, with the exception of greenhouse uses, which may result in chronic (>180 days) exposure. For handler assessments that consider exposure to ETU, non-cancer short-term and intermediate-term risks were the same, but chronic risks were assessed using a different toxicological dose and endpoint. For the metiram handler assessments, metiram dermal and inhalation exposures could not be combined, since the endpoints (toxic effects) selected for risk assessment were different. For non-cancer assessments that consider ETU, dermal and inhalation exposures were combined because the endpoints selected as the basis for risk (thyroid effects) assessment were similar.

No chemical-specific handler exposure studies were submitted in support of the reregistration of metiram, so Pesticide Handler Exposure Database (PHED, Version 1.1, 1998) data were used to calculate unit exposure values to estimate occupational handler exposures to metiram and ETU during application to crops and ornamentals. There are no recent or adequate data (either chemical-specific or in PHED) that reflect the specifics of the potato seed-piece treatment scenario; therefore, PHED data for other scenarios were extrapolated to approximate seed-piece treatment. Moreover, standard assumptions were used for the number of acres treated, body weight, hours worked, etc. for most handler scenarios. For the potato seed-piece use, assumptions were based on conversations with experts in the potato industry.

Occupational handler assessments are conducted using increasing levels of protection. The Agency typically evaluates all exposures with minimal protection and then considers additional

protective measures using a tiered approach (going from minimal to maximum levels of protection) in an attempt to assess reduction in exposure achieved by each protective measure. The lowest tier is represented by the baseline clothing scenario (i.e., single layer clothing, socks, and shoes), followed by, if MOEs are of concern, increasing levels of risk mitigation, such as personal protective equipment (PPE) and engineering controls (EC). End-use product PPE will be assessed on a product-by-product basis. Metiram labels currently require double layer PPE and a chemical resistant apron for mixing/loading and double layer PPE without the apron for application. The labels do not require respiratory protection.

1) Agricultural and Greenhouse Handler Risks

To assess occupational agricultural and greenhouse handler risks, the Agency conducted the following risk assessments:

- Metiram - (Non-cancer)
  - Short-term dermal (MOEs)
  - Intermediate-term dermal (MOEs)
  - Inhalation (combined short and intermediate-term MOEs)
- ETU - (Non-cancer - combined dermal and inhalation MOEs)
- ETU - (Cancer)

Metiram short-term dermal and ETU non-cancer (combined dermal and inhalation) MOEs are greater than the target MOE of 100 for all scenarios at baseline protection, and are not of risk concern. Therefore, to simplify this occupational risk summary, only metiram intermediate-term dermal MOEs, metiram inhalation (combined short and intermediate-term) MOEs, and ETU cancer risk estimates are tabulated in this section. Dermal and inhalation metiram risks for occupational agricultural and greenhouse handlers are summarized in Tables 14 and 15, respectively. ETU cancer risks for agricultural and greenhouse use are summarized in Table 16.

Table 14. Summary of Metiram Intermediate Term Dermal MOEs for Agricultural Crops

Exposure Scenario	Crop Type	Application Rate (lb ai/acre)	Acres Treated per Day	Dermal MOES			
				Base-line PPE	Single Layer PPE	Double Layer PPE	Eng Cont
Mixer/Loader							
Mix/Load DF for Aerial Application or Chemigation	apples (pre-bloom) potatoes leatherleaf ferns	4.8 1.6 1.6	350 350 40	**25** **76** 660	**25** **76** 660	**35** 106 930	No Data No Data No Data
Mix/Load DF for Groundboom	potatoes leatherleaf ferns	1.6 1.6	80 40	330 660	331 660	465 930	No Data No Data

Table 14. Summary of Metiram Intermediate Term Dermal MOEs for Agricultural Crops

Exposure Scenario	Crop Type	Application Rate (lb ai/acre)	Acres Treated per Day	Dermal MOES			
				Base-line PPE	Single Layer PPE	Double Layer PPE	Eng Cont
Mix/Load DF for Airblast	apples (pre-bloom)	4.8	40	220	220	310	No Data
Mix/Load DF for HP Handwand	ferns	1.6	10	>1000	>1000	>1000	No Data
Applicator							
Aerial Application	apples (pre-bloom) potatoes	4.8 1.6	350 350	Not Applicable			330 1000
Groundboom Application	potatoes, ferns	1.6	40 to 80	>1000	>1000	>1000	>1000
Airblast Application	apples (pre-bloom)	4.8	40	**41**	100	120	770
HP Handwand Application	ferns	1.6	10	≥140	≥450	≥600	No Data
Mixer/Loader/Applicator							
Mix/Load/Apply DF with LP Handwand	ferns	1.6	0.4	ND	>500	>700	NA
Mix/Load/Apply DF with Backpack Sprayer	ferns	1.6	0.4	No Data			
Flagger							
Flag Aerial Applications (8)	apples (pre-bloom) potatoes	4.8 1.6	350 350	150 460	140 420	150 450	7600 23000

Note - The target MOE is 100. MOEs less than 100 are of concern and are shown in bold font.
MOE = Margin of Exposure = NOAEL/estimated exposure. The target MOE for metiram and ETU is 100.
PPE = Personal Protective Equipment: The various levels of PPE are defined as follows:

Baseline = long-sleeved shirt, long pants, shoes, socks, and no gloves.
Single Layer = Baseline + gloves.
Double Layer = Single Layer + Coveralls.
Eng. Controls = Enclosed cockpit or cab, water soluble packaging, closed loading systems. Eng. Controls are not applicable to hand-held application methods.

Table 15. Summary of Metiram Inhalation MOEs for Agricultural Crops

Exposure Scenario	Crop	Application Rate (lb a.i. per acre)	Acres Treated per Day	Inhalation MOEs			
				Baseline (No Resp)	PF5 Respirator	PF10 Respirator	Eng Control
Mixer/Loader							

Table 15. Summary of Metiram Inhalation MOEs for Agricultural Crops

Exposure Scenario	Crop	Application Rate (lb a.i. per acre)	Acres Treated per Day	Inhalation MOEs			
				Baseline (No Resp)	PF5 Respirator	PF10 Respirator	Eng Control
Mix/Load DF for Aerial Application or Chemigation	apples potatoes ferns	4.8 1.6 1.6	350 350 40	**27** **81** 710	140 420 3600	270 810 7100	No Data No Data No Data
Mix/Load DF for Groundboom	potatoes ferns	1.6 1.6	80 40	360 710	>1000 >1000	>1000 >1000	No Data No Data
Mix/Load DF for Airblast	apples	4.8	40	240	>1000	>1000	No Data
Mix/Load DF for HP Handwand	ferns	1.6	10	>1000	>1000	>1000	No Data
Applicator							
Aerial Application	apples potatoes	4.8 1.6	350 350	Not Applicable			310 920
Groundboom Application	potatoes ferns	1.6 1.6	80 40	370 >1000	>1000 >1000	>1000 >1000	>1000 >1000
Airblast Application	apples	4.8	40	**41**	200	400	400
HP Handwand Application	ferns	1.6	10	>500	>1000	>1000	No Data
Mixer/Loader/Applicator (M/L/A)							
M/L/A DF with Low Pressure Handwand	ferns	1.6	0.4	**50**	250	500	NA
M/L/A DF with Backpack Sprayer	ferns	1.6	0.4	No Data			
Flagger							
Flag Aerial Applications	apples potatoes	4.8 1.6	350 350	**60** 180	300 890	600 1800	3000 8900

Note - The target MOE is 100. MOEs less than 100 are of concern and are shown in bold font.
MOE = Margin of Exposure = NOAEL/estimated exposure. The target MOE for metiram and ETU is 100.
PPE = Personal Protective Equipment: The various levels of PPE are defined as follows:
Baseline = long-sleeved shirt, long pants, shoes, socks, and no gloves or respiratory protection.
PF5 = Respirator with 80% protection (dust/mist).
PF10 = Respirator with 90% protection (half face with dust/mist filters).

Metiram Dermal and Inhalation Risks: All of the short-term dermal MOEs for metiram are greater than 100 and, therefore, the risks are not of concern and not presented in detail in this section. The intermediate-term dermal MOEs for metiram are of concern with label required PPE for only one scenario; mixing/loading for aerial application (Table 14). However, Agency information indicates that the aerial application method is used on apples less than 5% of the time; thus, it is unlikely that intermediate-term exposures occur. The inhalation MOEs for metiram are of concern with baseline PPE for two mixer/loader scenarios, one application scenario, one mixer/loader/applicator scenario, and one flagger scenario (Table 15). These risks can be managed in all cases by the addition of PF5 respiratory protection (dust/mist respirator). Also, the risks for mixing/loading/applying dry flowable formulations with a low pressure hand-wand are based upon wettable powder data and are considered to be an overestimate.

ETU Non-Cancer Risks: The short/intermediate-term MOEs are all 1000 or greater for all of the scenarios at all levels of PPE, which is well above the target MOE of 100. The chronic MOEs for ETU are 260 or greater for all scenarios, which is also greater than the target MOE and not of risk concern. Because these risks are not of concern, they are not tabulated in this section.

Table 16. Summary of ETU Cancer Risks for Crop Treatment (30 Days per Year)

Exposure Scenario	Crop	Application Rate (lb ai/acre)	Acres Treated per Day	Single Layer	Double Layer	Single Layer PF5	Single Layer PF10	Double Layer PF10	Eng Control
Mixer/Loader									
Mix/Load DF for Aerial	apples potatoes	2.2 1.5	350 350	3e-06 2e-06	3e-06 2e-06	2e-06 1e-06	2e-06 1e-06	1e-06 1e-06	ND ND
Mix/Load DF for Chemigation	potatoes ferns	1.5 1.3	350 40	2e-06 3e-07	2e-06 2e-07	1e-06 2e-07	1e-06 2e-07	1e-06 1e-07	ND ND
Mix/Load DF for Groundboom	potatoes ferns	1.5 1.3	80 40	5e-07 3e-07	5e-07 2e-07	3e-07 2e-07	3e-07 2e-07	2e-07 1e-07	ND ND
Mix/Load DF for Airblast	apples	2.2	40	4e-07	3e-07	3e-07	2e-06	2e-07	ND
Mix/Load DF for HP Handwand	ferns	1.3	10	7e-08	6e-08	4e-08	4e-08	3e-08	ND
Applicator									
Aerial Application	apples potatoes	2.2 1.5	350 350	N/A					3e-07 2e-07
Groundboom Application	potatoes ferns	1.5 1.3	80 40	3e-07 1e-07	3e-07 1e-07	1e-07 5e-08	8e-08 4e-08	7e-08 3e-08	4e-08 2e-08
Airblast Application	apples	2.2	40	2e-06	1e-06	7e-07	6e-07	5e-07	2e-07

HP Handwand Application	ferns	1.3	10	4e-07	3e-07	3e-07	2e-07	2e-07	NA
Mixer/Loader/Applicator (M/L/A)									
M/L/A DF with Backpack Sprayer	ferns	1.3	0.4	No Data					
M/L/A DF with LP Handwand	ferns	1.3	0.4	2e-06	2e-06	5e-07	3e-07	3e-07	NA
Flagger									
Flag Aerial Spray Applications	apples potatoes	2.2 1.5	350 350	1e-06 7e-07	1e-06 7e-07	5e-07 3e-07	4e-07 3e-07	3e-07 2e-07	2e-08 1e-08
Note - None of the cancer risks are greater than $1.0x10^{-4}$ at any level of PPE.									

ETU Cancer Risks: All of the ETU cancer risk estimates are within the range of an increased cancer risk of 1×10^{-6} (i.e., negligible) with single layer PPE. The ETU cancer risks are summarized in Table 16 above.

2) Handler Risk for Potato Seed-Piece Treatment

To assess occupational handler potato seed-piece treatment risks, the Agency conducted the following risk assessments:

- Metiram - (Non-cancer)
  - Short-term dermal (MOEs)
  - Intermediate-term dermal (MOEs)
  - Inhalation (combined short and intermediate-term MOEs)
- ETU - (Non-cancer - combine dermal and inhalation MOEs)
- ETU - (Cancer)

Table 17. Metiram Intermediate Term Dermal MOEs for Seed Piece Treatment						
Exposure Scenario	**Treatment Rate**	**Amount Treated per day**	**Dermal MOEs**			
			Baseline PPE	**Single Layer PPE**	**Double Layer PPE**	**Eng Control**
Load Dusts for Commercial Seed Piece Treatment (1)	0.105 lb a.i./cwt	10000 cwt	**1**	**16**	**21**	270
Load Dusts for On-Farm Seed Piece Treatment (2)		800 cwt	**9**	200	260	>1000
Apply Dusts During Commercial Seed Piece Treatment (3)	0.105 lb a.i./cwt	10000 cwt	No Data			
Apply Dusts During On-Farm Seed Piece Treatment (4)		800 cwt				
Load Treated Seed Pieces for Planting (5)	2.1 lb a.i./acre	40 acres	>1000	>1000	>1000	No Data
Plant Treated Seed Pieces (6)			>1000	>1000	>1000	>1000

Table 18. Metiram Inhalation MOEs for Seed Piece Treatment						
Exposure Scenario	**Treatment Rate**	**Amount Treated per Day**	**Inhalation MOEs**			
			Baseline (No Resp)	**PF5 Respirator**	**PF10 Respirator**	**Eng Control**
Load Dusts for Commercial Seed Piece Treatment (1)	0.105 lb a.i./cwt	10000 cwt	**1**	**4**	**8**	140
Load Dusts for On-Farm Seed Piece Treatment (2)		800 cwt	**10**	**48**	97	1700
Apply Dusts During Commercial Seed Piece Treatment (3)	0.105 lb a.i./cwt	10000 cwt	No Data			
Apply Dusts During On-Farm Seed Piece Treatment (4)		800 cwt	No Data			
Load Treated Seed Pieces for Planting (5)	2.1 lb a.i./acre	40 acres	240	1200	2400	No Data
Plant Treated Seed Pieces (6)			350	1700	3500	1900

Metiram Non-Cancer Risks: All of the metiram short-term dermal exposures exceed the target MOE with single layer PPE (the current product labels require double layer PPE) and are greater than the corresponding intermediate-term dermal MOEs, and therefore are not tabulated in this section. Intermediate-term dermal (see Table 17) and inhalation (see Table 18) risks of concern are indicated for handlers loading dusts for commercial seed-piece treatment, and would require engineering controls to achieve the target MOE of 100.

ETU Non-Cancer Risks: The ETU short/intermediate-term dermal and inhalation MOEs for seed piece treatment are greater than the corresponding MOEs for metiram, and are above 100 for all of the scenarios if single layer PPE with a PF5 respirator is worn. As such, these risk estimates are not tabulated in this section. Also, chronic risks were not calculated for the seed piece treatment scenarios, because the treatment of potato seed-pieces only occurs for several weeks per year during the potato planting season.

Table 19. Cancer Risks for Metiram Seed Piece Treatment (30 Exposure Days per Year)

Exposure Scenario	Application Rate	Area Treated per day	Single Layer	Double Layer	Single Layer PF5	Double Layer PF10	Eng Control
Mixer/Loader							
Load Dusts for Commercial Seed Piece Treatment	0.105 lb a.i./cwt	10000 cwt	**1.3e-04**	**1.3e-04**	3e-05	5e-06	1e-06
Load Dusts for On-Farm Seed Piece Treatment		800 cwt	1e-05	1e-05	2e-06	4e-07	8e-08
Applicator							
Apply Dusts During Commercial or On-Farm Seed Piece Treatment	0.105 lb a.i./cwt	800 to 10000 cwt	no data are available				
Secondary Handler							
Load Treated Seed Pieces	2.1 lb a.i.	40 acres	4e-07	4e-07	1e-07	5e-08	No Data
Plant Treated Seed Pieces			3e-07	3e-07	8e-08	1e-08	6e-08

Cancer risks that exceed 1.0e-04 are shown in bold font.

ETU Cancer Risks: The cancer risks for loading dusts for commercial seed-piece treatment exceed 1 x 10^{-4} with label required PPE (i.e. double layer). Engineering controls would be needed for this scenario to achieve a cancer risk within the range of 1 x 10^{-6}. The risks of handling the treated seed pieces is less than 1 x 10^{-6} with baseline PPE (Table 19).

b. Post-Application Assessments

The post-application occupational risk assessment considers exposure to chemical metiram and metiram-derived ETU from entering treated fields, orchards, and greenhouses. Given the nature of activities in these locations and that metiram is applied at various times during plant growth, contact with treated surfaces is likely. A variety of post-application exposure scenarios were identified by the type of activity involved and by the range of exposure expected, i.e., low, medium and high exposure activities. Examples of low exposure activities include irrigation and scouting; medium exposure activities may involve scouting of mature plants, or in greenhouses, hand pinching certain plants. Potential high exposure activities include hand harvesting leatherleaf ferns, and thinning and pruning

apples. In the Worker Protection Standard, a Restricted-Entry Interval (REI) is defined as the duration of time which must elapse before residues decline to a level so entry into a previously treated area and engaging in any task or activity would not result in exposures which are of concern.

Occupational Post-Application Exposures and Assumptions

One chemical-specific dislodgeable foliar residue (DFR) study was submitted for metiram, and was used, along with transfer coefficients selected from the Agricultural Re-entry Task Force (ARTF) data, to estimate post-application exposure and risk for all crops/ornamentals potentially treated with metiram. The DFR study was conducted on apples in California, and is considered likely to provide high-end estimates of post-application exposures calculated for ferns, as well as for crops grown under more humid conditions or with more rainfall.

Metiram Non-Cancer Post-Application Risks: Current label requirements specify a 24 hour REI. All of the short-term metiram MOEs exceed 100 on day 0 and, as such, are not of concern to the Agency and not presented in this section. The intermediate/chronic MOEs for metiram are shown below in Table 20. The time needed to achieve a metiram MOE of 100 is 28 days for high exposure activities with apples (pruning, training, and tying).

Table 20. Metiram Post-Application Non-Cancer Risks (Intermediate/Chronic)

Crop Group	Application Rate (lb ai/acre)	MOE on Day 0 (Days when MOE> 100)			
		Very Low Exposure	Low Exposure	Medium Exposure	High Exposure
Leather Leaf Fern Cuttings	1.6	NA	NA	NA	90
Leather Leaf Ferns in Containers	1.6	NA	2200	1400	610
Apples	2.4	1600	160	NA	**54 (28)**
Potatoes	1.6	NA	810	160	NA

ETU Non-Cancer Post-Application Risks: All of the short/intermediate-term MOEs for ETU exceed 100 at day zero, and, as such, are not of concern and are not presented in this section. EPA also assessed chronic ETU non-cancer risks for greenhouse grown ferns, which are assumed to have chronic re-entry exposures. The chronic ETU MOE for fern cutting harvesting is 73 at day zero. This MOE increases to 100 twenty days after treatment (Table 21).

Table 21. ETU Post-Application Chronic Non-Cancer Risks

Crop Group	Application Rate (lb ai/acre)	Chronic MOE on Day 0 (Days when MOE>100)			
		Very Low Exposure	Low Exposure	Medium Exposure	High Exposure
Leather Leaf Fern Cuttings	1.3	NA	NA	NA	**73(20)**

Table 21. ETU Post-Application Chronic Non-Cancer Risks					
Crop Group	Application Rate (lb ai/acre)	Chronic MOE on Day 0 (Days when MOE>100)			
		Very Low Exposure	Low Exposure	Medium Exposure	High Exposure
Leather Leaf Fern Plants	1.6	NA	1800	1100	490

ETU Cancer Post-Application Risks: The ETU cancer risks are #9 x 10^{-6} on the day of application for all of the scenarios, with risks exceeding the range of 1 x 10^{-6} only in two high exposure scenarios (Table 22).

Table 22. ETU from Metiram Post-Application Cancer Risks					
Crop Group	Application Rate (lb ai/acre)	Cancer Risk on Day 0			
		Very Low Exposure	Low Exposure	Medium Exposure	High Exposure
Leather Leaf Fern Cuttings	1.3	NA	NA	NA	4e-06
Leather Leaf Fern Plants	1.6	NA	3e-07	4e-07	9e-07
Apples	2.4	3e-07	3e-06	NA	9e-06
Potatoes	1.5	NA	6e-07	3e-06	NA

c. Human Incident Data

The most recent assessment of metiram incident reports was completed in 2002. Information sources consulted included the OPP Incident Data System (IDS); the Poison Control Centers (1993 - 1998); the California Department of Pesticide Regulation survey information collected from 1982 to present; and the National Pesticide Telecommunications Network (NPTN). In all, only one occupational incident was reported for metiram, through the Poison Control Centers; the incident involved exposure to the eye for one adult, and only minor effects were noted.

B. Environmental Risk Assessment

A summary of the Agency's environmental risk assessment is presented below. For detailed discussions of all aspects of the environmental risk assessment refer to, *Environmental Fate and Ecological Risk Assessment for Metiram, Section 3 Reregistration for Control of Fungal Diseases on Apples, Potatoes, Potato Seed, Certain Ornamental Plants and Tobacco Seedling Plants (Phase 3 Response)*, dated June 21, 2005, which is available on the internet and in the public docket.

1. Environmental Fate and Transport

Metiram is a high molecular weight polymer composed of repeating single units containing zinc ions. Parent metiram is nearly insoluble in water, but is expected to decompose rather quickly by hydrolytic reactions into a multi-species residue (the metiram complex) consisting of transient species and degradates, including the degradate of concern ETU and its degradates. Most of the species present in the metiram residue are expected to partition into the soil/sediment particles; with varied strength of bonding. These soil associated materials are not largely affected by abiotic degradation, but are susceptible to very slow bio-degradation possibly further producing degradates, including ETU, at a very slow rate.

Due to rapid hydrolytic decomposition (1 week), parent metiram is expected to exist in most natural environment for a short duration (few days) when moisture is available. Parent metiram appears to be stable in alkaline (75 hours at pH 9) compared to neutral (44 hours at pH 7) to acidic (33 hours at pH 5) conditions. Metiram has low octanol/water partition coefficients (K_{ow}), especially in neutral to alkaline aqueous environments (pH = 5-8.5), which strongly suggest that it would not be significantly bio-concentrated by aquatic organisms such as fish. Furthermore, metiram has a very low vapor pressure, thus indicating that volatilization is not an important dissipation pathway.

The degradate of concern (ETU) is predicted to be susceptible to leaching due to its high solubility and mobility. In the soil environment, ETU lacks stability which can limit its leaching; however, its possible slow and steady formation from metiram complex can overcome the lack of stability and make it available for leaching at low concentrations. ETU has an aerobic soil half-life of about 3 days; in the absence of data, the aquatic aerobic metabolism half-life was assumed to be about 6 days, or double the soil half life. The measured anaerobic aquatic metabolism half-life, however, is substantially longer (149 days) possibly leading to the periodic detections in groundwater. ETU is highly soluble in water (20,000 ppm), highly vulnerable to indirect photolysis (half-life= 1 day), and moderately mobile (288 L/kg). It also has a high vapor pressure, but high solubility reduces the possibility of losses from surface water due to volatilization.

2. Ecological Risk Presumptions

The pesticide use profile, exposure data, and toxicity information are used to determine risk estimates to non-target terrestrial and aquatic organisms. The estimated environmental concentrations (EECs) are used to calculate RQs. An RQ is the estimated ratio of exposure concentration to the toxicity endpoint. The calculated RQs use the EECs that are based on the maximum single application rate of metiram, which would yield the maximum metiram exposure estimates. The RQ is then compared to the Level of Concern (LOC) to predict if exposure to metiram and its degradates could pose a risk to non-target organisms. Table 23 outlines the Agency's LOCs and the corresponding risk presumptions.

Table 23. Agency's LOCs and Risk Presumptions			
If RQ > LOC value given below.....			**Then EPA presumes .....**
Terrestrial Organisms	**Aquatic Organisms**	**Plants**	**Risk Presumption**
0.5	0.5	1	**Acute Risk -** there is potential for acute risk; regulatory action may be warranted in addition to restricted use classification.
0.2	0.1	N/A	**Acute Restricted Use -** there is potential for acute risk, but may be mitigated through restricted use classification.
0.1	0.05	1	**Acute Endangered Species -** endangered species may be adversely affected; regulatory action may be warranted.
1	1	N/A	**Chronic Risk -** there is potential for chronic risk; regulatory action may be warranted.

Note that the following ecological risks are based on parent metiram only. EPA did not estimate ETU exposure or potential ecological risk from ETU as a result of use of metiram. The Agency expects ecological ETU exposure and risk resulting from metiram's uses to be encompassed by ETU exposure and risk resulting from mancozeb's uses because the EBDCs share similar application patterns. The Agency chose ETU from mancozeb uses as a surrogate assessment to determine exposure and risk from any ETU because mancozeb has the broadest use pattern of the EBDCs, thus providing a comprehensive view of risks posed by ETU. ETU exposure and risk as a result of mancozeb application are addressed in the mancozeb RED.

In summary, chronic mammalian ETU RQs exceed the LOC for most of mancozeb's use patterns, especially for small- and medium-sized mammals. ETU is practically acutely nontoxic to mammals, and EPA does not expect acute risks to mammals from ETU exposure. EPA does not have any toxicity data to evaluate ETU's toxicity to birds. In aquatic habitats, RQs are less than the LOCs for ETU's acute risk to freshwater fish, freshwater invertebrates, and nonvascular plants from use of mancozeb. The Agency does not have data to evaluate ETU's acute risks to estuarine/marine fish and invertebrates, and vascular aquatic plants. Overall, based on available toxicity data, the ETU ecological risks assessed for mancozeb use are less than the corresponding metiram parent risks. As such, measures to address ecological risk from metiram parent, as part of this RED, will address potential metiram-derived ETU exposures as well.

3. Risk to Terrestrial Species

a. Birds and Mammals Exposure and Toxicity

The Agency assessed exposure to terrestrial species by first predicting the amount of metiram residues found on animal food items and then using information on typical food consumption by various species of birds and mammals, to predict the amount of pesticide that could be consumed. The amount

of residues on animal feed items are based on the Fletcher nomogram which is a model developed by Hoerger and Kenaga (1972) and modified by Fletcher (1994). Thus, EPA modeled the maximum and mean residues of metiram, immediately following a single application at 1 lb ai/A. EPA's estimates of metiram residues on various wild animal food items are summarized in Table 24. EPA used these EECs and standard food consumption values to estimate dietary exposure levels for metiram to birds and mammals.

Table 24. Estimated Environmental Concentrations on Avian and Mammalian Food Items

Food Items	EEC (ppm) Predicted Maximum Residue[1]	EEC (ppm) Predicted Mean Residue[1]
Short grass	240	85
Tall grass	110	36
Broadleaf plants and small insects	135	45
Fruits, pods, seeds, and large insects	15	7

[1] Predicted maximum and mean residues are for a 1 lb ai/a application rate and are based on Hoerger and Kenaga (1972) as modified by Fletcher and others. (1994).

Metiram is categorized as practically nontoxic to avian species and small mammals on an acute oral basis. However, metiram as slightly toxic to avian species on a subacute dietary basis. The acute toxicity profile for birds and mammals is summarized in Table 25.

Table 25. Metiram Acute Toxicity Endpoints for Birds and Mammals

Toxicity Study	Test Species	% a.i.	Endpoint	Toxicity Category	MRID or Accession No.
Acute (Single dose by gavage)					
Avian Oral	Bobwhite Quail	95	LD50 = >2,150 mg/kg/day	Practically nontoxic	406569901
Mammalian Oral	Laboratory Rat	Technical	LD50 = >10,000 (male) & 8,000 (female) mg/kg/day	Practically nontoxic	009768
Mammalian Oral	Laboratory Rat	80	LD50 = >5,000 (male & female) mg/kg/day	Practically nontoxic	009926
Subacute (Five days of treated feed)					
Avian Dietary	Bobwhite Quail	80	LC50 = 3,712 ppm ai	Slightly toxic	00108005
Avian Dietary	Mallard Duck	80	LC50 = >3,712 ppm ai	Slightly toxic	00108004

In a metiram avian reproduction study using the mallard duck, chronic toxic effects seen included the following: reduced egg production; reduced mean egg weight; reduced fertility rate;

reduced number of hatched ducklings; reduced number of 14-day old survivors; and an increased rate of early embryonic deaths. Results from a chronic 3-generation reproduction study in rats for metiram indicate parental and reproductive toxicity with parental toxicity resulting in decreased body weight during gestation and lactation for females, and reproductive toxicity resulting in decreased mating performance (increased precoital time) in the F2 generation (two generations removed from the original parent generation). The chronic toxicity endpoints for birds and mammals are summarized in Table 26.

Table 26. Metiram Chronic Toxicity Endpoints for Birds and Mammals

Test Species	% a.i	NOAEC or NOAEL (ppm)	LOAEC or LOAEL (ppm)	Effects at LOAEC or LOAEL	MRID or Accession No.
Mallard Duck	97	50	300	Reduced hatchling survival at 14 days	42539102
Laboratory rat	96.8	40	320	Reduced body weight and mating in offspring	247214

NOAEC / LOAEC = No Observable Adverse Effect Concentration, the highest dose at which no adverse health effect is observed./ Lowest Observable Adverse Effect Concentration, the lowest dose at which an adverse health effect is observed.
NOAEL / LOAEL= No Observable Adverse Effect Level, the highest dose at which no adverse health effect is observed / Lowest Observable Adverse Effect Level, the lowest dose at which an adverse health effect is observed.

b. Birds and Mammals Risk

Avian and mammalian RQs exceed the chronic LOCs for almost all use metiram modeled exposures. Based on multiple applications, the chronic RQs for birds range from 76 on apples to a low of 1 on ornamentals using a default half-life value of 35 days. The 35-day value is a standard Agency default value when total foliar dissipation half-life is unknown for a pesticide. Table 27 summarizes the avian acute (based on maximum EEC values) and chronic (based on maximum and mean EEC values) RQs, from multiple applications of metiram.

Table 27. Avian Acute/Chronic RQs from Metiram Application

Crop	Maximum Application Rate (lbs a.i./A)	Avian Acute RQs (LC_{50}=3,712 ppm)	Avian Chronic RQs (NOAEC= 50 ppm)	
		Based on maximum EECs	Based on maximum EECs	Based on mean EECs
		Range = Shortgrass - Seeds		
Apples	4.8	1.02 - 0.06	76 - 5	27 - 2
Potatoes	1.6	0.55 - 0.03	41 - 3	14 - 1
Ornamentals (nonflowering plants)	1.6	0.27 - 0.02	20 - 1	7 - 0.6

Chronic RQs for mammals ranged from a high of 95 on apples to a low of 1 on ornamentals using a 35 day default half-life. The Agency expects risk to metiram to be below the LOC for acute risk to mammals, because metiram is practically nontoxic (rat LD_{50} > 5,000 mg/kg) to mammals on an acute basis. Thus, RQs for acute mammalian exposure were not calculated. Table 28 summarizes the mammalian chronic RQs from multiple applications of metiram, based on maximum and mean EEC values.

Table 28. Mammalian Chronic RQs from Metiram Application

Crop	Maximum Application Rate (lbs a.i./A)	Mammalian Chronic RQs (NOAEL= 40 ppm)	
		Based on maximum EECs	Based on mean EECs
		Range = Shortgrass - Seeds	
Apples	4.8	95 - 6	34 - 3
Potatoes	1.6	51 - 3	18 - 1
Ornamentals (nonflowering plants)	1.6	25 - 2	9 - 0.7

c. Non-Target Plant Risk

Terrestrial plants inhabiting dry and semi-aquatic areas may be exposed to pesticides from direct applications via runoff, spray drift, or volatilization. RQs could not be calculated because toxicity data for plants are not available; however, metiram is applied directly to a wide variety of terrestrial plants with no adverse effects. The potential for acute risks to terrestrial plants at use sites are unknown. Currently, the Agency does not perform chronic risk assessments for terrestrial plants.

d. Non-Target Insect Risk

Metiram is practically nontoxic to honeybees from acute contact exposure (acute contact LD_{50} = 437 µg/bee). The Agency does not expect metiram exposure to pose acute risk to non-target insects, because metiram is practically nontoxic to honeybees and there are no incident data reporting adverse effects to honeybees.

4. Risk to Aquatic Species

a. Fish and Invertebrate Exposure and Toxicity

Unlike the drinking water assessment described in the human health risk assessment section of this document, the ecological water resource assessment does not include the Index Reservoir (IR) and Percent-Crop Area (PCA) factor refinements. The IR and PCA factors represent a drinking water

reservoir, not the variety of aquatic habitats, such as ponds adjacent to treated fields, relevant to a risk assessment for aquatic animals. Therefore, the EEC values used to assess exposure to aquatic animals are not the same as the values used to assess human dietary exposure from drinking water sources.

EECs were estimated using tier II modeling, the linked PRZM and EXAMS models (PRZM/EXAMS). In modeling, metiram uses on apples and potatoes were chosen, because they are the major uses for metiram and PRZM-EXAMS modeling scenarios exist for these uses. The EECs are used for assessing acute and chronic risks to aquatic organisms. Acute risk assessments are performed using peak EEC values for single and multiple applications. Chronic risk assessments are performed using the 21-day EECs for invertebrates and 60-day EECs for fish. Table 29 summarizes the aquatic EECs for metiram.

Table 29. Tier II Estimated Environmental Concentrations (EECs) of Metiram in Surface Water (ppb)

Crop	Rate (lbs ai/A)	Number of Applications	Interval	Peak	96 Hour	21 Day	60 Day	90 Day	Annual Average
Apples (NC)	4.8	4	7	98.9	55.4	20.7	9.4	5.3	1.6
Potatoes (ME)	1.6	7	5	54.5	28.1	10.2	5.6	3.8	1.4

Acutely, metiram is highly toxic to coldwater freshwater fish (rainbow trout LC_{50} = 0.23 ppm based on measured, filtered samples). The acute daphnid study shows metiram to have a freshwater aquatic invertebrates EC_{50} value > 0.358 ppm based on measured, unfiltered samples. The study using freshwater green algae, *Ankistrodesmus bibraianus* shows metiram to be toxic to aquatic plants (EC_{50} = 0.077 ppm based on nominal concentrations). Metiram acute toxicity endpoints for freshwater aquatic fish and invertebrates are summarized in Table 30.

Table 30. Acute Toxicity Endpoints for Aquatic Species

Toxicity Study	Test Species	% a.i.	LC_{50} or EC_{50} (ppm)	Toxicity Category	MRID
Freshwater Fish (flow-through 96-hr)	Rainbow Trout	71.04	0.23	Highly Toxic	43525001
Freshwater Invertebrate (static 48-hr)	Daphnid	70	>0.358	Highly Toxic	44301101

b. Fish and Invertebrate Risk

The Agency expects metiram to reach aquatic environments through drift and runoff since metiram is not labeled for direct application to aquatic environments. Metiram is insoluble in water but the Agency expects it to decompose rather quickly, by hydrolytic reactions, into a multi-species residue (metiram complex) consisting of transient species and degradates, including the degradate of concern,

ETU. Once metiram reaches the aquatic environment, the Agency believes the metiram complex will be the portion of the metiram that is biologically available to aquatic organisms. The Agency expects most of the transient species present in the metiram complex to partition into the sediment particles with varied strength of bonding. Over time, ETU is the dominant transformation product of the metiram complex. These metiram complex residues are short-lived in aquatic media, but ETU is persistent in this media unless it is subjected to rapid degradation by microbes and/or indirect photolysis.

The Agency did not evaluate acute risks to estuarine/marine animals because of the lack of data (acute toxicity endpoints). Also, because of a lack of chronic toxicity endpoints data, the Agency did not evaluate chronic risks for freshwater aquatic animals from exposure to metiram residues. The Agency is reserving the need for chronic studies for estuarine/marine aquatic organisms at this time, until acute studies for estuarine/marine organisms are received and reviewed, because the acute toxicity for estuarine/marine organisms is unknown. Metiram acute risk quotients for freshwater fish and invertebrates are summarized below in Table 31.

Table 31. Acute RQs for Fish and Invertebrates from Metiram Application

Crop	Maximum Single Application Rate (lbs a.i./A)	Peak EEC (ppb)	Freshwater Acute RQ	
			Fish (LC_{50}= 230 ppb)	Invertebrates (EC_{50}= >358 ppb)
Apples	4.8	98.9	0.43	0.28
Potatoes	1.6	54.5	0.24	0.15

c. Non-Target Aquatic Plant Risk

Like terrestrial plants, non-target aquatic plants may be exposed to pesticide from run-off, spray drift or volatization of metiram. Available information suggests that metiram may be toxic to nonvascular aquatic plants. The EC_{50} for freshwater green algae was 77 ppb based on nominal concentration, and a nominal NOAEC of 13.0 ppb. The potential for acute risks to terrestrial, semi-aquatic and aquatic vascular plants exposed to metiram at use sites is unknown. EPA will require plant data to assess acute risks to terrestrial, semi-aquatic and aquatic plants. Currently, the Agency is not assessing chronic effects on aquatic plants.

Exposure to non-target aquatic plants may occur through runoff or spray drift from adjacent treated sites. An acute aquatic plant risk assessment is usually made for aquatic vascular plants from the surrogate duckweed *Lemna gibba*. Non-vascular acute risk assessments are performed using either algae or a diatom, whichever is the most sensitive species. Runoff and drift exposure is computed from PRZM-EXAMS.

The risk quotient is determined by dividing the pesticide's initial or peak concentration in water by the plant EC_{50} value. Acute RQs for freshwater, non-vascular green alga (*Ankistrodesmus bibraianus*) plants are presented in Table 32. The results indicate that the non-vascular, non-target plant acute risk LOC of 1 is slightly exceeded for metiram's maximum application on apples.

Table 32. Acute RQs for Aquatic Non-Vascular Plants from Metiram Application

Crop	Maximum Single Application Rate (lbs a.i./A)	Peak EEC (ppb)	Acute RQ (EC_{50} = 77 ppb)
Apples	4.8	98.9	1.28
Potatoes	1.6	54.5	0.71

5. Risk to Federally Listed Endangered and Threatened Species

Based on available screening-level information, there is a potential concern for acute effects on listed birds and freshwater fish species, and chronic effects on listed birds and mammals should exposure actually occur. Even though metiram is only slightly acutely toxic to birds, RQs exceed the endangered species LOC (RQ range from 0.11 to 1.02) at maximum EEC levels. The Agency does not currently have data to quantify risks for metiram at the screening-level and can not preclude potential direct effects to the following taxonomic groups; listed non-target terrestrial plants, freshwater invertebrates, estuarine/marine fish, or vascular aquatic plants. These findings are based solely on EPA's screening-level assessment and do not constitute "may affect" findings under the Endangered Species Act (ESA) for any specific listed species.

The Agency has developed the Endangered Species Protection Program to identify pesticides whose use may cause adverse impacts on federally listed endangered and threatened species, and to implement mitigation measures that address these impacts. The ESA requires federal agencies to ensure that their actions are not likely to jeopardize listed species or adversely modify designated critical habitat. To analyze the potential of registered pesticide uses that may affect any particular species, EPA uses basic toxicity and exposure data developed for the REDs and considers ecological parameters, pesticide use information, the geographic relationship between specific pesticide uses and species locations and biological requirements and behavioral aspects of the particular species. When conducted, this analysis will consider regulatory changes recommended in this RED that are implemented a that time. A determination that there is a likelihood of potential effects to a listed species may result in limitations on the use of the pesticide, other measures to mitigate any potential effects, or consultations with the Fish and Wildlife Service or National Marine Fisheries Service as appropriate. If the Agency determines use of metiram "may affect" listed species or their designated critical habitat, EPA will employ the provisions in the Services regulations (50 CFR Part 402). Until that species specific analysis is completed, the risk mitigation measures being implemented through this RED will reduce the likelihood that endangered and threatened species may be exposed to metiram at levels of

concern.

6. Ecological Incidents

The Ecological Incident Information System (EIIS) indicated there were no adverse effect incidents to terrestrial or aquatic non-target organisms reported in association with metiram's use.

IV. RISK MANAGEMENT, REREGISTRATION AND TOLERANCE REASSESSMENT

A. Determination of Reregistration Eligibility

Section 4(g)(2)(A) of FIFRA calls for the Agency to determine, after submission of relevant data concerning an active ingredient, whether or not products containing the active ingredient are eligible for reregistration. The Agency has previously identified and required the submission of the generic (i.e., active ingredient-specific) data to support reregistration of products containing metiram as an active ingredient. The Agency has completed its review of these generic data, and has determined that the data are sufficient to support reregistration of all products containing metiram.

The Agency has completed its assessment of the dietary, occupational, residential (as a result of exposures from mancozeb), and ecological risk associated with the use of pesticide products containing the active ingredient metiram, including metiram-derived ETU and ETU from all sources. Based on a review of these data and on public comments on the Agency's assessments for the active ingredient metiram, the Agency has sufficient information on the human health and ecological effects of metiram to make decisions as part of the tolerance reassessment process under FFDCA and reregistration process under FIFRA, as amended by FQPA. The Agency has determined that metiram containing products are eligible for reregistration provided that: (i) current data gaps and confirmatory data needs are addressed; (ii) the risk mitigation measures outlined in this document are adopted; and (iii) label amendments are made to reflect these measures. Label changes are described in Section V. Appendix A summarizes the uses of metiram that are eligible for reregistration. Appendix B identifies the generic data requirements necessary as part of the Agency's determination of reregistration eligibility of metiram, and lists the submitted studies that the Agency reviewed and found acceptable. Data gaps are identified as generic data requirements that have not been satisfied with acceptable data.

Based on its evaluation of metiram, the Agency has determined that metiram products, unless labeled and used as specified in this document, would present risks inconsistent with FIFRA and FQPA. Accordingly, should a registrant fail to implement any of the risk mitigation measures identified in this document, the Agency may take regulatory action to address the risk concerns from the use of metiram. If all changes outlined in this document are incorporated into the product labels, then all current risks for metiram will be adequately mitigated for the purposes of this reregistration determination.

Although not currently registered, exposure from a proposed import use of metiram on wine grapes has been assessed. It has also been included in the risk assessment supporting this RED to assist the Agency in making a determination of whether to establish an import tolerance for metiram use on wine grapes. Because the determination of establishing this import tolerance is outside the scope of this RED, it will be made separately by the Agency.

B. Public Comments and Responses

Through the Agency's public participation process, EPA worked extensively with stakeholders and the public to reach its regulatory decisions for metiram. During the public comment period on the risk assessments, which closed on February 22, 2005, the Agency received comments from the registrant, growers and grower groups. These comments in their entirety and the Agency's response are available in the public docket (OPP-2005-0078) at http://www.epa.gov/edockets.

C. Regulatory Position

1. Food Quality Protection Act Findings

a. "Risk Cup" Determination

As part of the FQPA tolerance reassessment process, EPA assessed the risks associated with this pesticide. EPA has determined that risk from dietary (food sources only) exposure to metiram is within its own "risk cup." An aggregate assessment was conducted for exposures to metiram through food and drinking water only, since there are no registered residential uses of metiram. Because metiram and the other EBDC fungicides (maneb and mancozeb) degrade to ETU in the environment and metabolize to ETU in the body, the aggregate assessment considered ETU derived from metiram and other EBDCs. The Agency has determined that the human health risks from these combined exposures to both metiram and ETU are within acceptable levels, provided the mitigation measures stipulated in this document are implemented. In other words, EPA has concluded that the tolerances for metiram meet FQPA safety standards. In reaching this determination, EPA has considered the available information on the special sensitivity of infants and children, as well as aggregate exposure from metiram and ETU.

b. Determination of Safety to U.S. Population (including Infants and Children)

The Agency has determined that the established tolerances for metiram, with amendments and changes as specified in this document, meet the safety standards under the FQPA amendments to section 408(b)(2)(D) of the FFDCA, and that there is a reasonable certainty no harm will result to the general population or any subgroup from the use of metiram. In reaching this conclusion, the Agency has considered all available information on the toxicity, use practices and exposure scenarios, and the

environmental behavior of metiram and its ETU metabolite and degradate. EPA has also considered information on the toxicity of ETU, and the aggregate exposure to ETU, resulting both from the use of metiram and from the use of the other EBDC fungicides.

As discussed in Chapter III, acute, chronic and cancer dietary (food alone) risks from metiram are not of concern. Aggregate risk, which combined food, drinking water and residential exposures, where applicable, from metiram, metiram-derived ETU, and ETU from all sources are also not of concern. The aggregate risk assessment for ETU considers residential scenarios, because mancozeb has uses that may result in residential exposure, and degrade to ETU.

c. Endocrine Disruptor Effects

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

The available human health and ecological effects data for metiram suggest possible thyroid effects, which may indicate potential endocrine disruption. EPA has considered these effects in the human health risk assessment by selecting endpoints based on thyroid effects. To further address these effects, EPA is requiring a confirmatory comparative thyroid toxicity study for ETU. Data on ecological effects suggest possible hormonal effects to birds and mammals. These effects will be addressed when the Agency's Endocrine Disruptor Screening and Testing Advisory Committee develops appropriate screening and/or testing protocols. At that time, metiram may be subjected to additional screening and/or testing to better characterize effects related to endocrine disruption.

d. Cumulative Risks

Risks summarized in this document are those that result only from the use of metiram and its metabolite, ETU. The FFDCA, as amended by FQPA, requires that the Agency consider "available information" concerning the cumulative effects of a particular pesticide's residues and "other substances that have a common mechanism of toxicity." The reason for consideration of other substances is due to the possibility that low-level exposures to multiple chemical substances that cause a common toxic effect by a common toxic mechanism could lead to the same adverse health effect as would a higher

level of exposure to any of the substances individually. Metiram belongs to a group of pesticides called dithiocarbamates, which also includes the EBDC fungicides maneb and mancozeb. For the purposes of this RED, EPA has concluded that metiram does not share a common mechanism of toxicity with other substances. The Agency reached this conclusion after a thorough internal review and external peer review of the data on a potential common mechanism of toxicity. For more information, please see the December 19, 2001 memorandum, *"The Determination of Whether Dithiocarbamate Pesticides Share a Common Mechanism of Toxicity,"*which is available on the internet at http://www.epa.gov/oppsrrd1/cumulative/dithiocarb.pdf. However, the EBDCs share a common metabolite and degradate, ethylene thiourea (ETU), which is considered in this RED.

2. Tolerance Reassessment Summary

Metiram tolerances are established under 40 CFR §180.217 and are currently expressed in terms of residues of a fungicide that is a mixture of 5.2 parts by weight of ammoniates of [ethylenebis(dithiocarbamato)]zinc with 1 part by weight ethylenebis [dithiocarbamic acid] bimolecular and trimolecular cyclic anhydrosulfides and disulfides, calculated as zinc ethylenebisdithiocarbamate. Based on a reevaluation of the available plant and livestock metabolism studies, the Agency has reaffirmed that the residues of toxicological concern, i.e. to be included in risk assessment, are the parent EBDC.

For regulatory/enforcement purposes, the Agency recommends that tolerances in plant and livestock commodities at 40 CFR §180.217(a) be established for residues of metiram *per se*. The Agency has further proposed that EBDC (including metiram) tolerances be calculated as carbon disulfide rather than as zineb. The only established metiram tolerances are for apple (2.0 ppm) and potato (0.5 ppm). No metiram tolerances have been established for animal and processed food/feed commodities.

a. Tolerances Listed Under 40 CFR §180.217

Adequate residues of metiram and ETU in/on apple and potato have been submitted/evaluated to reassess the established tolerances. The maximum combined residues of metiram and ETU in/on apples following treatments were 0.5299 ppm, which is below the established tolerance of 2 ppm. Considering the conversion factor to CS_2 as 0.56x, the available residue data suggest expected combined residues of about 0.3 ppm and, therefore, the established apple tolerance should be lowered from 2 ppm to 0.5 ppm.

The maximum combined residues of metiram and ETU in/on potato tubers following treatments at 1x were <0.03 ppm, which is below the established tolerance of 0.5 ppm. The available residue data suggest that the established potato tolerance may be lowered from 0.5 ppm to 0.2 ppm to achieve numerical compatibility with the Codex's maximum residue limit (MRL) for dithiocarbamates on potato.

b. Tolerances To Be Proposed Under 40 CFR §180.217

The available apple data indicates that the combined residues of metiram and ETU concentrated 5x in wet pomace processed from whole apples bearing detectable residues. Based on a Highest Average Field Trial (HAFT) of 0.53 ppm and the observed concentration factor of 5x, the maximum expected combined residue in wet apple pomace is 2.65 ppm. Considering the conversion factor to CS_2 as 0.56x, the data suggest expected combined residues of about 1.7 ppm and, therefore, a tolerance for residues in wet apple pomace should be established at 2 ppm.

Table 33. Tolerance Reassessment Summary for Metiram.

Commodity	Tolerance Listed Under 40 CFR (ppm)	Maximum Residue Value [1] (ppm)	Reassessed Tolerance [2] (ppm)	Comment *[Correct Commodity Definition]*
Tolerance Listed Under 40 CFR §180.217				
Apple	2	0.5299	0.5	
Potato	0.5	<0.03	0.2	Harmonized
Tolerance To Be Proposed Under 40 CFR §180.217				
Apple, pomace, wet	None	0.53 (HAFT) x 5 (average concentration factor) = 2.65	2	

[1] Maximum combined residues of metiram and ETU (including ETU conversion factor for Metiram) in/on treated RAC sample(s) following applications of metiram formulation according to maximum registered use patterns.
[2] To be residues of metiram calculated as CS_2 (0.56 conversion factor is accounted for within).

c. Codex Harmonization

There are no established or proposed Codex MRLs for metiram residues *per se*, however, Codex limits for dimethyldithiocarbamates fungicides are grouped under dithiocarbamates. Maximum residue limits (MRLs) for the dithiocarbamates are established for several commodities resulting from the use of mancozeb, maneb, metiram, propineb, thiram, and ziram and are currently expressed as ppm carbon disulfide. The Agency is recommending harmonization of the tolerance expression with the Codex residue definition. A numerical comparison of the Codex MRLs and the corresponding reassessed U.S. tolerances for metiram are presented on the internet at the Food and Agricultural Organization database website: http://faostat.fao.org/faostat/collections?version=ext&hasbulk=0. The tolerance value for potatoes will be harmonized with the Codex MRL.

D. Regulatory Rationale

The following is a summary of the rationale for the mitigation measures necessary for reregistration eligibility and for managing risks associated with the use of metiram. Where labeling revisions are warranted, specific language is set forth in the summary table of Section V (Table 36 of this RED document).

1. Human Health Risk Management

a. Dietary (Food) Risk Mitigation

Acute, chronic, and cancer dietary (food only) exposure and risk from metiram, metiram-derived ETU, and ETU from all sources are below the Agency's level of concern. Acute, chronic, and cancer risks were also not of concern for metiram or metiram derived-ETU, even when residues from the proposed import use on wine grapes were included in the dietary assessment. Since there are no acute, chronic, cancer dietary (food only) risks of concern, no mitigation measures are necessary.

b. Dietary (Drinking Water) Risk Mitigation

The drinking water exposure assessment for metiram addresses concentrations of ETU only, since metiram is not expected to remain in water long enough to reach a location that would supply drinking water for human consumption, whether from surface or groundwater sources. Estimated concentrations of ETU, for both surface and ground water sources of drinking water, are low and not of concern; therefore, no mitigation is needed.

c. Residential Risk Mitigation

The Agency is not considering residential mitigation options for metiram, since there are no existing or proposed residential or other non-occupational sources of exposure, and metiram is not used in or around public buildings, schools or recreational areas where children or others might be exposed.

d. Aggregate Risk Mitigation

Aggregate risk refers to the combined risk from food, drinking water, and residential (as a result of residential exposures from mancozeb uses) exposures. In addition, aggregate risk can result from one-time (acute), short-term and/or chronic (non-cancer and cancer) exposures. Below is a discussion of the risk for each duration of exposure and any risks of concern.

Acute Aggregate: Since residues of metiram *per se* are not expected in drinking water, acute aggregate risks for metiram consist of acute exposures to metiram-derived ETU and ETU from all sources. Potential concentrations of metiram-derived ETU and ETU from all sources in drinking water, when combined with exposure through food, are below Agency's level of concern for acute aggregate risk (see Table 12). No mitigation measures are necessary for acute aggregate risk.

Short-term Aggregate: Short-term aggregate (food + drinking water + residential [as a result of residential exposures from mancozeb uses]) risk for ETU from all sources is below the Agency's level of concern for residential handlers, and children and adults exposed to ETU from re-entry activities (see Table 13). Therefore, no mitigation is required.

Chronic (Non-Cancer) Aggregate: The chronic aggregate risk to metiram-derived ETU and ETU from all sources were calculated using food and drinking water exposures only, because residential mancozeb exposure scenarios were considered to occur only on a short-term basis. Aggregate (food + drinking water) chronic risk to metiram-derived ETU and ETU from all sources are below the Agency's level of concern; therefore, no mitigation is required.

Cancer Aggregate: Aggregate (food + drinking water) cancer risk to metiram-derived ETU for the general U.S. population is below the Agency's level of concern. The cancer risks from ETU from all sources were aggregated using food, drinking water and residential/recreational (as a result of mancozeb uses) exposures. These risks range from 2.0×10^{-6} to 2.3×10^{-6} depending upon the drinking water source and the type of residential exposure, with the food exposure being the largest contributor of cancer risk (1.86×10^{-6}), followed by drinking water from groundwater sources. The Agency considers cancer risks as high as 3 in 1 million are within the negligible risk range; thus, cancer aggregate risks are not of concern. Therefore, the Agency believes no further mitigation is required for metiram.

e. Occupational Risk Mitigation

It is the Agency's policy to mitigate occupational risk to the greatest extent necessary and feasible. Mitigation measures may include reducing application rates, adding personal protective equipment (PPE) to end product labels, requiring the use of engineering controls, and other measures. A wide range of factors is considering in making risk management decisions for worker risks. These factors include, estimated margins of exposure (MOEs), cancer risk estimates, incident data, the nature and severity of adverse effects observed in animal studies, uncertainties in the risk assessment, alternative registered pesticides, the importance of the chemical in integrated pest management (IPM) programs, and other similar factors.

1) Agricultural and Greenhouse Handler Mitigation

Handler exposure assessments are completed by EPA considering the use of baseline PPE, and, if warranted, increasing levels of PPE and engineering controls in order to estimate their potential impact on exposure. The target MOE for occupational risk is 100, and MOEs greater than 100 do not exceed the Agency's level of concern. For occupational cancer risks, estimates in the general range of 1×10^{-6} (one in a million) generally do not exceed the Agency's level of concern. When occupational MOEs are less than 100 or occupational cancer risks exceed the general range of 1×10^{-6}, EPA strives to reduce worker cancer risks through the use of personal protective equipment and engineering controls or other mitigation measures. The Agency generally considers occupational cancer risks in the general range of 1×10^{-6} or less to be negligible, but may accept estimated risks as high as 1×10^{-4} (1 in 10,000 persons) when all mitigation measures that are feasible have been applied, particularly when there are critical pest management needs associated with the use of the pesticide. Levels of PPE considered and applicable to the proposed mitigation are described below:

- Baseline - long-sleeved shirt, long pants, and shoes and socks
- Single layer - baseline plus gloves
- Double layer - baseline plus gloves and coveralls
- PF5 - a dust/mist filtering respirator
- PF10 - a half face respirator with appropriate cartridges

Section 3 Use on Apples and Potatoes

As described in Section III.A.6. of this document, non-cancer (inhalation and dermal) and cancer risks to handlers mixing and loading and applying metiram are not of concern for several exposures at baseline PPE (MOEs and cancer risk estimates are also described below). The Agency is requiring the use of baseline PPE for these scenarios, as follows:

- Handlers mixing and loading dry flowable for groundboom application to potatoes (dermal and inhalation MOEs are 330 and 360; cancer risks are 5×10^{-7});
- Handlers mixing and loading dry flowable for airblast application to apples (dermal and inhalation MOEs are 220 and 240; cancer risks are 4×10^{-7});
- Handlers applying via groundboom to potatoes (dermal and inhalation MOEs are >1000 and 370; cancer risks are 3×10^{-7});

For other exposure scenarios, risks to handlers are above the Agency's level of concern at baseline PPE, as described in Section III.A.6. of this document. The Agency is requiring the use of additional PPE for these scenarios and other mitigation measures for these scenarios, as described in the paragraphs below.

For handlers mixing and loading dry flowable for aerial or chemigation application to apples or potatoes, the Agency is requiring the use of double-layer PPE and a PF5 respirator. Considering the use of this PPE, the dermal and inhalation MOEs for apples are 35 and 140 and for potatoes are 106 and 420, respectively. In addition, to help further mitigate the dermal risk associated with apples, the registrants have agreed to reduce the maximum application rates from 4.8 lb ai/A to 3.6 lb ai/A. This results in a dermal MOE of approximately 50, which is still less than the target MOE of 100; however, Agency information indicates that the aerial application method is an infrequent occurrence and used on apples less than 5% of the time (e.g., when it is too wet to use ground application equipment for this scenario). Thus, it is unlikely that intermediate-term exposures occur. Since the short-term dermal MOE is 420 at baseline, the Agency believes that the mitigation described here mitigates any risk of concern.

For handlers applying via airblast application to apples, the Agency is requiring single layer PPE plus a PF5 respirator. MOEs were both 41 with baseline PPE. The dermal MOE with the use of single layer PPE increases to 100 and the inhalation MOE with the use of a respirator is 200. The cancer risk estimate considering the use of the PPE being required is 7×10^{-7}. Considering the mitigation, there are no remaining risks of concern to the Agency.

For aerial applicators, the Agency is requiring the use of engineering controls (closed cockpits). With the use of engineering controls, dermal and inhalation MOEs are 330 and 310 for apples and 1000 and 920 for potatoes, respectively, and cancer risk estimates are 3×10^{-7} for apples and 2×10^{-7} for potatoes. Considering the mitigation, there are no remaining risks of concern to the Agency.

For flaggers, the Agency is requiring the use of baseline PPE (no gloves) plus a PF5 respirator. For use on apples, the dermal MOE for flaggers at baseline PPE is 150 and the inhalation MOE at baseline PPE is 60. MOEs for potatoes are all greater than 100. With the addition of a PF5 respirator, the inhalation MOE increases to 300. The cancer risk estimates with the use of a PF5 respirator are 5×10^{-7} for apples and 3×10^{-7} for potatoes; therefore, there are no remaining risks of concern to the Agency.

Short-term, intermediate term and non-cancer chronic risks were not of concern for metiram-derived ETU; MOEs were above 100 for all of the handler scenarios evaluated.

Section 24(c) Use on Leatherleaf Ferns

As described in Section III.A.6. of this document, non-cancer (inhalation and dermal) risks to handlers mixing, loading, and applying metiram to leatherleaf ferns with a low pressure handwand are not of concern at single layer PPE (baseline plus gloves) with a dermal MOE greater than 500, but resulted in an inhalation MOE of 50. Related to dermal exposure, MOEs could not be calculated without gloves due to the lack of data; however, the Agency understands that the use of gloves is common use practice for these handlers. The Agency believes that the inhalation MOE of 50 is not a risk of concern, because wettable powder unit exposure data were used to substitute for the dry flowable formulation; data specific to dry flowable formulations are not available for this scenario. The use of wettable powder data to substitute for the dry flowable formulation is highly conservative, because dry flowable formulations are significantly less dusty than wettable powders and, therefore, result in much less inhalation exposure.

Dermal and inhalation MOEs and cancer risk estimates were not able to be calculated for handlers mixing, loading, and applying metiram to ferns with a backback sprayer. The Agency believes that single layer PPE will mitigate any risks of concern for this scenario as well, because backpack sprayer and low pressure handwand are comparable application methods; the low pressure handwand dermal MOE is five times greater than the target MOE of 100; and inhalation exposures will not be greater than for handlers using the low pressure handwand.

Short-term, intermediate term and non-cancer chronic risks were not of concern for metiram-derived ETU; MOEs were above 100 for all of the handler scenarios evaluated.

2) Potato Seed-Piece Treatment Mitigation

As described in Section III.A.6. of this document, risks to handlers loading dust formulation for

commercial and on-farm potato seed-piece treatment are of concern to the Agency for dermal, inhalation, and cancer risks. As such, the end-use registrant has requested to voluntarily cancel the potato seed-piece treatment product registration and this scenario is no longer a risk of concern.

3) Post-Application Mitigation

When preparing post-application risk assessments, EPA considers dislodgeable foliar residue (DFR) data, application rates, transfer coefficients based on crop type and exposure scenario (low, medium, or high contact activities), and assumptions about average occupational workdays and adult body weight. In the case of metiram, both metiram and its degradate ETU were considered in the assessment. For the ETU cancer risk assessment, the Agency assumed that workers would be exposed for 30 days each year.

At the current REI of 24 hours, for high-end intermediate/chronic exposure scenarios, estimated MOEs are <100 only for apples and leather-leaf fern cuttings. For the ETU high-end chronic exposure scenario, the estimated MOE is <100 for leather-leaf fern cuttings. The only two post-application cancer risk scenarios with predicted risks exceeding the range of 1×10^{-6} are the high-end exposure scenarios for apples and leather-leaf fern cuttings; however, neither of these exceed 9×10^{-6}

For leatherleaf ferns, the Agency is requiring that use be restricted to a maximum of 1 application per week and 10 applications per year, but maintaining the existing 24 hour REI. Based on these restrictions, if 10 applications per year are made at weekly intervals, the expected use pattern based on information available from the user community, the exposure would be considered an intermediate-term duration and not a chronic duration. Thus, the chronic MOE as a result of ETU exposure (MOE of 74 at day 0 after treatment) is no longer applicable, considering these restrictions. The intermediate-term MOEs for metiram exposure are 90 at day 0 and 92 at day 1 after treatment, and for ETU the intermediate term MOE is greater than 100. MOEs of 90 and 92 are not significantly different than 100 and not of concern to the Agency.

For apples, a MOE of 54 is predicted for high intermediate-term exposure activities (pruning, tying, and training) at the current REI of 24 hours. Based on information provided to the Agency from the user community, these high exposure activities do not begin until several weeks after the last metiram application for apples grown in the East, including New England, and the central states. At 20 days after application, the metiram intermediate/chronic MOE is 84. For apples grown in the Southwest, West, and Pacific Northwest, high exposure activities can occur immediately after treatment, and may extend for greater than 30 days. This results in an intermediate-term MOE of 54. However, the Agency does not believe that there is a risk of concern to workers reentering treated apple orchards. The major metiram usage states are Michigan, New York, Virginia, North Carolina, Pennsylvania, Ohio, and South Carolina; and National Agricultural Statistical Services (NASS) data available to the Agency indicate very low metiram usage in the West. Further, IPM and resistance

management advantages from the use of this chemical as described in the Significance of the EBDCs section of this document (Section IV.E.3) are significant. Therefore, the Agency plans to maintain the current 24 hour REI for all apples.

2. Environmental Risk Mitigation

It is the Agency's policy to mitigate ecological risks to the greatest extent necessary and feasible. Mitigation measures may include lowering application rates, reducing the number of applications, restricting the timing of applications, minimizing runoff potential, and others.

a. Terrestrial Species Mitigation

From a short-term or acute metiram exposure, the Agency expects low risk to mammals and birds. However, the screening-level ecological risk assessment indicates some exceedance of the chronic screening LOCs for risk to birds and small mammals. In particular, the highest chronic RQs result from metiram use on apples. With a total of four applications at a rate of 4.8 lbs ai/A to apples, the corresponding avian chronic RQs based on mean EECs range from 27-2 and the mammalian chronic RQs range from 34-3. Predicted exposures from use of metiram on potatoes also exceed screening levels of concern for birds and mammals, with RQs ranging from 14-1 for birds and 18-1 for mammals, again based on mean EECs. These RQs are screening-level estimates, incorporating modeled estimated environmental concentrations. Nevertheless, to be more protective of terrestrial species that may be exposed on a chronic basis, the technical registrant has agreed to additional label changes to reduce potential risk. For example, the maximum application rate (pre-bloom) to apples is being reduced from 4.8 to 3.6 lbs ai/A, and the maximum number of applications is also being reduced from 4 to 3 times per year. Moreover, the maximum number of applications to potatoes is also being reduced from 7 to 6 times per year, thus reducing the yearly maximum application rate. Refer to Table 34 for summary of revisions to use site parameters.

The Agency does not expect metiram exposure to pose acute risk to non-target insects, because metiram is practically nontoxic to honeybees and there are no incident data reporting adverse effects to honeybees. Therefore, no bee precautionary labeling is required on metiram product labeling.

b. Aquatic Species Mitigation

Predicted acute risk to aquatic species (freshwater fish, freshwater invertebrates, and non-vascular plants) is low. Currently, there are no toxicity data on estuarine/marine species and no toxicity data to assess chronic risk to freshwater fish or freshwater invertebrates. The Agency is requiring additional acute and chronic toxicity data as part of this RED to address these data gaps.

Although the assessed acute RQs to aquatic species are relatively low, some LOC

exceedances exist. The same mitigation measures addressing terrestrial risks will also reduce these risks, including reducing single maximum application rates, and reducing maximum number of applications per year and maximum seasonal application rates. Refer to Table 34 for summary of revisions to use site parameters. For acute risks to aquatic non-vascular plants, the reduction of the maximum application rate for apples reduces the corresponding RQ below the LOC.

Table 34. Revised Use Site Parameters and Requirements for Metiram

Crop	Single Application Rates (lb ai/A)		Minimum Retreatment Interval (days)	Maximum Number of Applications Per Year		Yearly Maximum Rate (lb ai/A)	
	Previous	Revised		Previous	Revised	Previous	Revised
Apples	4.8	3.6	7	4	3	19.2	10.8
Potatoes	1.6	1.6	5	7	6	11.2	9.6
Leatherleaf Ferns	1.6	1.6	7	Unlimited	10	Unlimited	16

3. Significance of the EBDCs

As mentioned above, EPA received many comments in response to the Federal Register Notice published on November 24, 2004 (OPP-2004-0078) announcing the availability of the EBDC risk assessments and requests for risk reduction options. The majority of the comments supported the continued use of the EBDC products and data supporting the usefulness of the EBDCs to control plant diseases. The Agency also obtained information from internal expertise, USDA's Office of Pesticide Management and Policy (OPMP), and proprietary sources on several use sites.

Based on the information provided by a variety of resources, the Agency has determined that the EBDCs are a class of fungicides that are particularly significant to agriculture and integrated pest management (IPM) programs due to the use of the EBDCs in disease resistance management programs. The EBDCs have a multi-site mode of action, and, as such, are not considered susceptible to resistance development. This is supported by the fact that there has been no confirmed case of fungal resistance to the EBDCs after over 50 years of use. Because of these characteristics, the EBDCs are important resistance management partner chemicals for tank mixing or rotation with newer and lower risk fungicides that have single-site modes of action such as the sterol inhibitors and the strobilurins. This property helps to prolong the life of the newer and lower risk fungicides.

The Agency is committed to long-term pest resistance management strategies, and an important pesticide resistance management strategy is to avoid the repeated use of pesticides with the same or similar mode/target site of action in the same field (OPP PR Notice 2001-5). Because of this, the Agency has considered the advantages from the use of EBDCs as an important tool in fungicide resistance management programs while making its reregistration decision for all 3 EBDCs, mancozeb,

maneb, and metiram.

Further, comparing the cost per treatment of EBDCs with other fungicides, cost information demonstrated that the EBDCs are generally lower. The following paragraphs are summaries for specific use sites.

Apples

Mancozeb, maneb and metiram are registered to control several important fungal diseases on apples. The key alternatives to EBDCs include captan, strobilurins (e.g., trifloxystrobin), sterol inhibitors, and benzimidazoles. Copper, dodine, ziram, and cyprodinil are also used. However, none of these fungicides are considered to be a universal substitute for the EBDC fungicides. Fungal resistance to dodine, sterol inhibitor fungicides and benzimidazoles has developed, reducing the ability of these systemic fungicides to control apple diseases in orchards.

Dormant oil is used to decrease early season mite populations. This early mite population control reduces the total number of miticide applications needed during the course of the apple growing season. The advantage of mancozeb and metiram compared to captan is that captan cannot be used with dormant oil because this combination is phytotoxic to apple foilage. This phytotoxicity is not seen with mancozeb and metiram. Thus, indirectly, the use of EBDC fungicides in lieu of captan typically reduces the total number of miticide applications needed.

Potatoes

Mancozeb, maneb, and metiram are used to control early blight and late blight as well as several potato seed-piece diseases. The alternative fungicides include strobilurins (e.g. azoxystrobin, trifloxystrobin), chlorothalonil, propamocarb, dimethomorph, cymoxanil, copper, triphenylin hydoxide (TPTH), iprodione, and zoxamide fluazinam. However, there is no one alternative fungicide registered to control all the potato diseases for which EBDCs are registered. Because there has been reduced sensitivity of the strobilurins towards early blight on potatoes in some areas, rotational applications of strobilurins with fungicides with a different mode of action are required after every application.

Along with the EBDCs, chlorothalonil has been considered the standard early blight and late blight treatments for years. However, EBDCs are needed for use when the seasonal allowance of chlorothalonil per acre has been reached. Copper and tin products are less efficacious for early blight in some areas. Lastly, applications of TPTH may result in injury to foilage of sensitive varieties, but injury is reduced and efficacy is improved when TPTH is combined with an EBDC fungicide.

Leatherleaf Ferns 24(c) in Florida

Metiram is used to control anthracnose. Typically application occurs during high incidence of anthracnose (June through September). The key alternatives are chlorothalonil, mancozeb,

tebuconazole, cloroneb, fosetyl-aluminum, mefenoxam, thiophanate-methyl. Metiram and mancozeb provide an extra component of zinc in addition to disease control. The EBDCs' source of zinc fertilizer allows growers to apply a reduced number of zinc micro-nutrients, making the EBDCs favorable to growers due to the dual benefits.

4. Summary of Risk Mitigation Measures

The technical registrant has agreed to the following bulleted list that summarizes all mitigation measures necessary for the reregistration of metiram:

- Add a PF5 respirator to label PPE for some worker scenarios: mixer/loaders of dry flowables for aerial/chemigation applications; airblast applicators to apples; and flaggers,
- Add the use of engineering controls to labels for aerial applicators (enclosed cockpits),
- Reduce apple pre-bloom maximum application rate from 4.8 to 3.6 lbs ai/A,
- Reduce maximum number of applications for apples from 4 to 3 per year,
- Reduce maximum number of applications for potatoes from 7 to 6 per year, and
- Limit the number of applications to leatherleaf ferns to 1 per week and 10 per year.
- Metiram use on roses and dust and wettable powder formulations have been voluntarily cancelled prior to completion of the RED. Further, as a result of the voluntary cancellation of the dust formulation by the technical registrant and risks associated with this formulation, the end-use registrant has requested voluntary cancellation of their active potato seed treatment fungicide product registration (EPA Registration No. 2935-540).

E. Other Labeling Requirements

In order to be eligible for reregistration, various use and safety information will be included in the labeling of all end-use products containing metiram. For the specific labeling statements and a list of outstanding data, refer to Section V of this RED document.

1. Endangered Species Considerations

Based on available screening-level information, there is a potential concern for acute effects on listed birds and freshwater fish species, and chronic effects on listed birds and mammals should exposure actually occur. Even though metiram is only slightly acutely toxic to birds, RQs exceed the endangered species LOC (RQ range from 0.11 to 1.02) at maximum EEC levels. The Agency does not currently have data to quantify risks for metiram at the screening-level and can not preclude potential direct effects to the following taxonomic groups; listed non-target terrestrial plants, freshwater invertebrates, estuarine/marine fish, or vascular aquatic plants. These findings are based solely on EPA's screening-level assessment and do not constitute "may affect" findings under the Endangered Species Act (ESA) for any specific listed species.

The Agency has developed the Endangered Species Protection Program to identify pesticides whose use may cause adverse impacts on federally listed endangered and threatened species, and to implement mitigation measures that address these impacts. The ESA requires federal agencies to ensure that their actions are not likely to jeopardize listed species or adversely modify designated critical habitat. To analyze the potential of registered pesticide uses that may affect any particular species, EPA uses basic toxicity and exposure data developed for the REDs and considers ecological parameters, pesticide use information, the geographic relationship between specific pesticide uses and species locations and biological requirements and behavioral aspects of the particular species. When conducted, this analysis will consider regulatory changes recommended in this RED that are implemented a that time. A determination that there is a likelihood of potential effects to a listed species may result in limitations on the use of the pesticide, other measures to mitigate any potential effects, or consultations with the Fish and Wildlife Service or National Marine Fisheries Service as appropriate. If the Agency determines use of metiram "may affect" listed species or their designated critical habitat, EPA will employ the provisions in the Services regulations (50 CFR Part 402). Until that species specific analysis is completed, the risk mitigation measures being implemented through this RED will reduce the likelihood that endangered and threatened species may be exposed to metiram at levels of concern.

2. Spray Drift Management

The Agency has been working closely with stakeholders to develop improved approaches for mitigating risks to human health and the environment from pesticide spray and dust drift. As part of the reregistration process, we will continue to work with all interested parties on this important issue.

From its assessment of metiram, as summarized in this document, the Agency concludes that no drift management measures are needed for metiram. In the future, metiram product labels may need to be revised to include additional or different drift label statements. Current, drift label statements are listed in the "spray drift management" section of the label table (Table 36) in Chapter V of this RED document.

V. WHAT REGISTRANTS NEED TO DO

The Agency has determined that metiram is eligible for reregistration provided that: (i) additional data are submitted to confirm this decision; (ii) the risk mitigation measures outlined in this document are adopted; and (iii) label amendments are made to reflect these measures. To implement the risk mitigation measures, the registrants will be required to amend their product labeling to incorporate the label statements set forth in the Label Summary Table (Table 36). In the near future, the Agency intends to issue Data Call-In Notices (DCIs) requiring product-specific data and additional generic (technical grade) data at which time required label amendments will be submitted. Generally, registrants will have 90 days from receipt of a DCI to complete and submit response forms or request time extension and/or waiver requests with a full written justification. For product-specific data, the registrant will have eight months to submit data and amended labels. For generic data, due dates can

vary depending on the specific studies being required. Below are additional generic data and label amendments that the Agency intends to require for metiram to be eligible for reregistration.

A. Manufacturing-Use Products

Generic Data Requirements

The generic data base supporting the reregistration of metiram for the above eligible uses has been reviewed and determined to be substantially complete. However, the data listed below are necessary to confirm this RED.

Table 35. Outstanding and Confirmatory Generic Data Requirements for Metiram and ETU

Guideline Study Name	New OPPTS Guideline No.	Old Guideline No.
Human Health		
Preliminary Analysis (technical)	830.1700	62-1
Confined Accumulation in Rotational Crops	860.1850	165-1
2-Generation Reproduction - Rat*	870.3800	83-4
Developmental Toxicity - Rabbit**	870.3700	83-3
Acute Neurotoxicity - Rat	870.6200	81-8
Developmental Neurotoxicity - Rat**	870.6300	83-6
Comparative Thyroid Assay **	Special Study	-----
UV/Visible Absorption	830.7050	None
Ecological		
Acute Fish Toxicity Bluegill	850.1075	72-1A
Acute Aquatic Invertebrate Toxicity	850.1010	72-2A
Whole Sediment Acute Toxicity Invertebrates, Freshwater	850.1735	None
Acute Estuarine/Marine Toxicity - Fish	850.1075	72-3A
Acute Estuarine/Marine Toxicity - Mollusk	850.1025	72-3B
Acute Estuarine/Marine Toxicity - Shrimp	850.1025	72-3C
Whole Sediment Acute Toxicity Invertebrates, Estuarine/Marine	850.1740	None

Table 35. Outstanding and Confirmatory Generic Data Requirements for Metiram and ETU		
Guideline Study Name	**New OPPTS Guideline No.**	**Old Guideline No.**
Early Life Stage Fish - Estuarine/Marine	850.1350	72-4A
Life Cycle Aquatic Invertebrate - Estuarine/Marine	850.1350	72-4B
Aquatic Plant Growth - Tier I	850.5400	122-2
Seedling Germination and Seedling Emergence - Tier I	850.4225	122-1A
Vegetative Vigor - Tier I	850.4250	122-1B
Aquatic Plant Growth - Tier II	850.4400	123-2
* The study must be conducted under the current protocol. ** ETU data requirement		

Labeling for Manufacturing-Use Products

To ensure compliance with FIFRA, manufacturing-use product (MUP) labeling must be revised to comply with all current EPA regulations, PR Notices, and applicable policies. The MUP labeling must bear the labeling contained in Table 36.

B. End-Use Products

Additional Product-Specific Data Requirements

Section 4(g)(2)(B) of FIFRA calls for the Agency to obtain any needed product-specific data regarding the pesticide after a determination of eligibility has been made. Registrants must review previous data submissions to ensure that they meet current EPA acceptance criteria and if not, commit to conduct new studies. If a registrant believes that previously submitted data meet current testing standards, then the study MRID numbers should be cited according to the instructions in the Requirement Status and Registrants Response Form provided for each product. The Agency intends to issue a separate product-specific data call-in (PDCI), outlining specific data requirements.

Labeling for End-Use Products

To be eligible for reregistration, labeling changes are necessary to implement measures outlined in Section IV above. Specific language to incorporate these changes is specified in Table 36. Generally, conditions for the distribution and sale of products bearing old labels/labeling will be established when the label changes are approved. However, specific 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.

C. Labeling Changes Summary Table

In order to be eligible for reregistration, amend all product labels to incorporate the risk mitigation measures outlined in Section IV. The following table (Table 36) describes how language on the labels should be amended.

Table 36. Summary of Labeling Changes for Metiram		
Description	**Amended Labeling Language**	**Placement on Label**
Manufacturing Use Products		
For all Manufacturing Use Products	"Only for formulation as a dry flowable fungicide for use on apples and potatoes. Only for formulation as a dry flowable fungicide for Section 24(c) -- Special Local Need use on leatherleaf ferns in Florida (FL980001). Technical and end-use product labels must be revised to delete all references to and use directions for all other formulations and use patterns."	Directions for Use
One of these statements may be added to a label to allow reformulation of the product for a specific use or all additional uses supported by a formulator or user group	"This product may be used to formulate products for specific use(s) not listed on the manufacturing use product label if the formulator, user group, or grower has complied with U.S. EPA submission requirements regarding support of such use(s)." "This product may be used to formulate products for any additional use(s) not listed on the manufacturing use product label if the formulator, user group, or grower has complied with U.S. EPA submission requirements regarding support of such use."	Directions for Use
Environmental Hazards Statements Required by the RED and Agency Label Policies	"Do not discharge effluent containing this product into lakes, streams, ponds, estuaries, oceans, or other waters unless in accordance with the requirements of a National Pollutant Discharge Eliminations System (NPDES) permit and the permitting authority has been notified in writing prior to discharge. Do not discharge effluent containing this product to sewer systems without previously notifying the local sewage treatment plant authority. For guidance, contact your State Water Board or Regional Office of the Environmental Protection Agency."	Precautionary Statements
End-Use Products Intended for Occupational Use (WPS and non-WPS)		

Table 36. Summary of Labeling Changes for Metiram

Description	Amended Labeling Language	Placement on Label
PPE Requirements Established by the RED for Dry Flowable (DF) Formulation for Section 3 use on Apples and Potatoes	"Personal Protective Equipment (PPE)" "Some materials that are chemical-resistant to this product are [registrant inserts correct material(s)]. If you want more options, follow the instructions for category [insert A, B, C, D, E, F, G or H] on an EPA chemical-resistance category selection chart." "Mixers and loaders supporting aerial applications or use in chemigation systems and handlers cleaning up spills must wear: - coveralls over long-sleeved shirt and long pants - chemical-resistant gloves, - chemical-resistant footwear plus socks, - chemical-resistant apron, and - a dust/mist filtering respirator (MSHA/NIOSH approval number prefix TC-21C), or a NIOSH approved respirator with any N*, R, P, or HE filter." *Instructions to registrant: Drop the "N" type filter from the respirator statement if the pesticide product contains or is used with oil. "All other handlers must wear: - long-sleeved shirt, - long pants, - shoes and socks, - chemical resistant gloves when applying by airblast sprayer, and - a dust/mist filtering respirator (MSHA/NIOSH approval number prefix TC-21C), or a NIOSH approved respirator with any N*, R, P, or HE filter when	Immediately following/below Precautionary Statements: Hazards to Humans and Domestic Animals

Table 36. Summary of Labeling Changes for Metiram

Description	Amended Labeling Language	Placement on Label
	applying by airblast sprayer and when flagging." *Instructions to registrant: Drop the "N" type filter from the respirator statement if the pesticide product contains or is used with oil. "See engineering controls for additional options and requirements"	
PPE Requirements Established by the RED for Dry Flowable (DF) Formulations labeled for the 24(c) Special Local Need Use on Leatherleaf Ferns	"Personal Protective Equipment (PPE)" "Some materials that are chemical-resistant to this product are [registrant inserts correct material(s)]. If you want more options, follow the instructions for category [insert A, B, C, D, E, F, G or H] on an EPA chemical-resistance category selection chart." "Mixers, loader, applicators, and other handlers must wear: - long-sleeved shirt, - long pants, - shoes and socks, and - chemical-resistant gloves. "See engineering controls for additional options and requirements"	Immediately following/below Precautionary Statements: Hazards to Humans and Domestic Animals

Table 36. Summary of Labeling Changes for Metiram

Description	Amended Labeling Language	Placement on Label
Engineering Controls: Enclosed Cockpits for Aerial Applicators Handlers for Section 3 (apples and potatoes) and Section 24(c) (leatherleaf ferns) labels	Enclosed Cockpits "Engineering Controls: Pilots must use an enclosed cockpit that meets the requirements listed in the Worker Protection Standard (WPS) for agricultural pesticides [40 CFR 170.240(d)(6)] and must wear a long-sleeve shirt, long pants, shoes, and socks.	Immediately following/below Precautionary Statements: Hazards to Humans and Domestic Animals
Engineering Controls: Optional Use by Handlers for Section 3 (apples and potatoes) and Section 24(c) (leatherleaf ferns) labels	Engineering Control Statement for Optional Use (WPS Only) "Engineering Controls: When handlers 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)(5)], the handler PPE requirements may be reduced or modified as specified in the WPS."	Immediately following/below 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 exist, use detergent and hot water. Keep and wash PPE separately from other laundry." "Discard clothing or other absorbent materials that have been drenched or heavily contaminated with this product's concentrate. Do not reuse them."	Precautionary Statements: Hazards to Humans and Domestic Animals immediately following the PPE requirements

Table 36. Summary of Labeling Changes for Metiram

Description	Amended Labeling Language	Placement on Label
User Safety Recommendations	**"USER SAFETY RECOMMENDATIONS"** "Users should wash hands before eating, drinking, chewing gum, using tobacco, or using the toilet." "Users should remove clothing/ PPE immediately if pesticide gets inside, then wash thoroughly and put on clean clothing." "Users should remove PPE immediately after handling this product. Wash the outside of gloves before removing. As soon as possible, wash thoroughly and change into clean clothing."	Precautionary Statements under: Hazards to Humans and Domestic Animals (Must be placed in a box.)
Restricted-Entry Interval for the Section 3 label (apples and potatoes)	"Do not enter or allow worker entry into treated areas during the restricted entry interval (REI) of 24 hours."	Directions for Use, in Agricultural Use Requirements box
Restricted-Entry Interval for the (24(c) Special Local Need Use on Leatherleaf Ferns)	"Do not enter or allow worker entry into treated areas during the restricted entry interval (REI) of 24 hours."	Directions for Use, in Agricultural Use Requirements box
Early Reentry Personal Protective Equipment Interval for the Section 3 label (apples and potatoes) and for the (24(c) Special Local Need Use on Leatherleaf Ferns)	"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 soil or water, is: - Coveralls, - Shoes and socks, and - Chemical-resistant gloves made of any waterproof material.	Directions for Use, in Agricultural Use Requirements Box

Table 36. Summary of Labeling Changes for Metiram

Description	Amended Labeling Language	Placement on Label
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."	Place in the Directions for Use directly above the Agricultural Use Box
Application Restrictions for Section 3 labels (apples and potatoes)	Apples: Limit to 3 applications per year. Maximum application rate per application is 3.6 lb ai/A. (Label also must list this as pounds of formulated product per acre) Potatoes: Limit to 6 applications per year.	Directions for Use
Application Restrictions for Section 24(c) labels (leatherleaf ferns)	Leatherleaf Fern: Limit to a maximum of 1 application per week and 10 applications per year.	Directions for Use
Environmental Hazards Statements Required by the RED and Agency Label Policies	"This pesticide is toxic aquatic organisms. Do not apply directly to water, or to areas where surface water is present, or to inter-tidal areas below the mean high water mark. Do not contaminate water when cleaning equipment or disposing of equipment washwaters or rinsate. Apply this product only as specified on the label."	Precautionary Statements: Hazards to Humans and Domestic Animals
Spray Drift Label Language for Products Applied as a Spray	**"SPRAY DRIFT MANAGEMENT"** "A variety of factors including weather conditions (e.g., wind direction, wind speed, temperature, relative humidity) and method of application (e.g., ground, aerial, airblast, chemigation) can influence pesticide drift. The applicator must evaluate all factors and make appropriate adjustments when applying this product." **Wind Speed** "Do not apply at wind speeds greater than 15 mph. **Temperature Inversions** "If applying at wind speeds less than 3 mph, the applicator must determine if a)	Directions for Use under General Precautions or Restrictions and/or Application Instructions

Table 36. Summary of Labeling Changes for Metiram		
Description	**Amended Labeling Language**	**Placement on Label**
	conditions of temperature inversion exist, or b) stable atmospheric conditions exist at or below nozzle height. Do not make applications into areas of temperature inversions or stable atmospheric conditions." **Other State and Local Requirements** "Applicators must follow all state and local pesticide drift requirements regarding application of metiram. Where states have more stringent regulations, they must be observed." **Equipment** "All aerial and ground application equipment must be properly maintained and calibrated using appropriate carriers or surrogates." *Additional requirements for aerial applications:* 1. "The boom length must not exceed 75% of the wingspan or 90% of the rotor blade diameter." 2. "Release spray at the lowest height consistent with efficacy and flight safety. Do not release spray at a height greater than 10 feet above the crop canopy unless a greater height is required for aircraft safety." 3. "When applications are made with a crosswind, the swath must be displaced downwind. The applicator must compensate for this displacement at the up and downwind edge of the application area by adjusting the path of the aircraft upwind." *Additional requirements for ground boom application:* 1. "Do not apply with a nozzle height greater than 4 feet above the crop canopy."	

APPENDICES

Appendix A: METIRAM (CASE 0644): USE PATTERNS ELIGIBLE FOR REREGISTRATION

Application Type Timing Equipment	Formulation [EPA Reg. No.]	Max. Single App. Rate	Max. No. of Apps. Per Year	Minimum Retreatment Interval	Pre-harvest Interval (PHI)	Restrictions/Comments
Apple						
Foliar Pre-bloom schedule Aerial or Ground (Broadcast)	80% AI Dry Flowable [7969-105]	3.6 lb ai/A	3	7	Not Specified (NS)	Do not combine or integrate the 'pre-bloom' and 'extended application' schedules. Applications after bloom are prohibited. Ground applications may be made in a minimum of 20 gal/A; aerial applications may be made in a minimum of 10 gal/A. Do no apply more than 24 pounds of active ingredient per season. Do not graze livestock in treated areas.
Foliar Extended schedule Aerial or Ground (Broadcast)	80% AI Dry Flowable [7969-105]	2.4 lb ai/A	7	7	77	Do not combine or integrate the 'pre-bloom' and 'extended ' application schedules. Ground applications may be made in a minimum of 20 gal/A; aerial applications may be made in a minimum of 10 gal/A. Do no apply more than 21 pounds of active ingredient per season. Do not graze livestock in treated areas.
Potato						
Foliar Aerial, Ground (Broadcast) or Chemigation	80% AI Dry Flowable [7969-105]	1.6 lb ai/A	6	5	14; 3 in CT, DE, FL, MA, ME, MI, NH, NY, OH, PA, RI, VT	Vine kill should occur 14 days prior to harvest. Grazing of livestock in treated areas is prohibited. Ground applications may be made in a minimum of 15 gal/A; aerial applications may be made in minimum of 5 gal/A; and chemigation may be made only by sprinkler irrigation systems.

Appendix A: METIRAM (CASE 0644): USE PATTERNS ELIGIBLE FOR REREGISTRATION

Application Type Timing Equipment	Formulation [EPA Reg. No.]	Max. Single App. Rate	Max. No. of Apps. Per Year	Minimum Retreatment Interval	Pre-harvest Interval (PHI)	Restrictions/Comments
Seed Treatment	80% AI Dry Flowable [7969-105]	0.105 lb ai/100lbs of seed pieces	1	5	NS	In addition to the maximum number of foliar applications permitted, a single seed treatment application may be made on potatoes.
Leatherleaf Ferns						
Foliar Ground (Broadcast)	80% AI Dry Flowable [7969-105]	1.6 lb ai/A	10	7	NS	Limit to a maximum of 1 application per week and 10 applications per year. 24(c) Special Local Need (SLN) use in Florida only.

Appendix B

Data Supporting Guideline Requirements for the Reregistration of Metiram

GUIDE TO APPENDIX B

Appendix B contains a listing of data requirements which support the reregistration for active ingredients within the chemical case covered by this RED. It contains generic data requirements that apply in all products, including data requirements for which a "typical formulation" is the test substance.

The data table is organized in the following formats:

1. Data Requirement (Columns 1, 2 & 3). The data requirements are listed in the order of New Guideline Number and appear in 40 CFR §158. The reference numbers accompanying each test refer to the test protocols set in the Pesticide Assessment Guidance, which are available from the National Technical Information Service, 5285 Port Royal Road, Springfield, VA 22161-0002, (703) 487-4650.

2. Use Pattern (Column 4). This column indicates the use patterns for which the data requirements apply. The following letter designations are used for the given use patterns.

   A. Terrestrial food
   B. Terrestrial feed
   C. Terrestrial nonfood
   D. Aquatic food
   E. Aquatic nonfood outdoor
   F. Aquatic nonfood industrial
   G. Aquatic nonfood residential
   H. Greenhouse food
   I. Greenhouse nonfood
   J. Forestry
   K. Residential
   L. Indoor food
   M. Indoor nonfood
   N. Indoor medical
   O. Indoor residential

3. Bibliographical Citation (Column 5). If the Agency has acceptable data in its files, this column lists the identification number of each study. Normally, this is the Master Record Identification (MRID) Number, but may be a "GS" number if no MRID number has been assigned. Refer to the Bibliography (Appendix D) for a complete citation of the study.

Appendix B. Data Supporting Guideline Requirements for the Reregistration of Metiram				
New Guideline Number	**Old Guideline Number**	**Requirement**	**Use Pattern**	**Bibliographical Citation(s)**
PRODUCT USE CHEMISTRY				
830.1550	61-1	Product Identity and Composition	All	Not Applicable [1]
830.1600	61-2A	Starting Materials and Manufacturing Process	All	40507102
830.1620	61-2B	Description of Production Process	All	40507102
830.1670		Discussion of Formation of Impurities	All	
830.1700	62-1	Preliminary Analysis (Technical)	All	Data Gap*
830.6302	63-2	Color	All	00149526
830.6303	63-3	Physical State	All	
830.6304	63-4	Odor	All	
830.7050	None	UV/Visible Absorption	All	New Data Requirement (Confirmatory)
830.7200	63-5	Melting Point/Melting Range	All	00149526
830.7300	63-7	Density, Relative Density, Bulk Density	All	00149526
830.7840 830.7860	63-8	Solubility	All	40507101, 40507102, 00157997
830.7950	63-9	Vapor Pressure	All	00149526
830.7370	63-10	Dissociation Constant in Water	All	40507102
830.7550	63-11	Octanol/Water Partition Coefficient	All	00157997
830.7000	63-12	pH of Water Solutions or Suspensions	All	40507102
830.6313	63-13	Stability	All	00149526
ECOLOGICAL EFFECTS				
850.2100	71-1A	Avian Acute Oral Toxicity, Bobwhite Quail	A, B, C	40656901
850.2200	71-2A	Avian Subacute Dietary Toxicity, Bobwhite Quail	A, B, C	00108004
	71-2B	Avian Subacute Dietary Toxicity, Mallard Duck	A, B, C	00108005
850.2300	71-4A	Avian Reproduction, Bobwhite Quail	A, B, C	41082001
	71-4B	Avian Reproduction, Mallard Duck	A, B, C	42539102

Appendix B. Data Supporting Guideline Requirements for the Reregistration of Metiram				
New Guideline Number	**Old Guideline Number**	**Requirement**	**Use Pattern**	**Bibliographical Citation(s)**
850.1075	72-1A	Fish Acute Toxicity, Bluegill Sunfish	A, B, C	Data Gap*
	72-1C	Fish Acute Toxicity, Rainbow Trout	A, B, C	43525001, 45933402
850.1010	72-2A	Invertebrate Toxicity	A, B, C	44301101, Data Gap*
None	72-3A	Acute Estuarine/Marine Toxicity, Fish	A, B, C	New Data Requirement (Confirmatory)
850.1025	72-3B	Acute Estuarine/Marine Toxicity, Mollusk	A, B, C	New Data Requirement (Confirmatory)
850.1035	72-3C	Acute Estuarine/Marine Toxicity, Shrimp	A, B, C	New Data Requirement (Confirmatory)
850.1300	72-4A	Early Life Stage Fish, Freshwater	A, B, C	New Data Requirement (Confirmatory)
850.1350	72-4B	Life Cycle Aquatic Invertebrate, Freshwater	A, B, C	Data Gap*
854.1450	72-4D	Early Life Stage, Estuarine/Marine Fish	A, B, C	Reserved
850.1500	72-5	Life Cycle Fish	A, B, C	Reserved
850.1735	None	Whole Sediment Acute Toxicity Invertebrates, Freshwater	A, B, C	New Data Requirement (Confirmatory)
850.1740	None	Whole Sediment Acute Toxicity Invertebrates, Estuarine/Marine	A, B, C	New Data Requirement (Confirmatory)
850.4100	122-1A	Seedling Emergence, Tier 1	A, B, C	New Data Requirement (Confirmatory)
850.4150	122-1B	Vegetative Vigor, Tier 1	A, B, C	New Data Requirement (Confirmatory)
850.4225	123-1A	Seedling Germination and Seedling Emergence, Tier 2 on TEP	A, B, C	Reserved
850.4250	123-1B	Vegetative Vigor, Tier 2 on TEP	A, B, C	Reserved
850.5400	122-2A	Aquatic Plant Growth, Tier 1 on TEP	A, B, C	Data Gap New Data Requirement (Confirmatory)
850.4400	123-2B	Aquatic Plant Toxicity Test Using *Lemma spp.*, Tier 2	A, B, C	43199601, Data Gap*
850.3020	141-1	Honey Bee Acute Contact Toxicity	A, B, C	66220 (Duplicate of 132710)
TOXICOLOGY				
870.1100	81-1	Acute Oral Toxicity, Rat	A, B, C	40497002, 40497005

Appendix B. Data Supporting Guideline Requirements for the Reregistration of Metiram

New Guideline Number	Old Guideline Number	Requirement	Use Pattern	Bibliographical Citation(s)
870.1200	81-2	Acute Dermal Toxicity, Rabbit/Rat	A, B, C	40497007, 40497008
870.1300	81-3	Acute Inhalation Toxicity, Rat	A, B, C	40497010
870.2400	81-4	Primary Eye Irritation, Rabbit	A, B, C	40497012
870.2500	81-5	Primary Skin Irritation	A, B, C	40497004
870.2600	81-6	Dermal Sensitization	A, B, C	40497006
870.6200	81-8	Acute Neurotoxicity Screening Battery	A, B, C	New Data Requirement (Confirmatory)
870.3100	82-1A	90-Day Subchronic Feeding, Rodent	A, B, C	126738 (Acc. No 249885), 40290601, 42539101, 42595001
870.3150	82-1B	90-Day Subchronic Feeding, Nonrodent	A, B, C	31591 (Acc. No 242190)
870.3200	82-2	21-Day Dermal, Rabbit/Rat	A, B, C	40497001
870.3465	82-4	90-Day Inhalation, Rat	A, B, C	164083 (Acc. Nos. 263914, 263915), 40044701, 40713301
870.4100	83-1A	Chronic Feeding Toxicity, Rodent	A, B, C	98449, 98450 (Acc. Nos.247209-247213), 41163101
	83-1B	Chronic Feeding Toxicity, Nonrodent (Dog)	A, B, C	42133101, 42491401
870.4200	83-2B	Chronic Carcinogenicity (Feeding), Mouse	A, B, C	30245 (Acc. Nos. 242192, 242193)
870.3700	83-3A	Prenatal Developmental Toxicity, Rat	A, B, C	30565 (Acc. No. 242188)
	83-3B	Prenatal Developmental Toxicity, Rabbit	A, B, C	40711401, Reserved
870.3800	83-4	2-Generation Reproduction and Fertility Effects, Rat	A, B, C	98431 (Acc. No. 247214), Data Gap*
870.4300	83-5	Combined Chronic Toxicity/Carcinogenicity Study, Rat	A, B, C	24720913, 41163101
870.6300	83-6	Developmental Neurotoxicity Study, Rat	A, B, C	Reserved
870.5100	84-2	Bacterial Reverse Gene Mutation Assay Test	A, B, C	0148682
870.5300		Detection of Gene Mutations in Somatic Cells in Culture, Mammalian	A, B, C	00148680
870.5385		Structural Chromosomal Aberrations	A, B, C	00163786
870.5900		Cytogenics	A, B, C	00148681

Appendix B. Data Supporting Guideline Requirements for the Reregistration of Metiram				
New Guideline Number	**Old Guideline Number**	**Requirement**	**Use Pattern**	**Bibliographical Citation(s)**
870.5500	84-4	Other Genotoxic Effects (Unscheduled DNA Synthesis)	A, B, C	00149528
870.7485	85-1	General Metabolism, Rat	A, B, C	155160, 155161 (Acc. No 259892)
870.7600	85-2	Dermal Absorption (Penetration), Rat	A, B, C	155160, 155161 (Acc. No 259892)
OCCUPATIONAL/RESIDENTIAL EXPOSURE				
875.2100	132-1A	Foliar Residue Dissipation	A, B, C	41339901 (Apple DFR)
ENVIRONMENTAL FATE				
835.2120	161-1	Hydrolysis	A, B, C	00146764, 00155189, 00161937
835.2240	161-2	Photodegradation, Water	A, B, C	00155190, 00161938
835.2410	161-3	Photodegradation, Soil	A, B, C	00157031
835.4100	162-1	Aerobic Soil Metabolism Study	A, B, C	45906901, 45145203, 00155288
835.4200	162-2	Anaerobic Soil Metabolism Study	A, B, C	00155288, Reserved
835.4400	162-3	Anaerobic Aquatic Metabolism Study	A, B, C	Reserved
835.4300	162-4	Aerobic Aquatic Metabolism Study	A, B, C	459334401
835.1240		Leaching	A, B, C	40576301, 00155288
835.6100	164-1	Terrestrial Field Dissipation Study	A, B, C	00161935, 41440801, 41440802
835.1950	165-4	Bioaccumulation in Fish	A, B, C	Waived
RESIDUE CHEMISTRY				
860.1100	171-2	Chemical Identity	A, B, C	40507102
860.1200	171-3	Directions for Use	A, B, C	Product Labels
860.1300	171-4A	Nature of the Residue, Plants	A, B, C	00088894, 00160789, 00160790, 41695901, 41695902, 41695907, 41695908, 41695909, 41695910, 43064001
	171-4B	Nature of the Residue, Livestock	A, B, C	00088894, 00157034, 00160534, 00161338, 41171601, 41695903, 41695904, 41695905, 41695906, 43064001

Appendix B. Data Supporting Guideline Requirements for the Reregistration of Metiram				
New Guideline Number	**Old Guideline Number**	**Requirement**	**Use Pattern**	**Bibliographical Citation(s)**
860.1340	171-4C	Residue Analytical Method, Plants	A, B, C	00063821, 00098644, 00098677, 00098689, 00157032, 00157033, 00160784, 00160785, 40540009, 40540010, 40587401, 40587402, 40587403, 40587404, 40581405, 40587406, 41076201, 41076202, 41076203, 41076204, 41076205, 41076206, 42078601, 43357201
	171-4D	Residue Analytical Method, Animals	A, B, C	00098685, 00160639, 00160786, 00161939, 42078601
860.1360	171-4M	Multiresidue Methods	A, B, C	40730001, 40730002
860.1380	171-4E	Storage Stability, Plants	A, B, C	40540001, 40540002, 40540003, 40540004, 40540005, 40540006, 40540007, 40540008, 40540010, 40587407, 40587601, 40617401, 40617402, 40642101, 40642102, 40655101, 40655102, 40838901, 40962801, 41112201, 41112202, 41112203, 41112204, 41137601, 41188601, 41188602, 41188603, 41188604, 41188605, 41188606, 41188607, 41294401, 43064001, 43357201
		Storage Stability, Livestock	A, B, C	40587601, 40962801
860.1480	171-4J	Magnitude of Residues in Meat, Milk, Poultry and Eggs	A, B, C	40062801, 40063802
860.1850	165-1	Confined Rotational Crops	A, B, C	41904801, Data Gap*
860.1900	165-2	Field Rotational Crops	A, B, C	Reserved
Pome Fruits Group				
860.1500	171-4K	Crop Field Trials (Apple)	A, B, C	40587406, 41076203, 41731801, 41831501, 42036901, 43357201
Root and Tuber Vegetables Group				
860.1500	171-4K	Crop Field Trials (Potato)	A, B, C	40540009
Processed Food/Feed Group				
860.1520	171-4L	Processed Food (Apple)	A, B, C	40587402
		Processed Food (Potato)	A, B, C	40540010

[1] Data are not required for the unregistered TGAI.
* These studies were required under a previous DCI (GDCI-014601-16149), therefore data remain outstanding.

APPENDIX B2

Data Supporting FIFRA Guideline Requirements for the EBDC Metabolite/Degradate ETU

Guideline Requirement			Use Pattern	MRID Citation
Guideline Number		Study Title		
New	Old			
	ECOLOGICAL EFFECTS			
850.1010	72-2A	Acute Aquatic Invertebrate Toxicity - *Daphnia magna*	All	405910402, 46020901
850.1075	72-1	Acute Toxicity - Estuarine/Marine Fish	All	New Data Requirement (Confirmatory)
850.1025	72-3B	Acute Toxicity - Estuarine/Marine Mollusk	All	New Data Requirement (Confirmatory)
	72-3C	Acute Toxicity - Estuarine/Marine Shrimp	All	New Data Requirement (Confirmatory)
850.1075	72-1A	Acute Fish Toxicity - Bluegill	All	New Data Requirement (Confirmatory)
850.1075	72-1C	Fish Toxicity Rainbow - Trout	All	45910401, 46020903
850.1300	72-4B	Life Cycle Aquatic Invertebrate for freshwater and estuarine/marine	All	Reserved - Potential New Data Requirement
850.1400	72-4	Fish Early Life Stage for freshwater and estuarine/marine	All	Reserved - Potential New Data Requirement
850.4400	122-2	Aquatic Plant Growth, Tier I	All	Data Gap*
	123-2	Aquatic Plant Growth, Tier II	All	45910403, 46020902 (supplemental), Data Gap*

Guideline Requirement			Use Pattern	MRID Citation
Guideline Number		Study Title		
New	Old			
TOXICOLOGY				
870.3700	83-3	Developmental Toxicity Study in Rabbits	All	New Data Requirement (Confirmatory)
870.3800	83-4	2 Generation Reproductive Toxicity Study	All	New Data Requirement (Confirmatory)
870.4100	83-1A	Chronic Feeding Toxicity - Rodent	All	NTP Bioassay
870.4100	83-1B	Chronic Feeding Toxicity - Non-Rodent	All	42338101, 42338102
870.6300	None	Developmental Neurotoxicity Study	All	New Data Requirement (Confirmatory)
None	None	Comparative Thyroid Toxicity Study in Young and Adult Rats	All	New Data Requirement (Confirmatory)
ENVIRONMENTAL FATE				
835.2120	161-1-SS	Hydrolysis	All	40466103
835.2240	161-2-SS	Photodegradation - Water	All	40466102
835.2410	161-3-SS	Photodegradation - Soil	All	40466101
835.4100	162-1-SS	Aerobic Soil Metabolism	All	40838701, 45156401, 45225101 (all supplemental)†
835.4400	162-3-SS	Anaerobic Aquatic Metabolism	All	00163335†
835.1240	163-1-SS	Leaching/Adsorption/Desorption	All	40588301 (supplemental)
835.6100	164-1-SS	Terrestrial Field Dissipation	All	00088923 (supplemental)
None	165-4-SS	Bioaccumulation in Fish	All	Waived

* These studies were required under a previous DCI, GDCI-014504-16148, which was issued in April 1987. Data remain outstanding.

† Registrants must completely characterize bound species to fulfill these guideline requirements.

Appendix C

TECHNICAL SUPPORT DOCUMENTS

Additional documentation in support of this RED is maintained in the OPP docket, located in Room 119, Crystal Mall #2, 1801 South Bell Street, Arlington, VA. It is open Monday through Friday, excluding legal holidays, from 8:30AM to 4PM.

Public docket OPP-2004-0078 initially contained preliminary risk assessments and related documents as of November 24, 2004. Ninety days later the first public comment period closed. The EPA then considered comments, revised the risk assessment, and added the formal "Response to Comments" document and the revised risk assessment to docket OPP-2005-0177 in December 2005.

All documents, in hard copy form, may be viewed in the OPP docket room or downloaded and/or viewed via the Internet at the following Federal Docket Management Docket (FDMS) site:

http://www.regulations.gov

These documents include:

HED Documents:

1. Kit Farwell. *Metiram. Health Effects Division (HED) Human Health Risk Assessment to Support Reregistration.* June 13, 2005.
2. Christine Olinger. *ETU from EBDCs: Health Effects Division (HED) Human Health Risk Assessment for the Common Metabolite/Degradate ETU to Support Reregistration.* June 8, 2005.
3. Felecia Fort. *Mancozeb, Maneb, and Metiram: Revised Aggregate Dietary Assessment of the Common Metabolite/Degradate Ethylene Thiourea (ETU) to Support the Reregistration including the Aggregate ETU Drinking Water Assessment.* May 26, 2005.
4. Felecia Fort. *Metiram Acute, Chronic, and Cancer Dietary Exposure Assessments for the Reregistration Eligibility Decision.* June 1, 2005.
5. Christine Olinger. *Metiram. Revised Residue Chemistry Chapter of the Reregistration Eligibility Decision.* June 23, 2005.
6. Timothy Dole. *Metiram. 2nd Revised Occupational and Residential Exposure Assessment and Recommendations for the Reregistration Eligibility Decision Document.* June 8, 2005.
7. Linda L. Taylor. *Metiram. Reregistration Branch 1/Health Effects Division Response to Comments by BASF Corporation - Agricultural Products [dated February 22, 2005, March 14, 2005, April 7, 2005].* July 6, 2005.

EFED Documents:

1. Gabe Patrick, Mohammed Ruhman, and Ronald Parker. *Environmental Fate and Ecological Risk Assessment for Metiram, Section 4 Reregistration for Control of Fungal Diseases on Apples, Potatoes, Potato seed, Certain Ornamental Plants and Tobacco Seedling Plants (Phase 3 Response).* June 21, 2005.
2. Gabe Patrick, Mohammed Ruhman, and Ronald Parker. *Environmental Fate and Ecological Risk Assessment for Ethylenethiourea (ETU) a Common Degradate of the Ethylenebisdithiocarbamate Fungicides (EBDCs): Metiram, Mancozeb, and Maneb. A Part of EFED Section 4 Reregistrations for Control of Fungal Diseases on Various Crops, A Forestry Use on Douglas Firs, Ornamental Plantings, and Turf.* June 21, 2005.

BEAD Documents:

1. Richard Michell, Bill Phillips, and David Donaldson. *BEAD Deliverables for the EBDC RED.* May 23, 2005.
2. Jenna Carter. *Usage Report in Support of the Metiram Reregistration*. March 31, 2005.

Appendix D

CITATIONS CONSIDERED TO BE PART OF THE DATA BASE SUPPORTING THE METIRAM REREGISTRATION DECISION (BIBLIOGRAPHY)

GUIDE TO APPENDIX D

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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30565	Palmer, A.K.; Simons, R. (1979) Effect of Metiram Technical on Pregnancy of the Rat: BSF 302/79616. (Unpublished study includ- ing submitter summary, received Apr 10, 1980 under 279-2514; prepared by Huntingdon Research Centre, submitted by FMC Corp., Philadelphia, Pa.; CDL:242188-A)
31591	Sortwell, R.J.; Allen, D.G.; Heywood, R.; et al. (1979) Metiram: (Containing 2.2% Ethylenethiourea) Oral Toxicity Study in Rhesus Monkeys: BSF 267/78263. Final Report. (Unpublished study in- cluding submitter summary, received Apr 10, 1980 under 279-2514; prepared by Huntingdon Research Centre, submitted by FMC Corp., Philadelphia, Pa.; CDL:242190-A)
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98431	Cozens, D.D.; Simons, R.; Clark, R.; et al. (1981) Effect of Metiram Technical on Reproductive Function of Multiple Genera- tions in the Rat: BSF 200/80692. (Unpublished study received Apr 8, 1982 under 279-2032; prepared by Huntingdon Research Centre, England, submitted by FMC Corp., Philadelphia, Pa.; CDL: 247214-A)
98449	Hunter, B.; Barnard, A.V.; Street, A.E.; et al. (1981) Metiram Toxicity and Tumorigenicity in Prolonged Dietary Administration to the Rat: BSF 199/80391; WNT No. 77/951. Final rept. (Unpublished study received Apr 8, 1982 under 279-2032; prepared by Huntingdon Research Centre, England, submitted by FMC Corp., Philadelphia, Pa.; CDL:247211-A; 247209; 247210; 247212; 247213)
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108004	Fink, R. (1974) Final Report: Eight-day Dietary LCI50^--Bobwhite Quail: Project No. 104-105. (Unpublished study received Apr 2, 1974 under 279-2032; prepared by Truslow Farms, Inc., submitted by FMC Corp., Philadelphia, Pa.; CDL:132451-A)
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155288	Keller, E.; Huber, R. (1985) [The Fate of Metiram in Soil]: Rep. No. 2208. Unpublished compilation prepared by BASF AG. 29 p.
157032	Novak, R. (1986) Determination of Residues of Polyram and Ethylene-thiourea in Apples: NPC Project No. 86-2001: FMC-01-85. Unpub- lished study prepared by NPC, Inc. and Enviro-Bio-Tech, Ltd. 27 p.
157033	Novak, R. (1986) Determination of Residues of Polyram and Ethylene-thiourea in Potatoes: NPC Project No. 86-2001: FMC-02-85. Un-published study prepared by NPC, Inc. and Enviro-Bio-Tech, Ltd. 20 p.
157034	Holloway, C.; Kargarotos, B.; Kurth, B.; et al. (1986) The Bioki- netics and Metabolism of Metiram Complex in Lactating Goats: NATEC Projects NA 85 9658, NA 85 9668, NA 85 9676 and NA 85 9678. Unpublished study prepared by NATEC Institute. 131 p.
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160639	Cameron, D.; Gummer, J. (1986) Residues of ETU (Ethylene Thiourea) in Milk and Tissues of Dairy Cows following Oral Administration of Metiram: HRC Report No. BSF/443/86353/b. Unpublished study prepared by Huntingdon Research Centre. 34 p.
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160786	Roberts, R.; Cameron, D.; Gummer, J. (1986) Residues of Metiram in Milk and Tissues of Dairy Cows: HRC Study No.: BSF/443/86353. Unpublished study prepared by Huntingdon Research Centre. 40 p.
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161939	Roberts, N.; Fairley, C.; Gummer, J.; et al. (1986) The Determination of Residues of Metiram in the Eggs and Tissues of the Laying Hen following Oral Gavage of Metiram: BSF 449BR/86777b. Unpublished study prepared by Huntingdon Research Centre Ltd. 133 p.
163786	Ivett, J. (1986) Mutagenicity Evaluation of Metiram Technical K38/ 33A in the Rat Bone Marrow: Cytogenetic Assay: Amended Final Rept.: LBI Proj. No. 22202. Unpublished study prepared by Lit- ton Bionetics, Inc. 29 p.
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40044701	Ulrich, C. (1986) Thirteen Week Subchronic Inhalation Toxicity Study on Metrim in Rats - Final Report: Laboratory Project ID: 312-015: BASF Doc. No. 86/0407. Unpublished study prepared by International Research and Development Corp. 385 p.
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Appendix E

PLACEHOLDER FOR GENERIC DATA CALL-IN (DCI)

This is a placeholder for the generic data call-in, which 1ists confirmatory studies for the active ingredient metiram that must be conducted as a condition of metiram's continued registration. The DCI will be issued at a future date.

Appendix F

PLACEHOLDER FOR PRODUCT SPECIFIC DATA CALL-IN (PDCI)

This is a placeholder for the product specific generic data call-ins, which 1ist studies necessary for the reregistration of products containing the active ingredient metiram. The PDCI will be issued at a future date.

Appendix G

EPA'S BATCHING OF METIRAM 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 METIRAM as the 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 that the Agency is not describing batched products as "substantially similar" since some products within 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 the 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 a batch, or to generate all the required acute toxicological studies for each of their own products. If a 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 a 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 today's 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, 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 a registrant supplies the data to support a batch of products, he/she must select 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.

Two products were found which contain Metiram as the active ingredient. These products have been placed a no batch group in accordance with the active and inert ingredients and type of formulation.

Batching Instructions:

No Batch: Each product in this Batch should generate their own data.

NOTE: The technical acute toxicity values included in this document are for informational purposes only. The data supporting these values may or may not meet the current acceptance criteria.

	EPA Reg. No.	Percent Active Ingredient
No Batch	7969-105	80.0

Appendix H

LIST OF REGISTRANTS SENT DATA CALL-IN (DCI)

This is a placeholder for the list of registrants, which will be generated at a future date, just before the DCI is mailed.

Appendix I

LIST OF ELECTRONICALLY AVAILABLE FORMS

Pesticide Registration Forms are available (in PDF format and require the Acrobat reader) at the EPA internet site: http://www.epa.gov/opprd001/forms/.

Instructions

1. Print out and complete the forms. (Note: Form numbers that are bolded can be filled out on your computer then printed.)

2. The completed form(s) should be submitted in hardcopy in accord with the existing policy.

3. Mail the forms, along with any additional documents necessary to comply with EPA regulations covering your request, to the address below for the Document Processing Desk.

DO NOT fax or e-mail any form containing 'Confidential Business Information' or 'Sensitive Information.'

If you have any problems accessing these forms, please contact Nicole Williams at (703) 308-5551 or by e-mail at williams.nicole@epa.gov.

The following Agency Pesticide Registration Forms are currently available via the internet: at the following locations:

8570-1	Application for Pesticide Registration/Amendment	http://www.epa.gov/opprd001/forms/8570-1.pdf
8570-4	Confidential Statement of Formula	http://www.epa.gov/opprd001/forms/8570-4.pdf
8570-5	Notice of Supplemental Registration of Distribution of a Registered Pesticide Product	http://www.epa.gov/opprd001/forms/8570-5.pdf
8570-17	Application for an Experimental Use Permit	http://www.epa.gov/opprd001/forms/8570-17.pdf
8570-25	Application for/Notification of State Registration of a Pesticide To Meet a Special Local Need	http://www.epa.gov/opprd001/forms/8570-25.pdf
8570-27	Formulator's Exemption Statement	http://www.epa.gov/opprd001/forms/8570-27.pdf
8570-28	Certification of Compliance with Data Gap Procedures	http://www.epa.gov/opprd001/forms/8570-28.pdf
8570-30	Pesticide Registration Maintenance Fee Filing	http://www.epa.gov/opprd001/forms/8570-30.pdf
8570-32	Certification of Attempt to Enter into an Agreement with other Registrants for Development of Data	http://www.epa.gov/opprd001/forms/8570-32.pdf
8570-34	Certification with Respect to Citations of Data (PR Notice 98-5)	http://www.epa.gov/opppmsd1/PR_Notices/pr98-5.pdf
8570-35	Data Matrix (PR Notice 98-5)	http://www.epa.gov/opppmsd1/PR_Notices/pr98-5.pdf

8570-36	Summary of the Physical/Chemical Properties (PR Notice 98-1)	http://www.epa.gov/opppmsd1/PR_Notices/pr98-1.pdf
8570-37	Self-Certification Statement for the Physical/Chemical Properties (PR Notice98-1)	http://www.epa.gov/opppmsd1/PR_Notices/pr98-1.pdf

Pesticide Registration Kit www.epa.gov/pesticides/registrationkit/

Dear Registrant:

For your convenience, we have assembled an online registration kit which contains the following pertinent forms and information needed to register a pesticide product with the U.S. Environmental Protection Agency's Office of Pesticide Programs (OPP):

1. The Federal Insecticide, Fungicide, and Rodenticide Act (FIFRA) and the Federal Food, Drug and Cosmetic Act (FFDCA) as Amended by the Food Quality Protection Act (FQPA) of 1996.

2. Pesticide Registration (PR) Notices

   a. 83-3 Label Improvement Program--Storage and Disposal Statements
   b. 84-1 Clarification of Label Improvement Program
   c. 86-5 Standard Format for Data Submitted under FIFRA
   d. 87-1 Label Improvement Program for Pesticides Applied through Irrigation Systems (Chemigation)
   e. 87-6 Inert Ingredients in Pesticide Products Policy Statement
   f. 90-1 Inert Ingredients in Pesticide Products; Revised Policy Statement
   g. 95-2 Notifications, Non-notifications, and Minor Formulation Amendments
   h. 98-1 Self Certification of Product Chemistry Data with Attachments (This document is in PDF format and requires the Acrobat reader.)

Other PR Notices can be found at http://www.epa.gov/opppmsd1/PR_Notices

3. Pesticide Product Registration Application Forms (These forms are in PDF format and will require the Acrobat reader).

   a. EPA Form No. 8570-1, Application for Pesticide Registration/Amendment
   b. EPA Form No. 8570-4, Confidential Statement of Formula
   c. EPA Form No. 8570-27, Formulator's Exemption Statement
   d. EPA Form No. 8570-34, Certification with Respect to Citations of Data
   e. EPA Form No. 8570-35, Data Matrix

4. General Pesticide Information (Some of these forms are in PDF format and will require the Acrobat reader).

   a. Registration Division Personnel Contact List
   b. Biopesticides and Pollution Prevention Division (BPPD) Contacts
   c. Antimicrobials Division Organizational Structure/Contact List

d. 53 F.R. 15952, Pesticide Registration Procedures; Pesticide Data Requirements (PDF format)
e. 40 CFR Part 156, Labeling Requirements for Pesticides and Devices (PDF format)
f. 40 CFR Part 158, Data Requirements for Registration (PDF format)
g.. 50 F.R. 48833, Disclosure of Reviews of Pesticide Data (November 27, 1985)

Before submitting your application for registration, you may wish to consult some additional sources of information. These include:

1. The Office of Pesticide Programs' website.

2. The booklet "General Information on Applying for Registration of Pesticides in the United States", PB92-221811, available through the National Technical Information Service (NTIS) at the following address:

   National Technical Information Service (NTIS)
   5285 Port Royal Road
   Springfield, VA 22161

   The telephone number for NTIS is (703) 605-6000.

3. The National Pesticide Information Retrieval System (NPIRS) of Purdue University's Center for Environmental and Regulatory Information Systems. This service does charge a fee for subscriptions and custom searches. You can contact NPIRS by telephone at (765) 494-6614 or through their website.

4. The National Pesticide Telecommunications Network (NPTN) can provide information on active ingredients, uses, toxicology, and chemistry of pesticides. You can contact NPTN by telephone at (800) 858-7378 or through their website: ace.orst.edu/info/nptn.

   The Agency will return a notice of receipt of an application for registration or amended registration, experimental use permit, or amendment to a petition if the applicant or petitioner encloses with his submission a stamped, self-addressed postcard. The postcard must contain the following entries to be completed by OPP:

   a. Date of receipt;
   b. EPA identifying number; and
   c. Product Manager assignment.

   Other identifying information may be included by the applicant to link the acknowledgment of receipt to the specific application submitted. EPA will stamp the date of receipt and provide the EPA identifying file symbol or petition number for the new submission. The identifying number should be used whenever you contact the Agency concerning an application for registration, experimental use permit, or tolerance petition.

To assist us in ensuring that all data you have submitted for the chemical are properly coded and assigned to your company, please include a list of all synonyms, common and trade names, company experimental codes, and other names which identify the chemical (including "blind" codes used when a sample was submitted for testing by commercial or academic facilities). Please provide a chemical abstract system (CAS) number if one has been assigned.