United States
Environmental Protection
Agency

Prevention, Pesticides
and Toxic Substances
(7508C)

EPA 738-R-04-014
September 30, 2004

Reregistration Eligibility Decision (RED) for

Cycloate

(*S*-ethyl cyclohexyl(ethyl)thiocarbamate)

UNITED STATES ENVIRONMENTAL PROTECTION AGENCY
WASHINGTON, D.C. 20460-0001

OFFICE OF
PREVENTION, PESTICIDES
AND TOXIC SUBSTANCES

CERTIFIED MAIL

Dear Registrant:

This is to inform you that the U.S. Environmental Protection Agency (hereafter referred to as EPA or the Agency) has completed its review of the available data and public comments received related to the risk assessments for the herbicide cycloate (*S*-ethyl cyclohexyl(ethyl)thiocarbamate). The enclosed Reregistration Eligibility Decision (RED) document for cycloate was approved on September 30, 2004. Public comments and additional data received were considered in this decision.

Based on its review, EPA has identified risk mitigation measures that the Agency believes are necessary to address the human health risks associated with the current use of cycloate. EPA is now publishing its reregistration eligibility and risk management decisions for the current uses of cycloate, and its associated human health risks. A Notice of Availability will be published in the *Federal Register* announcing a 60-day public comment period on the cycloate risk management decision. If substantive data or comments are received and indicate that any of the Agency's assumptions need to be refined and that alternate risk mitigation is warranted, EPA will make appropriate modifications at that time.

The RED and technical supporting documents for cycloate are available to the public through EPA's electronic public docket and comment system, EPA Dockets, under docket identification (ID) number **OPP-2004-0234**. The public may access EPA Dockets at *http://www.epa.gov/edockets*. In addition, the cycloate RED may be downloaded or viewed through the Agency's website at *http://www.epa.gov/pesticides/reregistration/status.htm*. Earlier information on cycloate, including public comments, can be found in EPA Dockets under docket ID number **OPP-2004-0077**.

The Cycloate RED was developed through EPA's public participation process, published in the *Federal Register* on May 14, 2004, which provides opportunities for public involvement in the Agency's pesticide tolerance reassessment and reregistration programs. Developed in partnership with USDA and with input from EPA's advisory committees and others, the public participation process encourages robust public involvement starting early and continuing throughout the pesticide risk assessment and risk mitigation decision-making process. The public participation process encompasses full, modified and streamlined versions that enable the Agency to tailor the level of review to the level of refinement of the risk assessments, as well as to the amount of use, risk, public concern and complexity associated with each pesticide. Using the public participation process, the Agency is attaining its strong commitment to both involve the public and meet statutory deadlines.

Please note that the risks summarized in the attached RED are those that result only from the use of cycloate. The Food Quality Protection Act 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 Agency has determined that some thiocarbamates (EPTC, molinate, pebulate and cycloate) share a common mechanism of toxicity, the inhibition of acetylcholinesterase. In September 2001, the Scientific Advisory Panel (SAP) concluded that there is insufficient evidence for grouping the thiocarbamate pesticides based on a common mechanism of toxicity for effects other than acetylcholinesterase inhibition. The Agency conducted a preliminary "screening level" cumulative food risk assessment for the thiocarbamates. The results of this assessment, using very conservative Tier 1 exposure assumptions, is that MOEs exceed 310 for all population subgroups. Any MOE greater than 100 is deemed acceptable by EPA. Therefore, at this time, EPA concludes that the potential cumulative risks from the thiocarbamates in general and cycloate in particular passes the "reasonable certainty of no harm" standard of the FQPA. For information regarding EPA's efforts to determine which chemicals have a common mechanism of toxicity and to evaluate the cumulative effects of such chemicals, see the policy statements released by OPP concerning common mechanism determinations and procedures for cumulating effects from substances found to have a common mechanism at *http://www.epa.gov/pesticides/cumulative*.

The Agency is in the process of developing criteria for characterizing and testing endocrine disrupting chemicals and plans to implement an Endocrine Disruptor Screening Program in the near future. Cycloate will be reevaluated at that time and additional testing may be required.

This RED also contains both generic and product-specific data that the Agency intends to require in Data Call-Ins (DCIs). Note that DCIs, with all pertinent instructions, will be sent to registrants at a later date. Additionally, for product-specific DCIs, the first set of required responses will be due 90 days from the receipt of the DCI letter. The second set of required responses will be due eight months from the receipt of the DCI letter.

As part of the RED, the Agency has determined that cycloate will be eligible for reregistration provided that all the conditions identified in this document are satisfied, including implementation of the risk mitigation measures outlined in Section IV of the document. Sections IV and V of this RED document describe labeling amendments for end-use products and data requirements necessary to implement these mitigation measures. Instructions for registrants on submitting the revised labeling can be found in the set of instructions for product-specific data that accompanies this document.

Should a registrant fail to implement any of the risk mitigation measures outlined in this document, the Agency will continue to have concerns about the risks posed by cycloate. Where the Agency has identified any unreasonable adverse effect to human health and the environment, the Agency may at any time initiate appropriate regulatory action to address this concern. At that time, any affected person(s) may challenge the Agency's action.

If you have any questions on this document or the label changes necessary for reregistration, please contact the Chemical Review Manager for cycloate, Carmen Rodia, at (703) 306-0327. For questions about product reregistration and/or the Product DCI that accompanies this document, please contact Moana Appleyard at (703) 308-8175.

/S/

Debra Edwards, Ph.D.
Director, Special Review and
Reregistration Division

Attachment

Reregistration Eligibility Decision

for

Cycloate
(*S*-ethyl cyclohexyl(ethyl)thiocarbamate)

List B
Case 2125

Approved By:

/S/

Debra Edwards, Ph.D.
Director, Special Review and
Reregistration Division

September 30, 2004

Date

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Glossary of Terms and Abbreviations

AGDCI	Agricultural Data Call-In
a.i.	Active Ingredient
aPAD	Acute Population Adjusted Dose
AR	Anticipated Residue
BCF	Bioconcentration Factor
CAS	Chemical Abstract Service
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
DWLOC	Drinking Water Level of Comparison
EC	Emulsifiable Concentrate Formulation
EC_{25} or EC_{50}	Effective Concentration (EC_{25} for terrestrial plants and EC_{50} for aquatic plants and invertebrates). The concentration of a chemical in water at which an effect is observed that is 25% or 50% of the maximum effect.
EEC	Estimated Environmental Concentration. The estimated pesticide concentration in an environment, such as a terrestrial ecosystem.
EP	End-Use Product
EPA	United States Environmental Protection Agency
FAO	Food and Agriculture Organization
FDA	Food and Drug Administration
FIFRA	Federal Insecticide, Fungicide and Rodenticide Act
FFDCA	Federal Food, Drug and Cosmetic Act
FQPA	Food Quality Protection Act
FOB	Functional Observation Battery
GENEEC	Tier I Surface Water Computer Model
GLC	Gas Liquid Chromatography
GLN	Guideline Number
HDT	Highest Dose Tested
IR	Index Reservoir
LC_{50}	Median Lethal Concentration. A statistically derived concentration of a substance that can be expected to cause death in 50% of test animals. It is usually expressed as the weight of substance per weight or volume of water, air or feed, e.g., mg/l, mg/kg or ppm.
LD_{50}	Median Lethal Dose. A statistically derived single dose that can be expected to cause death in 50% of the test animals when administered by the route indicated (oral, dermal, inhalation). It is expressed as a weight of substance per unit weight of an animal, e.g., mg/kg.
LEL	Lowest Effect Level
LOAEC	Lowest Observed Adverse Effects Concentration. The lowest concentration in an experiment at which an "adverse" health effect is seen (kg body weight/day).
LOAEL	Lowest Observed Adverse Effects Level
LOC	Level of Concern
LOD	Limit of Detection
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). The EPA's system of recording and tracking studies submitted.
MUP	Manufacturing-Use Product
NA	Not Applicable
NAWQA	USGS National Water Quality Assessment
NOAEC	No Observed Adverse Effect Concentration
NR	Not Required
NOAEC	No Observed Adverse Effects Concentration. The highest concentration of a substance a group of experimental animals is exposed to that demonstrates the absence of adverse effects observed or measured at higher concentration levels (kg body weight/day).
NOAEL	No Observed Adverse Effects Level
OPP	EPA Office of Pesticide Programs
OPPTS	EPA Office of Prevention, Pesticides and Toxic Substances
Pa	Pascal. The pressure exerted by a force of one newton acting on an area of one square meter.
PAD	Population Adjusted Dose
PCA	Percent Crop Area
PDP	USDA Pesticide Data Program
PHED	Pesticide Handler's Exposure Data
PHI	Preharvest Interval
ppb	Parts Per Billion
ppm	Parts Per Million
PPE	Personal Protective Equipment
PRN	Pesticide Registration Notice
PRZM/EXAMS	Pesticide Root Zone Model and Exposure Analysis Modeling System, which is a Tier II surface water computer model.
Q_1*	The Carcinogenic Potential of a Compound, Quantified by the EPA's Cancer Risk Model
RAC	Raw Agriculture Commodity
RBC	Red Blood Cell
RED	Reregistration Eligibility Decision
REI	Restricted Entry Interval
RfD	Reference Dose
RQ	Risk Quotient
SCI-GROW	Screening Concentration in Ground Water modeling system, which is a 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(c) of FIFRA)
TC	Toxic Concentration. The concentration at which a substance produces a toxic effect.
TD	Toxic Dose. The dose at which a substance produces a toxic effect.
TEP	Typical End-Use Product
TGAI	Technical Grade Active Ingredient
TLC	Thin Layer Chromatography
torr	A unit of pressure needed to support a column of mercury 1 mm high under standard conditions.
TRR	Total Radioactive Residue
UF	Uncertainty Factor
USDA	United States Department of Agriculture
USEPA	United States Environmental Protection Agency
USGS	United States Geological Survey
WPS	Worker Protection Standard

Executive Summary

This document presents the Agency's decision regarding the reregistration eligibility of the registered uses of cycloate. This document also presents the Agency's tolerance reassessment decision for cycloate, which includes the consideration of risk to infants and children for any potential dietary, drinking water, dermal, inhalation or oral exposures. The Agency made its tolerance reassessment decision based on the data required for reregistration, the current guidelines for conducting acceptable studies to generate such data, and published scientific literature. The Agency has found that the current uses of cycloate on garden beets, spinach and sugarbeets are eligible for reregistration, provided the changes specified in this document are made to the labels.

Use Summary

Cycloate is a broad-spectrum, pre-emergent herbicide registered for the control of annual grasses, certain perennial grasses and many broadleaf weeds on garden beets, spinach and sugarbeets. A new use on Swiss chard has been proposed by the IR-4 program. Cycloate is not for homeowner/garden use.

Sugarbeets account for more than 90% of cycloate usage. EPA estimates that approximately 679,000 pounds of active ingredient (a.i.) are used annually on a total of approximately 288,000 acres. Spinach accounts for almost 7% of cycloate usage with 45,000 pounds of a.i. applied per year on average. Garden beets receive about 17,000 pounds of a.i. annually on just under 8,000 acres treated, nearly 100% crop treated on garden beet acres.

Carcinogenicity Classification

Cycloate is classified as “not likely to be a carcinogen to humans,” therefore, no assessments were performed for cancer.

Dietary Risks

No population subgroup, including infants and children, exceeded the Agency’s level of concern for either acute or chronic dietary exposure to cycloate based upon aggregated exposure to food plus water; therefore, no mitigation was warranted for dietary exposure to cycloate.

Worker Risks

The Agency has determined that there is potential for short- and intermediate-term exposures in occupational settings from handling cycloate products during the application process (i.e., mixer/loader, applicator and mixer/loader/applicator). Short- and intermediate-term dermal risk estimates for most scenarios exceed the Agency’s level of concern at baseline personal protective equipment (PPE). However, most of these exposures can be mitigated by some level of PPE and/or engineering controls. Risk estimates from inhalation exposures remain a concern for most scenarios, even with maximum PPE and/or engineering controls. Mitigation measures include the voluntary

cancellation of the chemigation application of cycloate, requiring engineering controls (including closed cabs and closed mixing/loading systems), prohibiting on-farm impregnation of cycloate onto dry bulk fertilizer, and requiring use data to better characterize exposure from dry bulk fertilizer applications.

Post-application exposures are expected to be negligible because cycloate is incorporated into the soil either immediately or within a few hours after application, or it is injected into the soil. As a result, post-application scenarios were not assessed. However, due to the volatility of cycloate, the REI will be increased from the current 12 hours to 48 hours.

Residential and Other Nonoccupational Risks

Cycloate is not registered for any residential (home/garden) or other nonoccupational use, nor is it to be used in or around public buildings, schools or recreational areas where children or others might be exposed. Thus, there is no residential exposure to aggregate with the dietary exposure.

Ecological Risks

Cycloate use on garden beets, spinach and sugarbeets may cause adverse ecological effects at the current maximum application rate of 4 lbs. a.i./acre. Chronic risks are potentially a concern for small mammals, birds and estuarine/marine fish and invertebrates. Based on the Agency's screening level assessment, levels of concern have been exceeded for endangered species of small mammals (chronic risk) and potentially for birds (chronic risk). These findings are based solely on EPA's screening level assessment and do not constitute "may affect" findings under the ESA.

Currently, the Agency does not have data to determine the risk from cycloate use on spinach near estuarine areas to nontarget terrestrial plants. In addition, no acceptable chronic avian reproduction data were available, so chronic risks for avian species could not be assessed. Data are required to address these gaps in the ecological assessment.

Cumulative Risk

Section 408(b)(2)(D)(v) of the FFDCA requires that, when considering whether to establish, modify or revoke a tolerance, 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." OPP has determined that some thiocarbamates (EPTC, molinate, pebulate and cycloate) share a common mechanism of toxicity, the inhibition of acetylcholinesterase. In September 2001, the Scientific Advisory Panel (SAP) concluded that there is insufficient evidence for grouping the thiocarbamate pesticides based on a common mechanism of toxicity for effects other than acetylcholinesterase inhibition. Although structural and metabolic similarities exist among the thiocarbamates and there is evidence that the thiocarbamates may produce a common effect (neuropathology); however, this evidence is not definitive. The Agency has conducted a preliminary "screening level" cumulative food risk assessment for the thiocarbamates.

The results of the screening level cumulative food risk assessment, using very conservative Tier 1 exposure assumptions (using tolerance level residues, assuming 100% of all crops treated and including exposures from molinate, which is being phased out), is that MOEs exceed 310 for all population subgroups. These results are reported in a memorandum dated December 19, 2001 from Marcia Mulkey entitled, "Thiocarbamates: A Determination of the Existence of a Common Mechanism of Toxicity and a Screening Level Cumulative Food Risk Assessment." This document can be found under thiocarbamates at the EPA website entitled, "Public Comment Period Opened: Common Mechanism Determination for Thiocarbamate and Dithiocarbamate Pesticides" at *http://www.epa.gov/oppsrrd1/cumulative/thiocar.htm*. Since any MOE greater than 100 is deemed acceptable, the Agency has concluded that the potential cumulative risks from the thiocarbamates in general and cycloate in particular passes the "reasonable certainty of no harm" standard of the Food Quality Protection Act.

Summary of Mitigation

Pesticide mixer, loader and applicator risks will be mitigated by a combination of increased personal protective equipment, use of engineering controls and revised label language. Specifically, the following mitigation measures will reduce risks to agricultural workers:

- Voluntary cancellation of chemigation application of cycloate;
- Extend the cycloate REI to 48-hours;
- Require engineering controls including closed cabs and closed mixing/loading systems;
- Prohibit on-farm impregnation of cycloate onto dry bulk fertilizer; and
- Require use data to better characterize exposure from dry bulk fertilizer applications.

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 hazards arising from the currently registered uses of the pesticide; to determine the need for additional data on health and environmental effects; and to determine whether or not the pesticide meets the "no unreasonable adverse effects" criteria of FIFRA. Congress also passed the Pesticide Registration Improvement Act of 2003 to set time frames for the issuance of Reregistration Eligibility Decision (RED) documents.

On August 3, 1996, the Food Quality Protection Act of 1996 (FQPA) was signed into law. FQPA amends FIFRA to require reassessment of all tolerances that were in existence at the time of enactment by 2006. The Agency has decided that, for those chemicals that have tolerances and are undergoing reregistration, the tolerance reassessment will be completed through the reregistration process.

FQPA also amends the Federal Food, Drug and Cosmetic Act (FFDCA) to require a safety finding in tolerance reassessment based on factors including an assessment 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 mechanism could lead to the same adverse health effect as would a high level of exposure to any one of the other substances individually. OPP has determined that some thiocarbamates (EPTC, molinate, pebulate and cycloate) share a common mechanism of toxicity, the inhibition of acetylcholinesterase. Further, in September 2001, the SAP concluded that there is insufficient evidence for grouping the thiocarbamate pesticides based on a common mechanism of toxicity for effects other than acetylcholinesterase inhibition.

This document presents the Agency's decision regarding the reregistration eligibility of the registered uses of cycloate, including the consideration of risk to infants and children for any potential food, drinking water, dermal, inhalation or oral exposures. In an effort to simplify the RED, the information presented herein is summarized. More detailed information can be found in the technical supporting documents (risk assessments) for cycloate referenced in this RED. The risk assessments and related addenda are not included in this document, but are available on the Agency's website at *http://www.epa.gov/pesticides/reregistration/status.htm*, and in the OPP Public Docket.

This document consists of six sections. Section I is the introduction. Section II provides a profile of the use and usage of cycloate and its regulatory history. Section III gives an overview of the human health and environmental effects risk assessments, based on the data and information available to the Agency. Section IV presents the reregistration eligibility and risk management decisions for cycloate. Section V summarizes the label changes necessary to implement the risk

mitigation measures outlined in Section IV. Finally, in Section VI, the Appendices list all related documents and how to access them, and the Data Call-In (DCI) information.

II. Chemical Overview

A. Regulatory History

Cycloate (*S*-ethyl cyclohexyl(ethyl)thiocarbamate) was first registered in the United States on July 13, 1967, for use as a selective herbicide on sugarbeets and spinach by the Stauffer Chemical Company. The use of cycloate on garden beets was first approved on January 9, 1970. Stauffer Chemical Company transferred the cycloate registrations to ICI Americas, Inc. on December 23, 1987. On January 24, 1994, the registrant name was changed to Zeneca Agrochemicals. Zeneca Agrochemicals merged with Novartis Agribusiness in November 2000 to form Syngenta Crop Protection, Inc. Syngenta Crop Protection, Inc. sold all proprietary rights for cycloate to TRI AG, Inc. on December 1, 2000. Helm Agro US, Inc. is now the agent for TRI AG, Inc.

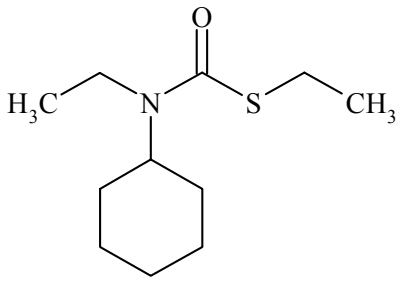
Cycloate was the subject of a Registration Standard Guidance Document that was issued on December 7, 1988 and the Residue Chemistry Science Chapter of the Guidance Document (Phase 4 reviews of available residue chemistry data) was issued on December 20, 1990. These documents summarized the regulatory conclusions based on available residue chemistry data and specified the updated generic and product-specific chemistry data required by the Agency to support the continued use of cycloate. In addition to the data requirements in the 1988 Guidance Document, Data Call-In (DCI) notices were issued on April 5, 1991 and October 18, 1995. The data received in response to the DCIs were used to reach the reregistration eligibility conclusions for cycloate that are presented in this RED.

In an effort to promote transparency of the reregistration process and include the public in developing regulatory decisions, the Agency has developed a public participation process that is used for pesticide tolerance reassessment and reregistration. This public participation process was developed in partnership with USDA, based on EPA's and USDA's experiences with the pilot public participation process used for the organophosphate pesticides, comments received from Tolerance Reassessment Advisory Committee and the public during the public comment period on the proposed process and EPA's experience with the interim process used in developing decisions for a number of non-organophosphate pesticides during the past few years. The public participation process encompasses full and modified versions that enable EPA to tailor the level of review to the level of refinement of the risk assessments, as well as to the amount of use, risk, public concern and complexity associated with each pesticide.

The Agency followed a 4-phase, modified public participation process for cycloate. Consistent with this process, EPA initiated Phase 1 of the process on March 1, 2004, by transmitting the preliminary human health and ecological risk assessments to the technical registrant for a 30-day error only correction review. In Phase 2, EPA considered the errors that were identified by the registrant and made changes in the risk assessments as appropriate. To initiate Phase 3 of the process

on May 12, 2004, the Agency published a *Federal Register* notice announcing the availability of the revised risk assessments and supporting documents for a 60-day public review and comment period. EPA received only 20 comments during this period, most expressing a need for the continued use of cycloate on garden beets, spinach and sugarbeets. None of the submitted comments were specific to the revised risk assessments or potential risk mitigation measures.

B. Chemical Identification



Pure cycloate is a colorless liquid and technical-grade cycloate is an amber liquid at room temperature with a density of 1.0243 g/ml at 20° C and an octanol/water partition coefficient (K_{ow}) of 13,000 at 20° C. Cycloate has a moderately high vapor pressure of 6.2 x 10^{-3} mm Hg at 25° C, so that losses due to volatilization or sublimation are expected to be significant. Henry's Law constant is therefore a relatively high 1.85 x 10^{-5} atm-m^3/mol. Cycloate has a moderate solubility in water of 93 mg/L at 25° C and is completely soluble in acetone, chlorobenzene, ethanol, kerosene, methyl chloride, xylene and n-octanol.

- **Common Name:** Cycloate [BSI, ISO & WSSA]
- **CAS NT-1 Systematic Chemical Name:** *S*-ethylcyclohexylethyl carbamothioate
- **Other Name:** *S*-ethyl cyclohexyl(ethyl)thiocarbamate [IUPAC]
- **Chemical Family:** Thiocarbamate
- **Case Number:** 2125
- **CAS Registry Number:** 1134-23-2
- **OPP Chemical Code:** 041301
- **Empirical Formula:** $C_{11}H_{21}NOS$
- **Molecular Weight:** 215.4 g/mole

- **Trade Name(s):** RO-NEET® 6-E and Cycloate 6-E

- **Basic Manufacturer(s):** TRI AG, Inc. and Helm Agro US, Inc.

C. Use Profile

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

Type of Pesticide: Herbicide

Summary of Use: Cycloate is a broad-spectrum, pre-emergent herbicide registered for the control of annual grasses, certain perennial grasses and many broadleaf weeds. Cycloate acts by interfering with the germination of seeds and development of seedlings.

Food: Cycloate is used on garden beets, spinach (fresh and processed) and sugarbeets. A new use on Swiss chard has been proposed by IR-4.

Non-Food: There are no registered non-food uses of cycloate products.

Residential: There are no registered residential uses of cycloate products.

Target Pests: Annual grasses; barley (*Hordeum spp.*); barnyardgrass, watergrass (*Echinochloa spp.*); black nightshade (*Solanum nigrum*); burning nettle, small stinging nettle (*Uteca urens*); common lambsquarters (*Chenopodium album*); common purslane (*Portulaca oleracea*); foxtail (*Setaria spp.*); hairy nightshade (*Solanum villosum*); henbit (*Lamium spp.*); nettleleaf goosefoot (*Chenopodium murale*); nutsedge (*Cyperus spp.*); pennsylvania smartweed (*Polygonum pensylvanicum*); redroot pigweed (*Amaranthus retroflexus*); shepherdspurse (*Capsella bursapastoris*); velvetleaf (*Abutilon theophrasti*); wild buckwheat (*Polygonum convolvulus*); and wild oat (*Avena fatua*).

Formulation Types: Formulated as an emulsifiable concentrate liquid, 73.9% active ingredient (a.i.).

Methods and Rates of Application:

Equipment: Cycloate is typically applied using groundboom equipment and then incorporated into the soil mechanically or by sprinkler irrigation (chemigation).

Application Rates: Typical application rates are similar on all three crops, ranging from 2 to 3 lbs. a.i./acre. Maximum labeled application rate is 4 lbs. a.i./acre.

Timing: Applied as a pre-plant or at-planting treatment.

Use Classification: General Use.

D. Estimated Usage of Pesticide

Table 1 summarizes the best estimates available for the uses of cycloate. The estimate for total domestic use (annual average) is approximately 679,000 pounds of a.i. on approximately 288,000 acres treated. More than 90% of cycloate's total usage is on sugarbeets, with an estimated annual average application of 617,000 pounds of a.i. used on 261,000 acres. Spinach accounts for almost 7% of cycloate usage with 45,000 pounds of a.i. applied per year on average. Garden beets receive about 17,000 pounds of a.i. annually on just under 8,000 acres treated, nearly 100% crop treated on garden beet acres.

Table 1. Cycloate Usage Summary.

Site	Lbs. Active Ingredient Applied (Weighted Average)[1]	Percent Crop Treated (Estimated Maximum)[2]	Percent Crop Treated (Weighted Average)
Garden Beets	17,000	100%	98%
Spinach, Fresh	32,000	68%	56%
Spinach, Processed	14,000	55%	42%
Sugarbeets	617,000	24%	17%

[1] Weighted Average = the most recent years and more reliable data are weighted more heavily.

[2] Estimated Maximum = the maximum percentage amount applied as estimated from available data.

Usage data primarily covers 1988 through 1999.

Calculations of the above numbers may not appear to agree because they are displayed as rounded:

- to the nearest 1,000 for acres treated or lbs. a.i.
- to the nearest whole percentage point for % of crop treated.

Sources: EPA proprietary data, USDA/NASS, CAL EPA and National Center for Food and Agricultural Policy.

III. Summary of Cycloate Risk Assessments

The following is a summary of EPA's human health and ecological effects risk findings and conclusions for the herbicide cycloate, as presented fully in the documents: "Cycloate In/On Spinach, Garden Beets, Sugarbeets and Swiss Chard. Health Effects Division (HED) Risk Assessment," dated January 28, 2004; "Cycloate: Reregistration Eligibility Document Science Chapter, PC Number 041301, Environmental Fate and Effects Division (EFED)," dated August 23, 2002; and any subsequent addenda which are cited within the RED.

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 cycloate. While the risk assessments and related addenda are not included in this RED, they are available in their entirety from the OPP Public Docket and may also be accessed on the Agency's website at *http://www.epa.gov/pesticides/reregistration/status.htm*.

A. Human Health Risk Assessment

1. Dietary Risk from Food

A brief overview of the toxicity studies used for endpoints in the dietary risk assessment is outlined below in Table 2. Further details on the toxicity of cycloate can be found in the "Cycloate In/On Spinach, Garden Beets, Sugarbeets and Swiss Chard. Health Effects Division (HED) Risk Assessment," dated January 28, 2004 and the "Cycloate Toxicology Disciplinary Chapter for the Reregistration Eligibility Decision Document," dated September 10, 2003.

Table 2. Summary of Cycloate Dietary Toxicity Endpoints.

Exposure Scenario	Dose (mg/kg/day)	Endpoint	Study (MRID No.)
Acute Dietary (U.S. General Population including infants and children)	LOAEL = 200 NOAEL = N/A UF = 300 UF_{DB} = 10 Total UF = 3,000	Neuronal cell necrosis in the pryriform cortex and/or dentate gyrus.[1]	Acute neurotoxicity study in rats (42921701, 43968001)
	Acute RfD = 0.066 mg/kg/day	**Acute PAD = 0.066 mg/kg/day**	
Chronic (Noncancer) Dietary	LOAEL = 3.1 NOAEL = 0.5 UF = 100	Spinal nerve axonal atrophy and femoral nerve alterations in female rats.[2]	Chronic toxicity/carcinogenicity study in rats (00137735)
	Chronic RfD = 0.005 mg/kg/day	**Chronic PAD = 0.005 mg/kg/day**	

[1] Cycloate may cause damage and death to nerve cells in various parts of the brain and spinal cord.

[2] Cycloate can cause damage to various nerves.

a. Toxicity of Cycloate

The Agency has reviewed all toxicity studies submitted for cycloate and has determined that the toxicological data base for cycloate is considered adequate for hazard characterization.

Acute Toxicity: A brief overview of the acute toxicity of cycloate is in Table 3. Cycloate has a low order of acute toxicity via the oral (Category III), dermal (Category IV) and inhalation (Category IV) routes of exposure. It is a moderate eye and dermal irritant (Category III) and is also a dermal sensitizer.

Table 3. Acute Toxicity Profile for Occupational Exposure to Cycloate.

Guideline Number	Study Type	MRID No.	Results	Toxicity Category
870.1100 (§81-1)	Acute Oral Toxicity (Rat)	00132791 (Ro-Neet 6-E)	LD_{50} = 3,250 mg/kg (♂) LD_{50} = 4,175 mg/kg (♀)	III
870.1200 (§81-2)	Acute Dermal Toxicity (Rabbit)	00132791 (Ro-Neet 6-E)	LD_{50} >5,000 mg/kg	IV
870.1300 (§81-3)	Acute Inhalation Toxicity (Rat)	00132792 (Ro-Neet 6-E)	LC_{50} >5.03 mg/L	IV
870.2400 (§81-4)	Acute Eye Irritation (Rabbit)	00132791 (Ro-Neet 6-E)	Moderate eye irritant.	III
870.2500 (§81-5)	Acute Dermal Irritation	00132791 (Ro-Neet 6-E)	Moderate dermal irritant.	III
870.2600 (§81-6)	Acute Dermal Sensitization	41729901 (Cycloate 98% TGAI)	Cycloate is a dermal sensitizer.	Not Applicable

Subchronic Toxicity: There are no subchronic oral toxicity studies in the rodent or dog identified in the data base for cycloate. However, the chronic oral studies in the rodent and dog (MRIDs 00077787, 00137735 and 40458401) provided frequent monitoring of clinical signs and interim measurements of body weights, food consumption, hematology, clinical chemistry and urinalysis, and the results provided insight into potential subchronic effects. In addition, a special 27-day oral neurotoxicity study and a subchronic oral neurotoxicity study (90-day) in the rat are available. Also, two subchronic inhalation toxicity studies in the rat have been conducted.

Developmental Toxicity: The data base for developmental toxicity is considered complete. The available data provided no indication of increased susceptibility (quantitative or qualitative) of rats or rabbits to *in utero* and/or post-natal exposure to cycloate.

Reproductive Toxicity: The data base for reproductive toxicity is considered complete. In a 2-generation reproduction study (MRID 41691901), cycloate was administered to rats at dose levels of 0, 2.5, 20 and 50 mg/kg/day. The parental systemic LOAEL is 20 mg/kg/day based on decreased pup body weight gain, decreased food consumption and histological findings in the nervous system (mineralization of the brain, sacral spinal cord white matter degeneration). The parental systemic NOAEL is 2.5 mg/kg/day. In the 3-generation reproduction study in the rat (MRID 00132795), the

parental systemic LOAEL is 24 mg/kg/day, based on decreased pup body weight/body weight gains. The parental systemic NOAEL is 8 mg/kg/day.

Chronic Toxicity: The data base for chronic toxicity is considered complete. In one combined chronic toxicity/carcinogenicity rat study (MRID 00137735), spinal nerve axonal atrophy and femoral nerve alterations were observed in females. The LOAEL is 3.1 mg/kg/day and the NOAEL is 0.5 mg/kg/day. In another combined chronic toxicity/carcinogenicity study in the rat (MRID 00077787), decreased cholinesterase activity (females) and neuromyopathy (cycloate can cause damage to various nerves and muscles) of the sciatic nerve and associated muscles (both sexes) were noted at the LOAEL of 8.0 mg/kg/day. A NOAEL was not achieved in this study. Dogs administered 50 mg/kg/day in the diet displayed clinical signs (loose stool), clinical chemistry alterations (increased alkaline phosphatase activity, decreased blood urea nitrogen) and histological findings in the liver (hepatocellular hypertrophy, portal tract fibrosis, central vein active-chronic inflammation), kidney (papillopathy) and adrenal gland (cortical hyperplasia and/or hypertrophy).

Carcinogenicity: The data base for carcinogenicity is considered complete. There was no evidence of carcinogenic potential of cycloate in the rat or mouse. Based on the available data, cycloate has been classified as "not likely to be carcinogenic in humans ."

Mutagenicity: Cycloate was negative in a reverse gene mutation assay in bacteria, in mammalian cell cytogenetics assays (chromosome aberration in human lymphocytes) and in a mouse bone marrow micronucleus assay. In mammalian cell cytogenetics assays (chromosome aberration and sister chromatid exchange - L5178Y mouse lymphoma cells), significant clastogenic responses at levels of high cytotoxicity and significant induction of SCEs were observed at the majority of assayed doses, which extended into the cytotoxic range. It was weakly mutagenic in the presence of S9 activation over a narrow range of severely cytotoxic levels in a mammalian cell gene mutation assay at the $TK^{+/-}$ locus in mouse lymphoma cells.

Neurotoxicity: Mammalian neurotoxicity studies for cycloate have been conducted. Acute, subchronic, chronic and reproductive toxicity and special neurotoxicity studies have demonstrated central nervous system (CNS) and peripheral nervous system (PNS) neuropathological findings in several species. Effects include cholinergic signs, abnormalities in gait and posture in the hind legs, decreased hind limb grip strength, muscle atrophy and lesions in the brain (including specific regions such as medulla and the dentate gyrus/pyriform cortex), spinal cord, spinal nerve, sciatic nerve, sural nerve and tibial nerve. Inhibition of cholinesterase and/or neurotoxic esterase activities has also been noted in several toxicity studies.

A developmental neurotoxicity study (DNT), including cholinesterase measures, in the rat has been identified as a data gap.

Dermal Absorption: A dermal absorption study in the rat (MRIDs 00164351, 40229701 and 43712502) indicated a 16% absorption of cycloate at 10 hours exposure.

Metabolism: Metabolism studies were conducted in the rat and the mouse (MRID 00132796). The predominant urinary metabolite identified in the rat and the mouse was N-ethylcyclohexylamine. There was no significant bioaccumulation of cycloate and/or its metabolites. Results indicated that cycloate was rapidly absorbed following oral administration with half-times suggesting the presence of a small population of slow metabolizers and/or excreters. The percent absorbed ranged from approximately 61% to 68%. Tissue radioactivity was low at 192 hours with most of the activity remaining in the liver and kidneys. Urinary excretion was the primary route of elimination. The predominant urinary metabolite identified was N-ethylcyclohexylamine.

b. FQPA Safety Factor

EPA has determined that a Database Uncertainty Factor (UF_{DB}) of 10x is needed to account for the lack of the DNT when assessing acute (single dose) exposure scenarios since the available data provide no basis to support reduction or removal of the default 10x factor. In addition, no special FQPA safety factor is needed since there are no residual uncertainties for pre- and/or post-natal toxicity. A 1x FQPA special safety factor for sensitivity in infants and children is to be applied across all of the risk assessments, except for occupational assessments.

c. 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 maximum acceptable dose (i.e., the dose which will result in no unreasonable adverse health effects). This dose 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. A risk estimate that is less than 100% of the PAD is not of concern to the Agency.

1) Acute PAD

For setting the aRfD, a LOAEL of 200 mg/kg/day was selected from the acute neurotoxicity study in rats. A NOAEL was not identified. There is a concern for potential developmental neurotoxicity resulting from exposure to cycloate. A UF_{DB} of 10x is needed to account for the lack of a DNT study when assessing acute (single dose) exposure scenarios. As discussed in Section III.A.1.b, no special FQPA safety factor is needed since there are no residual uncertainties for pre- and/or post natal toxicity. Thus the total uncertainty factor (UF) is 3,000 (10x for interspecies extrapolation; 10x for intraspecies variation; 3x for the lack of a NOAEL; and 10x to account for the lack of a DNT study). The aPAD was set at 0.066 mg/kg/day.

2) Chronic PAD

For setting the cRfD, a LOAEL of 3.1 mg/kg/day was selected from the combined toxicity/ carcinogenicity study in rats. The NOAEL in this study was 0.5 mg/kg/day. An uncertainty factor of 100 (10x for interspecies extrapolation; 10x for intraspecies variation; and a 1x special FQPA safety factor) was calculated. The cPAD was set at 0.005 mg/kg/day.

d. Exposure Assumptions

The acute and chronic dietary exposure/risk analysis for cycloate was conducted using the Dietary Exposure Evaluation Model-Food Commodity Intake Database (DEEM-FCID™, Version 1.30), which incorporates food consumption data from the U.S. Department of Agriculture's (USDA's) Continuing Surveys of Food Intakes by Individuals (CSFII) from 1994-1996 and 1998. The CSFII data are based on the reported food consumption by more than 20,000 individuals over two nonconsecutive survey days. For the acute and chronic exposure assessment, consumption data are averaged for the entire U.S. population and within population subgroups. Exposure estimates are reported in mg/kg body weight/day, and risk is expressed as a percent of the acute or chronic PAD.

The Agency's Metabolism Assessment Review Committee (MARC) has reviewed the cycloate toxicology and metabolism data (meeting date of November 5, 2003) and has concluded that cycloate and its cis- + trans- 3-hydroxycycloate (3HC) and cis + trans- 4-hydroxycycloate (4HC) metabolites are the residues of concern for risk assessment. Assessments for cycloate were performed using tolerance level residues at the screening Tier 1 level. Because these Tier 1 assessments were based upon tolerances, exposure is estimated for residues of cycloate and its 3HC and 4HC metabolites. Although percent crop treated data were available, they were not necessary to refine the assessment.

e. Dietary (Food) Risk Assessment

1) Acute Dietary Risk

Acute dietary risk is calculated considering what is eaten in one day and maximum, or high-end residue values in food. A risk estimate that is less than 100% of the acute population adjusted dose (aPAD), the dose at which an individual could be exposed on any given day and no adverse health effects would be expected, does not exceed the Agency's level of concern. The aPAD is the acute dietary reference dose (aRfD) adjusted for the FQPA Safety Factor.

For cycloate, the acute dietary (food only) risk does not exceed the Agency's level of concern for the U.S. population and all subgroups, including infants and children, using highly conservative assumptions. The acute dietary (food only) risk estimate is 1.1% of the aPAD at 95th percentile of exposure, for the most highly exposed population subgroup, children aged 3-5 years. Exposure and risk estimates are summarized in Table 4.

2) Chronic Dietary Risk

Chronic dietary risk is calculated by using the average consumption value for food and average residue values on those foods. A risk estimate that is less than 100% of the chronic population adjusted dose (cPAD), the dose at which an individual could be exposed over the course of a lifetime and no adverse health effect would be expected, does not exceed the Agency's level of concern. The cPAD is the chronic dietary reference dose (cRfD) adjusted for the FQPA Safety Factor.

The chronic dietary (food only) risk estimates from exposures to cycloate in food do not exceed the Agency's level of concern (i.e., they are less than 100% of the cPAD) for the U.S. population and all subgroups using highly conservative assumptions. The chronic dietary (food only) risk estimate is 5.5% of the cPAD for the most highly exposed population subgroup, children aged 3-5 years. Exposure and risk estimates are summarized in Table 4.

Table 4. Summary of Dietary Exposure and Risk for Cycloate.

Population Subgroups	Acute Dietary (95th Percentile)		Chronic Dietary	
	Dietary Exposure (mg/kg/day)	% aPAD	Dietary Exposure (mg/kg/day)	% cPAD
U.S. General Population	0.000408	<1.0	0.000119	2.4
All Infants (<1 year old)	0.000672	1.0	0.000172	3.4
Children (1-2 years old)	0.000720	1.1	0.000259	5.2
Children (3-5 years old)	0.000755	**1.1**	0.000277	**5.5**
Children (6-12 years old)	0.000556	<1.0	0.000205	4.1
Youth (13-19 years old)	0.000307	<1.0	0.000103	2.1
Adults (20-49 years old)	0.000261	<1.0	0.000083	1.7
Females (13-49 years old)	0.000278	<1.0	0.000088	1.8
Seniors (50+ years old)	0.000254	<1.0	0.000105	2.1

For more information on the dietary risk assessment, please refer to the Dietary Exposure and Risk Analysis sections of the "Cycloate In/On Spinach, Garden Beets, Sugarbeets and Swiss Chard. Health Effects Division (HED) Risk Assessment," dated January 28, 2004.

2. Dietary Risk from Drinking Water

Drinking water exposure to pesticides can occur through ground and surface water contamination. In assessing drinking water risks, EPA considers acute (one day), chronic (long-term) and cancer (lifetime) exposure, and uses either modeling or actual monitoring data if available, to estimate those risks. To determine the maximum allowable risk contribution from water, EPA first looks at how much of the overall allowable risk is contributed by food and then calculates a "drinking water level of comparison" (DWLOC) to determine whether modeled or monitoring exposure estimates exceed this level. The DWLOC represents the maximum contribution to the human diet that may be attributed from residues of a pesticide in drinking water after food exposure is subtracted from the aPAD or cPAD. Risks from drinking water are assessed by comparing the DWLOC to estimated environmental concentrations (EECs) in both surface and ground water. EECs that are less than the DWLOC are not of concern.

The Agency has determined that cycloate *per se* is the residue of concern in drinking water. Fate studies indicate that the major dissipation route for cycloate is volatilization, but when applied to soil in a manner to prevent volatilization, cycloate is moderately persistent and is expected to be moderately mobile. In various limited water monitoring studies, mostly in high use areas, cycloate was occasionally detected in ground water, but never in excess of 2 parts per billion (ppb). These data support the modeling conclusion that risks are below the Agency's level of concern (LOC) for all population subgroups. There is no information on the effects of water treatment on cycloate or any degradate.

According to the U.S. Geological Survey (1992 pesticide annual use data), about 94% of cycloate use was on sugarbeets, so EPA's water analysis focused on this use. The Minnesota sugarbeet use pattern was selected for both the surface and ground water assessments as this is expected to represent a reasonable worst case situation, that is, greatest potential for drinking water contamination. The maximum use rate on sugarbeets is 4 lbs. a.i./acre. One application per growing season (spring or fall) is allowed.

a. Surface Water

Modeling: The Tier II screening models, Pesticide Root Zone Model and Exposure Analysis Modeling System (PRZM/EXAMS), with the Index Reservoir and Percent Crop Area adjustment (IR-PCA PRZM/EXAMS) were used to estimate cycloate residues in surface water used for drinking water. These screening models provide more refined, less upper-bound assumptions.

For cycloate, the acute (peak) and chronic (90^{th} percentile) surface water EECs are 52 ppb and 10 ppb, respectively. The modeled EECs are less than the acute and chronic DWLOCs calculated for the U.S. General Population (2,296 ppb and 171 ppb, respectively) and all population subgroups. Acute DWLOCs were smallest (and were almost identical) for the population subgroups: infants <1 year of age, children aged 1-2 years, children aged 3-4 years and children aged 6-12 years. For these

subpopulations, available acute DWLOC values ranged from 652 to 654 ppb, which were still large compared to the acute EECs. Similarly, chronic DWLOCs were smallest (and were almost identical) for the population subgroups: infants <1 year of age, children aged 1-2 years, children aged 3-4 years and children aged 6-12 years. For these subpopulations, the chronic DWLOC values ranged from 47 to 48 ppb, all large when compared to the chronic EECs. Therefore, aggregate exposures to cycloate in food and water, both acute and chronic, were below the Agency's LOC for all population subgroups, including children (3-5 years), the population subgroup with the highest risk estimate (see Tables 5 & 6).

Monitoring: The state of Minnesota does not monitor for cycloate in the Red River of the North Valley (M. Zabel, Minnesota Department of Agriculture, November 2, 2000). North Dakota also does not monitor for cycloate (N. Bartleson, North Dakota Health Department, October 31, 2000). California has not conducted any monitoring studies for cycloate in surface water (K. Starner, California Department of Pesticide Regulation, October 31, 2000).

The only surface water monitoring information available is from the state of Washington's Department of Ecology where they monitored for cycloate (parent only) in 10 creeks in the Puget Sound area in April to May of 1998 (G. Bortleson and J. Ebbert, USGS WRIR 00-4118). No cycloate was detected (limit of detection is >0.14 ppb). The sampling locations did not appear to be in sugarbeet growing areas. However, garden beet and spinach seed production are located in that area.

b. Ground Water

Modeling: Estimated ground water concentrations are based on the Screening Concentration in Ground Water (SCI-GROW) model, which is a Tier I assessment that provides a high-end estimate. The SCI-GROW model generates a single EEC value of pesticide concentration in ground water used for drinking water and provides a ground water screening concentration for use in determining potential risk to human health from drinking water contaminated with a pesticide. Further, this EEC is used in assessments of both acute and chronic dietary risk. It is not unusual for the ground water EEC to be significantly lower than the surface water EECs.

For cycloate, the ground water EEC is 1 ppb. Since the modeled EEC is less than the aggregate DWLOCs calculated for the U.S. General Population and all population subgroups (2,296 ppb and 171 ppb, respectively), aggregate exposure to cycloate in food and drinking water from ground water sources, both acute and chronic, are below the Agency's LOC for all population subgroups, including children (3-5 years), the population subgroup with the highest risk estimate (see Tables 5 & 6).

Monitoring: Several states (Idaho, Michigan and Oregon), where cycloate is used, have monitored for cycloate (parent only) in ground water. The Idaho Department of Agriculture has sampled for cycloate in 45 wells in the Burley Perched Aquifer in Minidoka county, a sugarbeet growing area since 1998. Cycloate was detected in 1 well in 1999 at a concentration of 0.36 ppb.

Cycloate was not detected in 2000. In Michigan, 280 ground water samples from the 11 counties with the highest sugarbeet production were analyzed over a period of 8 years, with no detections of cycloate (personal communication with M. Schwartz, MI Department of Agriculture, November 13, 2000). The samples were taken from domestic wells, bulk agricultural chemical storage facilities and dairies.

The state of Oregon maintains a data base of water quality analyses called the Laboratory Analytical Storage and Retrieval Database (LASAR). For cycloate, the data base contains data for 615 ground water samples taken from 266 discrete locations (1990 to the present), from northern Malheur County, the lower Umatilla Basin, Clatsop Plains and the Ontario area (Malheur county). Malheur county is a heavy use area for cycloate (more than 4.745 lbs. a.i. per square mile in 1992 (USGS 1992 annual use map). The USGS map also indicates that cycloate is used in Umatilla county and possibly in Clatsop county. In 1998, only 1 detection of cycloate was reported in a City of Vale (North Malheur county) well 1.8 ppb.

Table 5. Comparison of Calculated Acute DWLOCs and EECs for Cycloate.

Population Subgroup	aPAD (mg/kg/day)	Acute Food Exposure (mg/kg/day)	Maximum Acute Water Exposure[1] (mg/kg/day)	Ground Water EEC[1] (ppb)	Surface Water EEC[2] (ppb)	Acute DWLOC (ppb)
U.S. Population	0.066	0.000408	0.065592	1.0	52	2,296
All Infants (<1 year)	0.066	0.000672	0.065328	1.0	52	653
Children (1-2 years)	0.066	0.000720	0.065280	1.0	52	653
Children (3-5 years)	0.066	**0.000755**	**0.065245**	1.0	52	**652**
Children (6-12 years)	0.066	0.000556	0.065444	1.0	52	654
Youth (13-19 years)	0.066	0.000307	0.065693	1.0	52	1,971
Adults (20-49 years)	0.066	0.000261	0.065739	1.0	52	2,301
Females (13-49 years)	0.066	0.000278	0.065722	1.0	52	1,972
Seniors (50+ years)	0.066	0.000254	0.065745	1.0	52	2,301

[1] Maximum water exposure (mg/kg/day) = aPAD (mg/kg/day) - food exposure (mg/kg/day)

[2] Sugarbeet was used.

Table 6. Comparison of Calculated Chronic DWLOCs and EECs for Cycloate.

Population Subgroup	cPAD (mg/kg/day)	Chronic Food Exposure (mg/kg/day)	Maximum Chronic Water Exposure[1] (mg/kg/day)	Ground Water EEC (ppb)	Surface Water EEC (ppb)	Acute DWLOC (ppb)
U.S. Population	0.005	0.000119	0.004881	1.0	10	171
All Infants (<1 year)	0.005	0.000172	0.004828	1.0	10	48.3
Children (1-2 years)	0.005	0.000259	0.004741	1.0	10	47.4
Children (3-5 years)	0.005	**0.000277**	**0.004723**	1.0	10	**47.2**
Children (6-12 years)	0.005	0.000205	0.004795	1.0	10	48.0
Youth (13-19 years)	0.005	0.000103	0.004897	1.0	10	147
Adults (20-49 years)	0.005	0.000083	0.004917	1.0	10	172
Females (13-49 years)	0.005	0.000088	0.004912	1.0	10	147
Seniors (50+ years)	0.005	0.000105	0.004895	1.0	10	171

[1] Maximum water exposure (mg/kg/day) = cPAD (mg/kg/day) - food exposure (mg/kg/day)

For more information on drinking water risks and the calculations of the DWLOCs, see the Water Exposure section of the "Cycloate In/On Spinach, Garden Beets, Sugarbeets and Swiss Chard. Health Effects Division (HED) Risk Assessment," dated January 28, 2004 and the Drinking Water Assessment section of the "Cycloate: Reregistration Eligibility Document Science Chapter, PC Number 041301, Environmental Fate and Effects Division (EFED)," dated August 23, 2002.

3. Residential and Other Nonoccupational Exposure

Cycloate is not registered for any residential (home/garden) use, nor is it used in or around public buildings, schools or recreational areas where children or the others might be exposed. Thus, there is no residential exposure to aggregate with the dietary exposure.

4. Aggregate Risk

The aggregate risk assessment for cycloate integrates the assessments conducted for food and drinking water exposure *only* since there are no residential uses for cycloate. For aggregate exposure, the Agency calculates a DWLOC which represents the maximum allowable exposure through drinking water after considering the dietary exposure to cycloate. If the EECs are less than the DWLOCs, the Agency does not have concern for aggregate exposure. No population subgroup exceeded EPA's level of concern for either acute or chronic dietary exposure to cycloate based upon aggregated exposure to food plus water. Given current uses, the Agency has no risk concerns for aggregate exposure to cycloate through food and water.

5. Occupational Risk

People can be exposed to a pesticide while working through mixing, loading and application activities and when re-entering a treated site. Occupational risks are estimated in terms of Margins of Exposure (MOEs). An MOE is the ratio of the NOAEL to the (occupational) exposure. Thus, an MOE of 10 means the NOAEL is 10 times the estimated exposure. Generally, for cycloate, MOEs greater than 100 for dermal exposure and 300 for inhalation exposure are not of concern. For workers entering a treated site, MOEs are calculated for each day after application to determine the minimum length of time required before workers can safely reenter.

Occupational risk is assessed for exposure of mixers, loaders and applicators (termed "handler" exposure) and for exposure following application (termed "post-application" or worker exposure). Handler risk is based on combining both dermal and inhalation exposures. Worker risk is assessed for activities such as scouting, irrigating, mechanical weeding and hand harvesting and is based primarily on dermal exposure.

The Agency has determined that there is a potential for short- and intermediate-term exposures in occupational settings from handling cycloate products during the application process (i.e., mixer/loader, applicator and mixer/loader/applicator). As a result, risk assessments have been completed for occupational handlers. Additionally, short-term exposures are anticipated from entering previously treated areas; however, since cycloate is incorporated into the soil either immediately or within a few hours after application, post-application exposures are expected to be negligible as compared to handler exposure.

An overview of the assumptions and calculations of potential risks to workers can be found in the "Cycloate: Occupational and Residential Exposure Assessment and Recommendations for the Reregistration Eligibility Decision (RED) Document," dated October 9, 2003 and the Occupational Exposure section of the "Cycloate In/On Spinach, Garden Beets, Sugarbeets and Swiss Chard. Health Effects Division (HED) Risk Assessment," dated January 28, 2004.

a. Occupational Toxicity

The toxicological endpoints that were used to determine short- (1 to 30 days) and intermediate-term (1 to 6 months) dermal and inhalation risk estimates were based upon separate dermal and inhalation studies, as reported by the Agency's Hazard Identification Assessment Review Committee (HIARC) on September 25, 2003. A LOAEL of 0.25 mg/kg/day, from a 21-day inhalation study in rats (MRID 43552101), is used for inhalation risk estimates. The dose selection is based on moderate respiratory epithelial cell hyperplasia of the nasal cavity in female rats and the weight-of-evidence in four separate studies. A NOAEL of 10 mg/kg/day, from a 21-day dermal study in rats (MRIDs 42090305 and 43323801), is used for dermal risk estimates. The dose selection is based on reduction in body weight gain in male rats.

Although the inhalation risk assessment for occupational exposures was based on respiratory effects, neurotoxic effects were also seen in the same rodent toxicity study. The risk assessment based on the respiratory endpoint is protective of all other effects seen in the study. In effect, the more sensitive respiratory endpoint used in the inhalation risk assessment is protective of potential neurotoxic effects. Dermal and inhalation risk estimates cannot be aggregated, because the endpoints/effects are different. Long-term (6 months to year-round) handler exposures are not anticipated from cycloate.

Cycloate has a low order of acute toxicity via the oral (Category III), dermal (Category IV) and inhalation (Category IV) routes of exposure. It is a moderate eye and dermal irritant (Category III) and is also a dermal sensitizer. Table 7 summarizes the toxicity endpoints used in the occupational risk assessment.

Table 7. Summary of Cycloate Occupational Toxicity Endpoints.

Exposure Scenario	Dose (NOAEL)	Dose (LOAEL)	Endpoint	Study
Dermal (both short- and intermediate-term)	10 mg/kg/day	50 mg/kg/day	Decreased body weight gain.	21-day rat dermal
Inhalation (both short- and intermediate-term)[1]	Not established	0.25 mg/kg/day	Short-term -- minimal-to-moderate respiratory epithelial cell hyperplasia of the nasal cavity of female rats.	21-day rat inhalation
			Intermediate-term -- increased incidence and severity of hypertrophy and/or hyperplasia of the anterior nasal epithelium.	

[1] For occupational exposure: short-term (1 to 30 days) and intermediate-term (1 to 6 months) inhalation exposure risk assessments, an MOE of 300 is required. This is based on the conventional uncertainty factor of 100x (10x for intraspecies extrapolation and 10x for interspecies variation) and an additional 3x factor for the lack of a NOAEL.

b. Occupational Exposure

It is the Agency's standard practice to use surrogate data from the Pesticide Handlers Exposure Database (PHED) Version 1.1 to assess handler exposures for regulatory actions when chemical-specific monitoring data are not adequate, acceptable or available. PHED uses standard assumptions about average body weight, work day, daily areas treated, volume of pesticide used, etc. The exposure factors (e.g., body weight, amount treated per day, protection factors, etc.) are all standard values used by the Agency, and the PHED unit exposure values are the best available estimates of exposure.

For cycloate, surrogate data from PHED were used to assess handler exposures. Use of the PHED unit exposures for risk assessment is a very conservative approach, because much of the data supporting these unit exposures are derived from passive dosimetry methods and from chemicals that

are not very volatile. Therefore, the resulting risk estimates using these PHED unit exposures should be considered very conservative, and may actually be over-estimates.

Guideline handler studies were not submitted for cycloate. Instead, the registrant submitted a cycloate biomonitoring handler (mixer/loader/applicator) exposure study. Biological monitoring was selected as the monitoring method for this study because "cycloate is a volatile pesticide and is not a suitable compound for passive dosimetry." This study determined the rate of volatilization of RO-NEET® 6-E on two types of dosimetry patches indicating that the half-lives of cycloate were 3.1 hours for gauze patches and 3.2 hours for t-shirt (cotton) patches.

The biomonitoring study was reviewed and found to be unacceptable due to some inadequacies and inconsistencies in the data; however, the data compiled and generated from the biomonitoring study are useful in the estimation, assessment and characterization of risks to handlers of cycloate since the results from the biomonitoring study are within the same order of magnitude as the unit exposure estimates generated by using the PHED data and assuming maximum application rates. Specifically, from the biomonitoring study, the dermal absorbed dose of cycloate for all test subjects ranged from 0.00001 to 0.074 mg/kg/day (mean = 0.011 mg/kg/day), and the inhalation exposure ranged from 0.23 to 45.63 µg/kg/day (mean = 5.16 µg/kg/day). Short-term baseline estimates from PHED for dermal exposure range from 0.00008 to 0.11 mg/kg/day, and for inhalation exposure from 5.1 to 36.0 µg/kg/day.

Anticipated use patterns, application methods and range of application rates were derived from current labeling. Application rates are the maximum application rates determined from EPA registered labels. Cycloate is typically applied using groundboom equipment. The maximum labeled application rate is 4 lbs. a.i./acre. Typical (average) application rates are similar on garden beets, spinach and sugarbeets, ranging from 2 to 3 lbs. a.i./acre.

Occupational handler exposure assessments are conducted using different 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 determine the protection needed to reduce risks to below the Agency's level of concern (LOC). The lowest tier is represented by the baseline exposure scenario (i.e., single layer clothing, socks, and shoes), followed by, if MOEs are still of concern, increasing levels of risk mitigation such as personal protective equipment (PPE) and engineering controls.

The cycloate label requires the use of a closed system or the following PPE for mixers/loaders and applicators: long-sleeved shirts, long pants, shoes plus socks and chemical-resistant gloves. The label specifies a 12 hour REI for all application methods. California (CA) requires additional worker protection. Mixers/loaders in CA must either use closed systems and PPE or chemical-resistant clothes over work clothes and a full face respirator. Applicators in CA must either use an enclosed cab or wear overalls over work clothes and wear a half-face respirator. CA also limits the amount of

cycloate that can be handled per day to 93 gallons (560 lbs. a.i.) per mixer/loader or applicator. The levels of protection that formed the basis for calculations of exposure from cycloate activities include:

Baseline:	Long-sleeved shirt and long pants, shoes and socks.
Minimum PPE:	Baseline + chemical-resistant gloves and dust/mist respirator.
Maximum PPE:	Baseline + chemical-resistant gloves, double layer of clothing and a NIOSH-approved respirator with an organic-vapor removing cartridge.
Engineering controls:	Engineering controls such as a package-based system (e.g., water-soluble packaging for wettable powders) or other closed mixing/ loading systems and enclosed cab or truck. Some engineering controls are not applicable for certain scenarios (e.g., for handheld application methods, there are no known devices that can be used to routinely lower the exposures).

c. Occupational Handler Risk Summary

The Agency has determined that there are potential exposures to handlers during the usual use patterns associated with cycloate. The anticipated use patterns and current labeling of cycloate indicate seven major occupational handler exposure scenarios (11 scenarios total) based on the types of equipment and techniques that potentially can be used to make cycloate applications. Five of these scenarios were assessed. Scenario 6 (applying sprays with soil injection equipment with an open/enclosed cab) and Scenario 7 (applying impregnated dry bulk fertilizers with tractor drawn spreader) were not assessed because exposure data were not available for these two scenarios and exposure through these scenarios is adequately covered by other scenarios. Groundboom PHED values were used as surrogates for the soil injection technique of Scenarios 6a and 6b. Because dermal and inhalation endpoints and uncertainty factors differ, separate dermal and inhalation exposure assessments have been conducted. The seven major occupational handler exposure scenarios were identified as follows**:**

- Scenario (1a) open mixing/loading of emulsifiable concentrate (EC) liquid formulation for chemigation;
- Scenario (1b) closed system mixing/loading of EC liquid formulation for chemigation;
- Scenario (2a) open mixing/loading of EC liquid formulation for groundboom or soil injection applications;
- Scenario (2b) closed system mixing/loading of EC liquid formulation for groundboom or soil injection applications;
- Scenario (3) closed system mixing/loading/incorporating of EC liquid formulation onto dry bulk fertilizers (on-farm technique);
- Scenario (4) closed system mixing/loading/incorporating of EC liquid formulation with liquid fertilizers (on-farm technique);

- Scenario (5a) applying sprays with groundboom equipment with an open cab;
- Scenario (5b) applying sprays with groundboom equipment with an enclosed cab;
- Scenario (6a) applying sprays with soil injection equipment with an open cab;
- Scenario (6b) applying sprays with soil injection equipment with an enclosed cab; and
- Scenario (7) applying impregnated dry bulk fertilizers with tractor drawn spreader.

MOE estimates were calculated for all scenarios at baseline, minimum PPE, maximum PPE and engineering control level exposures if necessary. Results of exposure and risk estimates for each occupational handler exposure scenario are presented in Table 8. For more information on the occupational risks, see the calculations in the occupational exposure section of the "Cycloate In/On Spinach, Garden Beets, Sugarbeets and Swiss Chard. Health Effects Division (HED) Risk Assessment," dated January 28, 2004.

Table 8. Summary of Short-/Intermediate-Term Occupational Exposure Scenarios/Risk Estimates for Cycloate Handlers.

Scenario No.	Crop/Use	Application Rate[1] (lbs. a.i./acre)	Daily Acreage Treated[2]	Engineering Controls Dermal UE[3] (mg/lb. a.i.)	Engineering Controls Inhalation UE[3] (mg/lb. a.i.)	Dermal Dose[4] (mg/kg/day)	Inhalation Dose[5] (mg/kg/day)	Dermal MOE[6] (Target MOE=100)	Inhalation MOE[7] (Target MOE=300)
Mixer/Loader									
(1) Closed Mixing/Loading of EC Liquid Formulation for Chemigation Application	sugarbeets	4	350	0.0086	8.3E-5	0.172	0.00166	**58**	**150**
	garden beets	4	350	0.0086	8.3E-5	0.172	0.00166	**58**	**150**
	spinach	4	350	0.0086	8.3E-5	0.172	0.00166	**58**	**150**
(2) Closed Mixing/Loading of EC Liquid Formulation for Groundboom Application	sugarbeets	4	200	0.0086	8.3E-5	0.0983	0.000949	102	**260**
	sugarbeets	4	80	0.0086	8.3E-5	0.0393	0.000379	250	660
	garden beets	4	200	0.0086	8.3E-5	0.0983	0.000949	102	**260**
	garden beets	4	80	0.0086	8.3E-5	0.0393	0.000379	250	660
	spinach	4	80	0.0086	8.3E-5	0.0393	0.000379	250	660
(3) Closed Mixing/Loading & Impregnation of EC Liquid Formulation onto Dry Bulk Fertilizers	sugarbeets	4	200	N/A	1.7E-4	N/A	0.00194	N/A	**130**
	sugarbeets	4	80	N/A	1.7E-4	N/A	0.000777	N/A	320
Applicator									
(4) Applying Liquids by Groundboom with Enclosed Cabs	sugarbeets	4	200	0.0051	4.3E-5	0.0583	0.000491	170	510
	sugarbeets	4	80	0.0051	4.3E-5	0.0233	0.000197	430	1,300
	garden beets	4	200	0.0051	4.3E-5	0.0583	0.000491	170	510
	garden beets	4	80	0.0051	4.3E-5	0.0233	0.000197	430	1,300
	spinach	4	80	0.0051	4.3E-5	0.0233	0.000197	430	1,300
(5) Applying Impregnated Dry Bulk Fertilizers with Enclosed Cabs	sugarbeets	4	200	0.002	2.2E-4	0.0229	0.00252	440	**99**
	sugarbeets	4	80	0.002	2.2E-4	0.0091	0.001	1,100	**250**

[1] Application rates are based on the maximum application rates listed on EPA registered labels for cycloate.

[2] Amount handled per day values are based on HED Exposure SAC Standard Operating Procedure # 009 "Standard Values for Daily Acres Treated in Agriculture," revised June 23, 2000.

[3] Unit Exposure (UE): Unless otherwise noted, dermal and inhalation unit exposure values from PHED v. 1.1 Surrogate Exposure Guide, August 1998. Engineering controls for mixers/loaders consist of closed systems or organic vapor respirator and enclosed cabs for applicators.

[4] Dermal dose = dermal unit exposure (mg/lbs. a.i.) x application rate (lbs. a.i./acre) x amount handled per day (acres/day) / body weight (70 kg).

[5] Inhalation dose = inhalation unit exposure (mg/lbs. a.i.) x application rate (lbs. a.i./acre) x amount handled per day (acres/day) / body weight (70 kg).

[6] Short-/Intermediate-term dermal MOE = NOAEL (10 mg/kg/day) / daily dermal dose (mg/kg/day). N/A= Not Applicable. **Bolded MOEs** have a risk concern at the engineering control level for corresponding scenarios.

[7] Short-/Intermediate-term inhalation MOE = LOAEL (0.25 mg/kg/day) / daily inhalation dose (mg/kg/day). **Bolded MOEs** have a risk concern at the engineering control level for corresponding scenarios.

The target MOE of 100 for dermal exposure was **met** or **exceeded** at either the *maximum PPE* or *engineering control* levels for most of the short- and intermediate-term occupational exposure scenarios for mixing, loading and applying cycloate to garden beets, spinach and sugarbeets.

In addition, the target MOE of 300 for inhalation exposure was **met** or **exceeded** at either the *maximum PPE* or *engineering control* levels for a number of the short- and intermediate-term occupational exposure scenarios for mixing, loading and applying cycloate to garden beets, spinach and sugarbeets.

The dermal MOEs were **less than** the target MOE of 100 with *maximum risk reduction measures* for the following occupational exposure scenario:

- Scenario (1) closed system mixing/loading of EC liquid formulation for chemigation application to garden beets, sugarbeets and spinach at 350 acres at 4 lbs. a.i./acre.

The inhalation MOEs were **less than** the target MOE of 300 with *maximum risk reduction measures* for the following occupational exposure scenarios:

- Scenario (1) closed system mixing/loading of EC liquid formulation for chemigation application to garden beets, sugarbeets and spinach at 350 acres at 4 lbs. a.i./acre;
- Scenario (2) closed system mixing/loading of EC liquid formulation for groundboom or soil injection applications to garden beets and sugarbeets at 200 acres at 4 lbs. a.i./acre;
- Scenario (3) closed system mixing/loading and incorporating of EC liquid formulation onto dry bulk fertilizers (on-farm technique) to sugarbeets at 200 acres at 4 lbs. a.i./acre; and
- Scenario (5) applying impregnated dry bulk fertilizers with enclosed cabs to sugarbeets at 80 and 200 acres at 4 lbs. a.i./acre.

1) Post-Application Occupational Risk

Post-application exposures are expected to be negligible compared to handler exposures because cycloate is applied to the soil and incorporated into the soil immediately or within a few hours after application, or it is injected directly into the soil.

2) California Air Monitoring

In California, the Air Resources Board, at the request of the California Department of Pesticide Regulation, conducted a study to determine the airborne concentrations of the pesticide cycloate. This study was completed on October 15, 2001. Application monitoring was conducted in Imperial County around the use of cycloate on sugarbeets. Ambient monitoring was conducted to coincide with the use of cycloate on sugarbeets also in Imperial County.

Of the 64 application samples collected, 10 were found to be above the estimated quantitation limit (EQL) of 63.0 ng/sample for cycloate, 29 sample results were equal to or above the method detection limit (MDL) of 12.6 ng/sample, 24 sample results were detected (above the MDL but below the EQL), and 1 sample was invalidated due to a sampling problem. The highest cycloate concentration was 500 ng/m^3 during the third sampling period.

Of the 115 ambient samples collected, 27 were found to be above the EQL of 63.0 ng/sample for cycloate, 43 sample results were below the MDL of 12.6 ng/sample, and 45 sample results were detected (above the MDL but below the EQL). The highest cycloate concentration was 220 ng/m^3 at the Heber Fire Department sampling site.

The application and ambient air concentrations from this study are well below the 21-day inhalation LOAEL of 1.2 mg/m^3 that was used in the Agency's occupational risk assessment. For more detailed information associated with the airborne concentrations of the pesticide cycloate in California, please refer to the "Final Report for the Application and Ambient Air Monitoring for Cycloate," dated October 15, 2001. The complete report may be accessed through the Air Resources Board's website at *http://www.arb.ca.gov*.

3) Human Health Incident Data

A review of human health incident data sources found only a few occupational incidents involving cycloate and that relatively few incidents of illness have been reported due to cycloate. Two incidents were due to workers not wearing label-specified PPE. A third incident was due to a worker being too close to a tractor while it was involved in spraying the soil.

Cycloate was not reported to be involved in any human incidents on the list of the top 200 chemicals for which the National Pesticide Information Center (NPIC) received calls from 1984 through 1991, inclusively.

B. Environmental Risk Assessment

A summary of the Agency's environmental risk assessment is presented below. More detailed information associated with the environmental risk from the use of cycloate may be found in the "Cycloate: Environmental Fate and Effects Division (EFED) Reregistration Eligibility Document Science Chapter," dated August 23, 2002. The complete environmental risk assessment is not included in this RED, but may be accessed in the OPP Public Docket and on the Agency's website at *http://www.epa.gov/pesticides/reregistration/status.htm*.

1. Fate and Transport

Cycloate has a moderate solubility (75 to 95 mg/L at 25° C) and moderately high vapor pressure (6.2 x 10^{-3} mm Hg at 25° C). Henry's Law constant is therefore a relatively high 1.85 x 10^{-5} atm-m^3/mol. Combined, these properties indicate that cycloate has a pronounced tendency to evaporate, especially from water or moist soil. In a laboratory volatilization study (MRID 41920602), cycloate volatilized (as the parent) with an average 12.1% of the applied radioactivity volatilized after 4 hours and 13.4% after 25 hours. This behavior was also observed in the anaerobic aquatic metabolism study (MRID 42997901), in which 50% of the parent compound volatilized over one year. Label directions for cycloate require incorporation into the soil immediately after application to slow down volatilization.

Cycloate is stable to hydrolysis and photolysis in water. However, a literature study (MRID 42541101) indicates that volatilized cycloate may have a short lifetime in air (5.2 hours) due to reaction with hydroxyl radicals. Therefore, nontarget organisms are expected to be exposed to cycloate via spray drift or volatility for several days after application.

Laboratory metabolism studies yielded half-lives of 43 days (aerobic soil, MRID 42812901), 68 days (anaerobic soil, Acc. 266125), and 192 days (anaerobic aquatic metabolism, MRID 42997901).

The one acceptable terrestrial field dissipation study (MRIDs 41582404-5), conducted in Orange Cove, CA, yielded a soil half-life of 11 days in the upper 3 inches. A second field study was compromised by irrigation of the study plot, which resulted in a failure to confirm the application rate.

Laboratory studies show that cycloate tends to sorb to soil under dry conditions, and that the sorption is not reversed if the soil is later flooded. However, if the soil is already flooded at the time of application, cycloate is easily desorbed and then volatilized over time. K_{oc} values (500 to 800 mL/g) indicate that cycloate is moderately mobile in soil.

Cycloate degradates in soil include the sulfoxide (which may revert to the parent under reducing conditions) and N-ethylcyclohexylamine. Two sets of ring-hydroxy and ring-keto degradates (the 4-hydroxy-, 4- keto-, 3-hydroxy- and 3-keto- degradates) are also formed in laboratory studies. Other degradates seen in laboratory studies include N-cyclohexyl-N-ethylformamide and N-ethyl-N-formyl-S-ethyl thiocarbamate.

In summary, cycloate applied to dry soil and immediately incorporated tends to remain sorbed to the soil and dissipates with a half-life on the order of 1 to 2 months. Cycloate volatilizes from moist soil if not immediately incorporated. Volatilized cycloate may be rapidly degraded by hydroxyl

radicals in the air. Available monitoring data for surface and ground waters indicate that cycloate is rarely detected in areas where it is used.

2. Ecological Risks

The Agency's ecological risk assessment compares toxicity endpoints from ecological toxicity studies to estimated environmental concentrations (EECs) based on environmental fate characteristics and pesticide use data. To evaluate the potential risk to nontarget organisms from the use of cycloate products, the Agency calculates a Risk Quotient (RQ), which is the ratio of the EEC to the most sensitive toxicity endpoint values, such as the median lethal dose (LD_{50}) or the median lethal concentration (LC_{50}). The most sensitive species tested is chosen for these RQ calculations, but the tests may not include the most sensitive species which may be exposed. These RQ values are then compared to the Agency's LOCs which indicate whether a chemical, when used as directed, has the potential to cause adverse effects on nontarget organisms. When the RQ exceeds the LOC for a particular category, the Agency presumes a potential risk of concern to that category. The LOCs and the corresponding potential risk presumptions are presented below in Table 9.

Table 9. LOCs and Associated Risk Presumptions.

IF...	THEN the Agency presumes...
Mammals and Birds	
The acute RQ > LOC of 0.5	Potential acute risk
The acute RQ >LOC of 0.2	Potential risk that may be mitigated through restricted use
The acute RQ > LOC of 0.1	Potential acute effects may occur in Endangered Species
The chronic RQ > LOC of 1	Potential chronic risk *and* chronic effects may occur in Endangered Species
Fish and Aquatic Invertebrates	
The acute RQ > LOC of 0.5	Potential acute risk
The acute RQ > LOC of 0.1	Potential risk that may be mitigated through restricted use
The acute RQ >LOC of 0.05	Potential acute effects may occur in Endangered Species
The chronic RQ > LOC of 1	Potential chronic risk *and* chronic effects may occur in Endangered Species

Risk Summary for Registered Uses of Cycloate

The uses of cycloate on garden beets, spinach and sugarbeets may cause adverse ecological effects at the maximum application rate of 4 lbs. a.i./acre. The potential risks include: (1) potential chronic risk to birds, including federally listed endangered and threatened species; (2) potential chronic risk to small mammals, including federally listed endangered and threatened species; (3) potential risk to estuarine/marine fish and invertebrates; and (4) potential acute and chronic risk to nontarget aquatic and terrestrial plants. Concern for potential chronic risk to small mammals is based on reproductive effects seen in 2- and 3-generation rat reproduction studies. This concern extends to the possibility of chronic effects in birds. These findings are based solely on EPA's screening level assessment and do not constitute "may affect" findings under the ESA. The Agency does not have

chronic data for birds and, in the absence of this data, we cannot preclude the possibility of chronic risk to birds. The Agency intends to issue a DCI as part of this RED to require additional data for: avian reproduction data; acute toxicity data for estuarine/marine animals; seedling emergence; vegetative vigor; and aquatic plant growth to address areas of uncertainty. These data are expected to confirm the conclusions of this screening level environmental risk assessment. In the absence of data, there is much uncertainty in the environmental risk assessment for cycloate.

For a more detailed explanation of the ecological risks posed by the use of cycloate, please refer to the Ecological Effects Hazard Assessment and Ecological Risk Assessment sections of the "Cycloate: Environmental Fate and Effects Division (EFED) Reregistration Eligibility Document Science Chapter," dated August 23, 2002.

a. Risk to Birds

1) Toxicity (Hazard) Assessment

Cycloate is considered practically nontoxic to birds on an acute oral basis since the LD_{50} value is >2,150 mg/kg and the LC_{50} is >5,000 ppm (see Table 10). These values are greater than the highest does tested (1,440 ppm). An LD_{50} is 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). An LC_{50} is a statistically estimated measure (concentration) expected to be lethal to 50% of the test population. Table 10 summarizes the data that support the acute toxicity endpoints used in assessing the risks to birds.

Table 10. Acute Toxicity Endpoints for Birds.

Toxicity Study	Test Species[1]	% a.i.	Endpoint	Toxicity Category	MRID or Accession No.
Acute (Single dose by gavage)					
Avian Oral	Northern Bobwhite Quail *(Colinus virginianus)*	98.6	LD_{50} = >2,150 mg/kg	Practically Nontoxic	Acc. 072166
Subacute (Eight days of treated feed)					
Avian Dietary	Mallard Duck *(Anas platyrhynchos)*	96.8	LC_{50} = >5,395 ppm	Practically Nontoxic	42090306
	Northern Bobwhite Quail *(Colinus virginianus)*		LC_{50} = >5,620 ppm		00145554

[1] Test species observed an additional three days while on untreated feed.

Currently, avian chronic toxicity tests have not been submitted to the Agency; therefore, it is not possible to determine the chronic effects to birds from cycloate use. Avian reproductive studies using the technical grade active ingredient (TGAI) are needed for cycloate because it is stable in the environment to the extent that potentially toxic amounts may persist in animal feed especially

preceding or during the breeding season and information derived from mammalian reproduction studies indicates reproduction in terrestrial vertebrates may be adversely affected by the anticipated use of the product.

2) Exposure and Risk

Exposure to birds will be primarily for edge-of-field habitats, where soil, water and food items may become contaminated with cycloate by direct application, spray drift or volatilization. Since cycloate is used before or at-planting, there are limited food items in the field; however, the animals feeding in the field are likely to be exposed to contaminated soil-dwelling organisms (e.g., invertebrates), seeds and soil rather than the crop itself.

Minimal acute risk is expected to birds from the registered uses of cycloate. However, no avian reproduction studies are available to assess chronic effects to birds. The acute RQs were not calculated for birds because the toxicity data on birds indicate that the RQs will be far below any Agency level of concern. The LC_{50} value for birds (>5,000 ppm) was greater than the highest dose tested (1,440 ppm), which is the highest application rate of 4 lbs. a.i./acre for short grass.

The Agency does not have chronic data for birds and, in the absence of this data, we cannot preclude chronic risk to birds.

b. Risk to Small Mammals

1) Toxicity (Hazard) Assessment

Cycloate is considered practically nontoxic to small mammals on an acute oral basis. Chronically, cycloate may affect small mammals subject to long-term exposure. The rat LD_{50} is 2,275 mg/kg (45,500 ppm), which is greater than the highest EEC of 960 ppm for 4 lbs. a.i./acre on short grass. In a 2-generation reproduction study (MRID 41691901) in the rat, cycloate was administered to multiple generations of rats at dose levels of 50, 400 and 1,000 mg/kg/day. The reproductive endpoint used in the cycloate mammalian wildlife risk assessment was based on decreased pup body weight gain with a NOAEL of 50 mg/kg/day and a LOAEL of 400 mg/kg/day. Table 11 discusses the data that support the acute and chronic toxicity endpoints used in assessing the risks to mammals.

Table 11. Mammalian Toxicity Endpoints for Rats Exposed to Cycloate.

Test Species	Test Type	Study Type	% a.i.	Toxicity Value (mg/kg)	Affected Endpoints	MRID No.
Laboratory Rat *(Rattus norvegicus)*	Mammalian Oral	Acute	98.0	LD_{50} = 3,200 (♂) LD_{50} = 2,275 (♀)	Mortality	00132790
	2-Generation Reproduction	Chronic	95.3	NOAEL = 50 LOAEL = 400	Reproduction	41691901

2) Exposure and Risk

Exposure to small mammals will be primarily for edge-of-field habitats, as with birds described in the preceding section, where soil, water and food items may become contaminated by direct application, spray drift or volatilization. Since cycloate is used before or at-planting, there are limited food items in the field; however, the animals feeding in the field are likely to be exposed to contaminated soil-dwelling organisms (e.g., invertebrates), seeds and soil rather than the crop itself. The fur on the small mammals will pick up cycloate residues as they burrow in the soil, thus exposing themselves directly to residues in the soil as they lick their fur.

Wild mammal testing is required on a case-by-case basis, depending on the results of lower tier laboratory mammalian studies, intended use patterns and pertinent environmental fate characteristics. Minimal acute risk to small mammals is expected from the registered uses of cycloate. Acute RQs were not calculated for mammals because the toxicity data on rats indicate that the RQs will be far below any Agency level of concern.

Chronic RQs range from 0.6 to 9.6 at the 2 lbs. a.i./acre (typical) application rate. At the higher 4 lbs. a.i./acre (maximum) application rate, the chronic RQs range from 1.2 to 19.2. Concern for chronic risk to mammals is based on reproductive effects seen in 2- and 3-generation rat reproduction studies. This concern extends to potential chronic effects in birds. See Table 12 for expected environmental residues of cycloate on various food items and resulting RQs.

Table 12. Cycloate Use: Chronic RQs for Mammals.

Application Rate (lbs. a.i./acre)	Food Items	EEC[1] (ppm)	Chronic RQ (ppm)
Mammalian Chronic NOAEL of 2.5 mg/kg/day for Rat (2.5 / 0.05 = 50 ppm)[2]			
2	Short grass	480	9.6
	Broadleaf plants	270	5.4
	Insects	220	4.4
	Seeds	30	0.6

Application Rate (lbs. a.i./acre)	Food Items	EEC[1] (ppm)	Chronic RQ (ppm)
4	Short grass	**960**	19.2
	Broadleaf plants	540	10.8
	Insects	440	8.8
	Seeds	60	1.2

[1] EEC is calculated based on the Kenaga nomogram [Hoerger and Kenaga, (1972); and as modified by Fletcher (1994)]. For maximum concentration, the application rate in lbs. a.i./acre is multiplied by 240 for Short Grass, 110 for Tall Grass, 135 for broad-leafed plants/small insects and 15 for fruits/pods/large insects/seeds. Additional applications are converted from lbs. a.i./acre to ppm on the plant surface and the additional mass added to the mass of the chemical still present on the surface on the day of application.

[2] The rat NOAEL (in ppm) is calculated by dividing the mammalian NOAEL (in mg/kg/day) by 0.05 (to correct for actual food consumption)

Note: Chronic RQ = EEC (ppm) / NOAEL (ppm)

c. Risk to Fish and Aquatic Invertebrates

Freshwater Species

1) Toxicity (Hazard) Assessment

The available acute toxicity data on cycloate, indicate that it is moderately toxic to freshwater fish, based on LC_{50} values ranging from 4.5 ppm to 10 ppm. Cycloate is classified as slightly toxic to freshwater invertebrates (EC_{50} = 24 ppm) on an acute oral basis. The LC_{50} value used for risk assessment purposes is 4.5 ppm (rainbow trout). Table 13 below displays the acute toxicity endpoints for freshwater fish and invertebrates.

Table 13. Acute Toxicity Endpoints for Freshwater Fish/Invertebrates.

Test Species	Test Type	% a.i.	Toxicity Value (ppm of a.i.)	Toxicity Category	MRID or Accession No.
Rainbow Trout *(Oncorhynchus mykiss)*	Fish Toxicity	97.8	(96-hour LC_{50}) 4.5	Moderately Toxic	Acc. 090620
Bluegill Sunfish *(Lepomis macrochirus)*		96.8	(96-hour LC_{50}) 4.6		00143654
		98.6	(96-hour LC_{50}) 6.8		Acc. 072166
Mosquito Fish *(Gambusia affinis)*		Formulation	(96-hour LC_{50}) 10		00084743
Scud *(Gammarus fasciatus)*	Invertebrate Toxicity	Technical	(48-hour EC_{50}) 2.6	Slightly Toxic	05001497
Water Flea *(Daphnia magna)*		96.8	(48-hour EC_{50}) 24		00143655

Although the EEC is not expected to reach 1% or greater of any acute LC_{50} or EC_{50} value, parent cycloate is persistent in the aquatic environment. An early life stage fish and a freshwater invertebrate life cycle test using the TGAI (Guidelines 850.1300 and 850.1350) are required. Without these data, the Agency cannot preclude chronic risks to aquatic organisms. The preferred test species for the invertebrate life cycle test is *Daphnia magna*.

2) Exposure and Risk

Acute RQs for both federally listed endangered and threatened species and nonendangered species of freshwater fish and aquatic invertebrates are all below Agency levels of concern. It is predicted that the aquatic EEC will generally be less than 1% of the LC_{50} for fish; however, this does not preempt the need for chronic fish or aquatic invertebrate studies if data show that terrestrial organisms may be chronically sensitive to cycloate. It is uncertain as to whether aquatic species may have chronic adverse impacts from cycloate use. Therefore, the early life study of fish and the aquatic invertebrate life cycle studies are required for cycloate. Table 14 below shows the RQs for the tested species for acute exposure to freshwater fish and invertebrates.

Table 14. Acute Risk Quotients for Acute Toxicity to Freshwater Fish/Invertebrates.

Test Species	Study Type	Toxicity Endpoint Value (ppb of a.i.)	Acute RQ
Bluegill Sunfish *(Lepomis macrochirus)*	(96-hour LC_{50})	4,600	0.007
		6,800	0.005
Mosquito Fish *(Gambusia affinis)*	(96-hour LC_{50})	10,000	0.003
Rainbow Trout *(Oncorhynchus mykiss)*	(96-hour LC_{50})	4,500	0.007
		5,600	0.006
		6,000	0.005
		7,000	0.004
Scud *(Gammarus fasciatus)*	(96-hour LC_{50})	2,600	0.012
Water Flea *(Daphnia magna)*	(48-hour LC_{50})	24,000	0.001

Estuarine/Marine Species

Cycloate is used on spinach near estuarine areas. As indicated previously in this RED, cycloate is expected to be persistent and moderately mobile in moist or flooded soils. As a result, EPA will require estuarine/marine fish and invertebrate acute toxicity data (Guideline 850.1035) for cycloate. In the absence of this data, risk assessment for estuarine/marine fish and invertebrates cannot be completed. In addition, since parent cycloate is persistent in the aquatic environment, an

early life stage fish test using the TGAI (Guideline 850.1300) is required for cycloate. Without these data, the Agency cannot preclude chronic risks to aquatic organisms.

d. Risk to Nontarget Insects

Available data from a honey bee acute contact toxicity study using the TGAI indicates that cycloate is practically nontoxic to the honeybee (with an LD_{50} of >29.01 µg/bee) and its uses on garden beets, spinach and sugarbeets are predicted to pose minimal risk to nontarget insects.

e. Risk to Nontarget Terrestrial and Aquatic Plants

The degree of risk (both acute and chronic) to nontarget terrestrial and aquatic plants is uncertain and cannot be assessed due to the complete lack of phytotoxicity data. Since cycloate is an herbicide, EPA must presume that there is a risk to nontarget terrestrial and aquatic plants. There is variability in phytotoxicity and specie selectivity among other thiocarbamate herbicides; therefore, it is highly uncertain as to the degree of phytotoxicity and the selectivity of species that are sensitive to cycloate without appropriate plant data. In the absence of these data, risk assessment to nontarget terrestrial and aquatic plants cannot be properly completed.

Terrestrial plant testing is necessary since cycloate is an herbicide with nonresidential terrestrial use patterns. The required terrestrial plant testing consists of seedling emergence and vegetative vigor tests with ten crop species. Tier 1 tests (Guidelines 850.4100 and 850.4150) may be conducted to measure the response of plants, relative to a control, at a test level that is equal to the highest use rate (expressed as lbs. a.i./acre) or three times the EEC for nontarget areas. Tier 2 tests (Guidelines 850.4225 and 850.4250) are required for any test species that shows a reduction in response equal to or greater than 25% in the Tier 1 tests.

Aquatic plant testing (Guideline 850.4400) is required for cycloate (TEP formulation) because it is an herbicide that has outdoor nonresidential terrestrial uses. The following species should be tested at Tier 2: *Kirchneria subcapitata*, *Lemna gibba*, *Skeletonema costatum*, *Anabaena flos-aquae* and a freshwater diatom. In the absence of data, there is much uncertainty in the nontarget aquatic plant risk assessment.

f. Risk to Federally Listed Endangered and Threatened 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 Endangered Species Act 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. This analysis will consider the risk mitigation measures that are being implemented as a result of this RED.

The screening level risk assessment indicates that cycloate exceeds the endangered species level of concern for chronic risks to mammals. These findings are based solely on EPA's screening level assessment and do not constitute "may affect" findings under the Endangered Species Act. Cycloate has no effect on federally listed endangered and threatened fish and aquatic invertebrates from acute and chronic exposures, and no effect on endangered and threatened birds from acute exposure. The absence of data for birds (chronic risk) and for aquatic and terrestrial plants does not permit EPA to preclude the potential for risks to endangered and threatened species in these areas. The risk mitigation measures stated in this RED, such as the elimination of the chemigation application of cycloate may potentially reduce exposure of any endangered species to this chemical. In addition, the usage information that the Agency is requesting from the registrant may provide EPA with sufficient data to reduce application rates in the future.

IV. Risk Management, Reregistration and Tolerance Reassessment Decision

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 required to support reregistration of products containing cycloate 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 cycloate.

Appendix B identifies the generic data requirements that the Agency reviewed as part of its determination of reregistration eligibility of cycloate. These data were sufficient to allow the Agency to determine that cycloate can be used without resulting in unreasonable adverse effects to humans and the environment. The Agency, therefore, finds that all products containing cycloate as the active ingredient are eligible for reregistration provided specified changes are made to the label and additional data identified in Section V of this RED confirm this conclusion. Actions needed to reregister particular products are addressed in Section V of this document.

The Agency may take appropriate regulatory action if new information comes to the Agency's attention regarding the reregistration of cycloate. The Agency may also require the submission of additional data (1) to support the registration of products containing cycloate; (2) if the data requirements for registration change; or (3) if the guidelines for generating such data change.

B. Regulatory Position

1. Food Quality Protection Act Findings

a. Determination of Safety for U.S. Population

The Agency has determined that the established tolerances for cycloate, 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, that there is a reasonable certainty of no harm for the U.S. general population and all population subgroups. In reaching this determination, EPA considered all available information on the toxicity, use practices and scenarios and the environmental behavior of cycloate. Cycloate is not registered for residential (home/garden) use, nor is it used in or around public buildings, schools or recreational areas where children or others might be exposed. Thus, there is no expected residential or other nonoccupational exposure. Therefore, EPA considered only dietary (food and drinking water) exposure sources in its aggregate risk assessment.

b. Aggregate Dietary Risks

The aggregate risk assessment for cycloate integrates the assessments conducted for food and drinking water exposure *only*, since there are no residential uses for cycloate. For aggregate exposure, the Agency calculates a DWLOC which represents the maximum allowable exposure through drinking water after considering the dietary exposure to cycloate. If the EECs are less than the DWLOCs, EPA does not have concern for aggregate exposure. No population subgroup exceeded the Agency's level of concern for either acute or chronic dietary exposure to cycloate based upon aggregated exposure to food plus water. Given current uses, the Agency has no risk concerns for exposure to cycloate through food and/or water.

For cycloate, the acute dietary (food only) risk does not exceed the Agency's level of concern for the U.S. general population and all subgroups, including infants and children, using highly conservative assumptions. The acute dietary (food only) risk estimate is 1.1% of the aPAD at 95% exposure, for the most highly exposed population subgroup, children aged 3-5 years. The chronic dietary (food only) risk estimates from exposures to cycloate in food do not exceed the Agency's level of concern (i.e., they are less than 100% of the cPAD) for the U.S. general population and all subgroups using highly conservative assumptions. The chronic dietary (food only) risk estimate is 5.5% of the cPAD, for the most highly exposed population subgroup, children aged 3-5 years.

For cycloate, the maximum acute EECs for both surface water (52 ppb) and ground water (1 ppb) are less than the aggregate acute DWLOC calculated for the U.S. Population (2,296 ppb). The maximum chronic EECs for both surface water (10 ppb) and ground water (1 ppb) are less than the aggregate chronic DWLOC calculated for the U.S. general population (171 ppb), indicating that aggregate chronic exposure to cycloate in food and water, both acute and chronic, were thus below

the Agency's level of concern for all population subgroups for cycloate and its metabolites given current uses.

For chronic (cancer) dietary risk assessment, the Agency has classified cycloate into the category *"not likely to be a carcinogen to humans;"* therefore a quantified carcinogenic assessment is not indicated for cycloate and no mitigation measures are necessary to address chronic (cancer) dietary risk for cycloate.

c. Determination of Safety for Infants and Children

EPA determined that the established tolerances for cycloate meet the safety standards under the FQPA amendments to section 408(b)(2)(C) of the FFDCA, that there is a reasonable certainty of no harm for infants and children. The safety determination for infants and children considers the factors noted above for the U.S. general population, but also takes into account the possibility of increased dietary exposure due to the specific consumption patterns of infants and children, as well as the possibility of increased susceptibility to the toxic effects of cycloate residues in this population subgroup.

As required by the Food Quality Protection Act (1996), the hazard database for cycloate was examined to determine the potential for increased susceptibility to infants and children from exposure to cycloate. On August 28, 2003, the Agency's HIARC determined that no FQPA special safety factor should be applied for special sensitivity of infants and children; and that a 10x data base uncertainty factor (UF_{DB}), for lack of a DNT study, should be applied to single dose (acute) exposures, but not to multiple dose (chronic) exposures. Based upon the above, the FQPA special safety factor has been reduced to 1x since there are no residual uncertainties for pre- and/or post-natal toxicity.

2. Endocrine Disruptor Effects

EPA is required under the FFDCA, as amended by FQPA on August 3, 1996, to develop a screening program to determine whether certain substances (including all pesticide active and other ingredients) *"may have an effect in humans that is similar to an effect produced by a naturally occurring estrogen, or other such endocrine effects as the Administrator may designate."* Following recommendations of its Endocrine Disruptor Screening and Testing Advisory Committee (EDSTAC), the Agency determined that there was 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 the Agency 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).

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

3. Cumulative Risks

Section 408(b)(2)(D)(v) of the FFDCA requires that, when considering whether to establish, modify or revoke a tolerance, 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 mechanism could lead to the same adverse health effect as would a high level of exposure to any one of the other substances individually. OPP has determined that some thiocarbamates (EPTC, molinate, pebulate and cycloate) share a common mechanism of toxicity, the inhibition of acetylcholinesterase. In September 2001, the Scientific Advisory Panel (SAP) concluded that there is insufficient evidence for grouping the thiocarbamate pesticides based on a common mechanism of toxicity for effects other than acetylcholinesterase inhibition. Although structural and metabolic similarities exist among the thiocarbamates and there is evidence that the thiocarbamates may produce a common effect (neuropathology), this evidence is not definitive. The Agency has conducted a preliminary "screening level" cumulative food risk assessment for the thiocarbamates. The results of the screening level cumulative food risk assessment, using very conservative Tier 1 exposure assumptions (using tolerance level residues, assuming 100% of all crops treated and including exposures from molinate, which is being phased out), is that MOEs exceed 310 for all population subgroups. Since any MOE greater than 100 is deemed acceptable, the Agency has concluded that the potential cumulative risks from the thiocarbamates in general and cycloate in particular passes the "reasonable certainty of no harm" standard of the Food Quality Protection Act.

These results are reported in a memorandum dated December 19, 2001 from Marcia Mulkey entitled, "Thiocarbamates: A Determination of the Existence of a Common Mechanism of Toxicity and a Screening Level Cumulative Food Risk Assessment." This document can be found under thiocarbamates at the EPA website entitled, "Public Comment Period Opened: Common Mechanism Determination for Thiocarbamate and Dithiocarbamate Pesticides" at *http://www.epa.gov/oppsrrd1/cumulative/thiocar.htm*.

C. Tolerance Reassessment Summary

The existing tolerances for residues of cycloate in/on plant commodities are established under 40 CFR §180.212. These tolerances are presently expressed in terms of cycloate (*S*-ethyl cyclohexyl(ethyl)thiocarbamate), *per se*. No cycloate tolerances for livestock commodities or processed food/feed commodities are currently established. The Agency has determined that the total toxic residues to be regulated in the target crops should consist of cycloate and the free and

conjugated forms of its metabolites (3HC and 4HC). The Agency is now recommending that the tolerance expression should be amended to reflect this determination.

The Agency has also determined that tolerances for milk, meat and meat byproducts of livestock are not required (Category 3, 40 CFR §180.6) for reregistration. There are no poultry feedstuffs associated with the registered food/feed uses; therefore, cycloate tolerances are not required for eggs and the meat and meat byproducts of poultry. A summary of cycloate tolerance reassessments is presented below in Table 15.

1. Tolerances Currently Listed Under 40 CFR §180.212

Adequate residue data are available to ascertain the adequacy of tolerances for Beet, garden, roots; Beet, garden, tops; and Spinach. For these commodities, the established tolerance levels have been increased to accommodate inclusion of the cycloate metabolites.

Adequate residue data are also available to support the registered Section 3 uses on Beet, sugar, roots and Beet, sugar, tops; however, inadequate data are available to support a Section 24(c) (CA780075) registration for use on sugarbeets, which specifies a higher rate of 6 lbs. a.i./acre. The reassessed tolerances for Beet, sugar, roots and Beet, sugar, tops assumes that the above Section 24(c) product will be canceled.

The group commodity definition "Garden beets (roots and tops)" should be revised to "Beet, garden, roots" and "Beet, garden, tops." The group commodity definition "Sugarbeets (roots and tops)" should be revised to "Beet, sugar, roots" and "Beet, sugar, tops."

2. Tolerance to Be Proposed Under 40 CFR §180.212

The registrant must propose a tolerance for Beet, sugar, molasses. The available data suggest that a tolerance level of 1.0 ppm is appropriate. The registrant must also propose a tolerance for Swiss chard. The Agency recommends 5.0 ppm.

Table 15. Tolerance Reassessment Summary for Cycloate.

Commodity	Current Tolerance[1] (ppm)	Reassessed Tolerance[2] (ppm)	Comment *[Corrected Commodity Definition]*
Tolerances Currently Listed Under 40 CFR §180.212			
Garden beets (roots and tops)	0.05	Roots: 0.50 Tops: 1.0	*[Beet, garden, roots]* *[Beet, garden, tops]*
Spinach	0.05	0.5	
Sugarbeets (roots and tops)	0.05	Roots: 0.3 Tops: 0.3	*[Beet, sugar, roots]* *[Beet, sugar, tops]*

Commodity	Current Tolerance[1] (ppm)	Reassessed Tolerance[2] (ppm)	Comment *[Corrected Commodity Definition]*
Tolerances To Be Proposed Under 40 CFR §180.212			
Beets, sugar, molasses	None	1.0	
Swiss chard	N/A	5.0	

[1] Expressed in terms of cycloate, *per se*.

[2] To be expressed in terms of cycloate and the free and conjugated forms of 3HC and 4HC. Reassessment is also contingent upon label revisions to specify minimum pre-harvest intervals of 60 days for garden beets, 120 days for sugarbeets and 60 days for spinach.

4. Codex Harmonization

No Codex maximum residue levels (MRLs) have been established for cycloate and its metabolites; therefore, issues of compatibility between Codex MRLs and U.S. tolerances do not exist.

5. Residue Analytical Methods

Adequate residue analytical methods are available for tolerance enforcement and data collection. No additional data pertaining to this guideline topic are required for reregistration. The available methods for determining cycloate residues of concern in/on plant commodities is described below.

Plants:

An analytical method based upon the steam distillation of cycloate from plants and measurement by GC using FID is currently listed in PAM II as Method A for determination of *S*-ethyl cyclohexyl(ethyl)thiocarbamate. The method was determined to be adequate for enforcement and collection of data on cycloate, *per se*, in/on plant commodities. (List B. Residue Analytical Methods Inventory, R. Perfetti, June 22, 1990). However, the Agency determined in 1992 that a new enforcement method was needed that would be capable of determining not only cycloate, but also its 3HC and 4HC metabolites in/on plants (CBRS No. 9028, DP Barcode D171952, C. Olinger, May 19, 1992). The analytical method(s) also was required to include a hydrolysis step to release any conjugated residues of 3HC or 4HC.

To meet this requirement, the registrant submitted a GC/NPD residue analytical method in 1995 (MRID 43523801), that can determine 3HC and 4HC, as well as cycloate, and includes the requisite hydrolysis step to release bound residues of 3HC and 4HC. The reported limit of quantification (LOQ) for each metabolite was 0.05 ppm. Residue identification can be confirmed by GC/MS. Although submitted validation data were acceptable for data collection and for tolerance enforcement, the recoveries tended to run too high (>120%) and also to have standard deviations that sometimes exceeded 20%. The submitted data did not support tolerance enforcement on spinach.

This method was subjected to an independent laboratory evaluation (ILV) on garden beet roots and tops, in accordance with PR Notice 96-1. This ILV incorporated certain modifications to improve performance. With these modifications, the ILV adequately supported use of this method on garden beet tops and also roots, but did not address spinach. Subsequent to this ILV, a field trial was submitted for Swiss chard. In this field trial, this same method was performed on Swiss chard by an IR-4 laboratory. The IR-4 laboratory had excellent recoveries and repeatabilities for all 5 analytes in Swiss chard, even at 0.05 ppm. After a review of this data, EPA concluded that the information from this field trial can be used as equivalent to an additional ILV and that, based upon performance of the method in this field trial, this method can be construed by weight-of-the-evidence to be adequate for enforcement of cycloate residues in/on all registered commodities, including spinach.

The requirement for radiovalidation of the new method has not yet been fulfilled. A radiovalidation study of this method must be submitted.

Animals:

No method is required for residues in livestock.

D. Regulatory Rationale

The regulatory rationale for each of the mitigation measures outlined below is discussed immediately after this list of mitigation measures. These mitigation measures will reduce risks to agricultural workers:

- Voluntary cancellation of chemigation application of cycloate;
- Extend the cycloate REI to 48-hours;
- Require engineering controls including closed cabs and closed mixing/loading systems;
- Prohibit on-farm impregnation of cycloate onto dry bulk fertilizer; and
- Require use data to better characterize exposure from dry bulk fertilizer applications.

The following is a summary of the rationale for the measures specified above which are necessary for reregistration eligibility and for managing risks associated with the use of cycloate. Where labeling revisions are warranted, specific language is set forth in the summary table of Section V (Table 16 of this RED document).

1. Human Health Risk Mitigation

a. Dietary Mitigation

(1) Acute Dietary (Food)

Acute dietary (food only) risk does not exceed the Agency's level of concern for the U.S. general population and all population subgroups, including infants and children, using highly conservative assumptions. The acute dietary (food only) risk estimate is 1.1% of the aPAD at 95% exposure, for the most highly exposed population subgroup, children aged 3-5 years. No mitigation is necessary for acute dietary (food only) exposure.

(2) Chronic Dietary (Food)

The chronic dietary (food only) risk estimates from exposures to cycloate in food do not exceed the Agency's level of concern (i.e., they are less than 100% of the cPAD) for the U.S. general population and all population subgroups using highly conservative assumptions. The chronic dietary (food only) risk estimate is 5.5% of the cPAD, for the most highly exposed population subgroup, children aged 3-5 years. No mitigation is necessary for chronic dietary (food only) exposure.

(3) Drinking Water

Estimated environmental concentrations of cycloate and its metabolites for both surface and ground water sources of drinking water are below the Agency's DWLOCs, indicating that aggregate chronic exposure to cycloate in food and water, both acute and chronic, were thus below the Agency's level of concern for all population subgroups. No mitigation is needed for drinking water.

(4) Residential

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

(5) Aggregate

Since there are no residential uses for cycloate, the aggregate risk assessment considered the combined risk from exposure through food and drinking water *only*. In general, combined risks from these exposures are less than 100% of the cPAD and are not considered to be a risk concern. No

population subgroup exceeded the Agency's level of concern for either acute or chronic dietary exposure to cycloate based upon aggregated exposure to food plus water. Given current uses, the Agency has no risk concerns for exposure to cycloate through food and/or water. No mitigation is necessary for aggregate exposure.

b. Occupational Risk Mitigation

(1) Handler Exposure

There is a potential risk for short- and intermediate-term dermal and inhalation exposures in occupational settings from mixing, loading and applying cycloate products. For the garden beet, spinach and sugarbeet uses, potential risks for the following occupational exposure scenarios can be addressed with engineering controls:

- Scenario (2) closed system mixing/loading of EC liquid formulation for groundboom applications to garden beets, spinach and sugarbeets (dermal exposure only);
- Scenario (4) applying liquid sprays by groundboom equipment with an enclosed cab to garden beets, spinach and sugarbeets (dermal and inhalation exposure); and
- Scenario (5) applying impregnated dry bulk fertilizers with tractor drawn spreader with an enclosed cab to sugarbeets (dermal exposure only).

Even taking into account maximum PPE and engineering controls, three (3) occupational exposure scenarios do not achieve the target MOE of 300 for inhalation exposure. In these instances, EPA first characterizes the handler risk estimates (high acreage/application rates) by examining the assumptions used in the risk assessment, the strengths and weaknesses of existing data and the potential for additional data to further refine the risk assessments. The Agency then considers the benefits of a pesticide's use, in making its risk management decision.

The following is a detailed consideration for the scenario where current estimates show MOEs of less than the specified target MOE of 100 for dermal exposure:

<u>Scenario (1) closed system mixing/loading of EC liquid formulation for chemigation application to garden beets, spinach and sugarbeets at 350 acres per day at 4 lbs. a.i./acre</u>

A current dermal MOE estimate of 58 was assessed, assuming maximum acreage at maximum application rate. Even with closed mixing/loading, the dermal risk estimate still exceeds the Agency's LOC (MOEs <100) for EC liquid formulation for chemigation application to garden beets, spinach and sugarbeets. **To address this handler concern, the Agency has proposed and the registrant has agreed to voluntarily cancel the chemigation application of cycloate.**

The following are detailed considerations for each scenario where current estimates show MOEs of less than the specified target MOE of 300 for inhalation exposure:

Scenario (1) closed system mixing/loading of liquid formulation for chemigation application to garden beets, spinach and sugarbeets at 350 acres at per day 4 lbs. a.i./acre

A current inhalation MOE estimate of 150 was assessed, assuming maximum acreage at maximum application rate. Even with closed mixing/loading, the inhalation risk estimate still exceeds the Agency's LOC (MOEs <300) for EC liquid formulation for chemigation application to garden beets, spinach and sugarbeets. **To address this handler concern, the Agency has proposed and the registrant has agreed to voluntarily cancel the chemigation application of cycloate.**

Scenario (2) closed system mixing/loading of liquid formulation for groundboom applications to garden beets and sugarbeets at 200 acres per day at 4 lbs. a.i./acre

The risk assessment for this scenario was conducted at the maximum application rate and at 80 and 200 acres treated daily. At 80 acres treated, the inhalation MOE is 660. At 200 acres treated, the inhalation MOE is 260. Information received from garden beet and sugarbeet growers indicates that, typically, less than 200 acres are actually treated with cycloate in a day. Comments from sugarbeet growers also indicate that less than the maximum application rate of 4 lbs. a.i./acre is used. Therefore, the Agency believes that the amount of cycloate handled in a day is actually less than the maximum value assessed by the Agency. **Use and usage information on the typical application rate and maximum daily acres treated for this scenario will be required.**

Scenario (3) closed system mixing/loading and impregnation of EC liquid formulation onto dry bulk fertilizers to sugarbeets at 200 acres per day at 4 lbs. a.i./acre; and

Scenario (5) applying impregnated dry bulk fertilizers with enclosed cabs to sugarbeets at 80 and 200 acres per day at 4 lbs. a.i./acre

The risk assessment for Scenario (3) was conducted at the maximum application rate and at 80 and 200 acres treated daily. At 80 acres treated per day, the MOE is 320. At 200 acres treated per day, the MOE is 130. For Scenario (5), current MOE estimates ranging from 250 at 80 acres treated per day to 99 for 200 acres treated per day, assuming maximum acreage at maximum application rate.

Information received from sugarbeet growers indicates that, typically, less than the maximum application rate of 4 lbs. a.i./acre is used during the impregnation process and, in many cases, may be at half the maximum application rate. Therefore, the Agency believes that the amount of cycloate handled in a day is actually less than the maximum value assessed by the Agency. **Use and usage information on the typical application rate and maximum daily acres treated for this scenario will be required.**

Comments from the sugarbeet growers also indicate that the on-farm impregnation of cycloate onto dry bulk fertilizer does not occur. The impregnation work is being conducted in commercial settings utilizing an enclosed mixing/loading system. **As such, the Agency has**

proposed and the registrant has agreed to prohibit on-farm impregnation of cycloate onto dry bulk fertilizer. Therefore, the impregnation of cycloate onto dry bulk fertilizer will be restricted to commercial settings only.

(2) Post-Application Exposure

Since cycloate is incorporated into the soil either immediately or within a few hours after application, post-application exposures are expected to be negligible. As a result, post-application scenarios were not assessed. **Due to the volatility of cycloate, the REI will be extended from the current 12 hours to 48 hours. However, workers will be allowed to enter the treated area during the first 48 hours following application to plant crops, provided they follow the early reentry language on the label.**

2. Environmental Risk Mitigation

a. Birds

Minimal acute risk is expected to birds from the registered uses of cycloate. However, no avian reproduction studies are available to assess chronic effects to birds. The acute RQs were not calculated for birds because the toxicity data on birds indicate that the RQs will be far below any Agency level of concern. The LC_{50} value for birds (>5,000 ppm) was greater than the highest dose tested (1,440 ppm), which is the highest application rate of 4 lbs. a.i./acre for short grass.

Currently, EPA does not have chronic toxicity data for birds and in the absence of this data, we cannot preclude chronic risks to birds, as discussed in Section V.A.1 of this document. The Agency reserves the right to impose environmental risk mitigation strategies for cycloate, once the avian chronic toxicity data has been reviewed.

b. Mammals

Minimal acute risk to small mammals is expected from the registered uses of cycloate. Acute RQs were not calculated for small mammals because the toxicity data on rats indicate that the RQs will be far below any Agency level of concern. Chronic RQs range from 0.6 to 9.6 at the 2 lbs. a.i./acre (typical) application rate. At the higher 4 lbs. a.i./acre (maximum) application rate, the chronic RQs range from 1.2 to 19.2. The chronic risk to small mammals will be primarily for edge-of-field habitats, as with birds described in the preceding section, where soil, water and food items may become contaminated by direct application, spray drift or volatilization. Since cycloate is used before or at-planting, there are limited food items in the field; however, the animals feeding in the field are more likely to be exposed to contaminated spoil-dwelling organisms (e.g., invertebrates), seeds and soil rather than the crop itself. The fur on the small mammals will pick up cycloate

residues as they burrow in the soil, thus exposing themselves directly to residues in the soil as they lick their fur.

c. Fish and Aquatic Invertebrates

Freshwater Species

Cycloate is moderately toxic to freshwater fish (based on LC_{50} values ranging from 4.5 ppm to 10 ppm) and slightly toxic to freshwater invertebrates (EC_{50} = 24 ppm). Acute RQs for both federally listed endangered and threatened species and nonendangered species of freshwater fish and aquatic invertebrates are all below Agency levels of concern.

Although the EEC is not expected to reach 1% or greater of any acute LC_{50} or EC_{50} value, parent cycloate is persistent in the aquatic environment. This does not preempt the need for chronic fish or aquatic invertebrate studies if data show that terrestrial organisms may be chronically sensitive to cycloate. It is uncertain as to whether aquatic species may have chronic adverse impacts from cycloate use. Since parent cycloate is persistent in the aquatic environment, an early life stage fish and a freshwater invertebrate life cycle test using the TGAI (Guidelines 850.1300 and 850.1350) are required. Without these data, the Agency cannot preclude chronic risks to aquatic organisms. The preferred test species for the invertebrate life cycle test is *Daphnia magna*.

Estuarine/Marine Species

Cycloate is used on spinach near estuarine areas and is expected to be persistent and moderately mobile in moist or flooded soils. As a result, EPA requires an estuarine/marine fish and invertebrate acute toxicity data (Guideline 850.1035) for cycloate. In the absence of this data, risk assessment for estuarine/marine fish and invertebrates cannot be completed.

d. Nontarget Insects

Available data indicate that technical cycloate is practically nontoxic to the honeybee. The labeled uses for cycloate on garden beets, spinach and sugarbeets are predicted to not exceed any LOC for risk to nontarget insects. No mitigation is necessary for nontarget insects.

e. Nontarget Terrestrial and Aquatic Plants

Exposure is expected to nontarget plants from runoff, volatility and spray drift (from Center-Pivot, Lateral Move, End Tow and Traveler irrigation systems). The degree of risk (both acute and chronic) to nontarget terrestrial and aquatic plants is uncertain and cannot be assessed by EPA due to the complete lack of phytotoxicity data. Since cycloate is an herbicide, EPA must presume that there

is a risk to nontarget terrestrial and aquatic plants. Terrestrial plant testing is necessary since cycloate is an herbicide with nonresidential terrestrial use patterns. The required Tier 1 terrestrial plant testing on cycloate (TEP formulation) consisting of seedling emergence and vegetative vigor tests with ten crop species (Guidelines 850.4100 and 850.4150). Tier 2 tests (Guidelines 850.4225 and 850.4250) will be required for any test species that shows a reduction in response equal to or greater than 25% in the Tier 1 tests. Therefore, Tier 2 tests are held in reserve, pending the outcome of the Tier 1 tests.

A Tier 2 aquatic plant growth test (Guideline 850.4400) is required for cycloate TEP because it is an herbicide that has outdoor nonresidential terrestrial uses. The following species should be tested at Tier 2: *Kirchneria subcapitata*, *Lemna gibba*, *Skeletonema costatum*, *Anabaena flos-aquae* and a freshwater diatom. Without the above data, the Agency must preclude acute and chronic risk to nontarget terrestrial and aquatic plants.

f. Summary of Environmental Risk Mitigation

The EFED risk assessment for cycloate is limited because of lack of data to assess chronic risk to birds and risk to plants. Therefore, avian reproduction data, seedling emergence, vegetative vigor and aquatic plant growth; and acute toxicity data for estuarine/marine animals are required. The registrant has agreed to submit data on cycloate, that will allow the Agency to adequately assess the ecological effects of cycloate, thus refining these risk estimates. The Agency reserves the right to impose environmental risk mitigation strategies for cycloate, once these data have been reviewed**.**

The following label statement is needed to address ecological concerns for cycloate:

Surface Water Label Advisory

"Do not apply directly to water, to areas where surface water is present or to intertidal areas below the mean high water mark. Do not apply when weather conditions favor drift from the target area. Do not contaminate water when disposing of equipment wash water."

E. Other Labeling Requirements

Other use and safety information needed for labeling of all end-use products containing cycloate are indicated in Table 16.

1. Endangered 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 Endangered Species Act 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. This analysis will consider the risk mitigation measures that are being implemented as a result of this RED.

A determination that there is a likelihood of potential impact to a listed species may result in limitations on use of the pesticide, other measures to mitigate any potential impact or consultations with the Fish and Wildlife Service and/or the National Marine Fisheries Service as necessary.

The Endangered Species Protection Program as described in a *Federal Register* notice (54 FR 27984-28008, July 3, 1989) is currently being implemented on an interim basis. As part of the interim program, the Agency has developed County Specific Bulletins that articulate many of the specific measures outlined in the Biological Opinions issued to date. The Bulletins are available for voluntary use by pesticide applicators on EPA's website at *http://www.epa.gov/espp*.

2. Spray Drift Management

Cycloate must be incorporated into the soil immediately after application, to be effective and to avoid substantial losses due to volatilization. The methods used to apply and incorporate cycloate into the soil affect the rate of volatilization. During chemigation, cycloate volatilizes at a higher rate than with mechanical incorporation methods, increasing the potential for off-site drift. The chemigation application of cycloate has been voluntarily cancelled by the registrants. Since all remaining application methods involve mechanical incorporation into the soil, EPA anticipates low potential for off-site drift.

3. For Commercial Use Only

There are no existing or proposed uses of cycloate for residential (home/garden) use, nor is it used in or around public buildings, schools or other recreational areas where children might be exposed. Cycloate is currently registered for use in commercial settings only. Non-commercial use is prohibited. All product labels will be amended to state that cycloate is "For commercial use only."

V. Actions Required of Registrants

A. Manufacturing-Use Products

1. Additional Generic Data Requirements

The generic database supporting the reregistration of cycloate for the eligible uses has been reviewed and determined to be substantially complete. The following confirmatory data requirements have been identified by the Agency:

Guideline Test Name	New OPPTS Guideline No.	Old Guideline No.
Stability on TGAI	830.6313	63-13
Ultraviolet/Visible Absorption	830.7050	None
Solubility	830.7840	63-8
Field Accumulation in Rotational Crops	835.1900	165-2
Terrestrial Field Dissipation Study #2	835.6100	164-1
Estuarine/Marine Fish Acute Toxicity on TGAI	850.1035	72-3A
Estuarine/Marine Invertebrate Acute Toxicity on TGAI		72-3C
Fish-Early Life Stage on TGAI	850.1300	72-4A
Invertebrate Life Cycle Test on TGAI	850.1350	72-4B
Avian Reproduction - Bobwhite Quail on TGAI	850.2300	71-4A
Avian Reproduction - Mallard Duck on TGAI		71-4B
Seedling Germination/Seedling Emergence, Tier 1 (10 most sensitive species from testing with parent compound) on TEP	850.4100	122-1A
Vegetative Vigor, Tier 1 (10 most sensitive species from testing with parent compound) on TEP	850.4150	122-1B
Aquatic Plant Growth, Tier 2 (5 most sensitive species) on TEP	850.4400	123-2
Multiresidue Methods (3- and 4-hydroxycycloate metabolites)	860.1360	171-4M
Developmental Neurotoxicity Study, Rat	870.6300	83-6

a. Product Chemistry Data

Acceptable data pertaining to thermal stability data have been submitted; however, data are required concerning the stability of the TGAI (Guideline 830.6313) upon exposure to metals and metal ions.

According to OPPTS Series 830, Product Properties Test Guidelines, the Agency requires data pertaining to ultraviolet/visible absorption (Guideline 830.7050) for the PAI.

Acceptable data pertaining to solubility in water have been submitted; however, data are required demonstrating the solubility of the TGAI in representative polar and nonpolar solvents at 20° or 25° C.

b. Environmental Fate Data

Limited field rotational crop trials (Guideline 835.1900) are required because cycloate residues of concern were detected in/on samples of rotational crop commodities from the reviewed field rotational crop study. The need for rotational crop tolerances and restrictions will be determined following submission of the required field rotational crop studies.

EPA generally requires two acceptable terrestrial field dissipation (TFD) studies (Guideline 835.6100). There is currently one acceptable TFD study from California; however, the Agency requires a second TFD be performed. A site in the Red River Valley of the North is preferable, and a module to measure volatilization as well as dissipation from the soil is requested. Based on uncertainties identified in the drinking water assessment, a monitoring study for cycloate sulfoxide should be incorporated into the TFD study.

There are outstanding data needs for the primary degradate, cycloate sulfoxide. Cycloate sulfoxide, is considered to be potentially bio-active according to OPP's Health Effects Division ("Results of October 31, 2000 MARC Committee Meeting on Molinate Degradates in Water," memo dated November 30, 2000; DP Barcode D270853). There are currently no fate and transport data available on the sulfoxide degradate of cycloate. In order to ascertain toxicity to the environment, a soil photodegradation study on cycloate sulfoxide (Guideline 835.2410) is held in reserve, pending the review of data submitted on parent cycloate.

c. Ecological Effects Data

Since cycloate is used on spinach near estuarine areas, EPA will require estuarine/marine fish and invertebrate acute toxicity data (Guidelines 850.1035) for the cycloate TGAI. In the absence of this data, risk assessment for estuarine/marine fish and invertebrates cannot be completed. In addition, since parent cycloate is persistent in the aquatic environment, an early life stage fish and a freshwater invertebrate life cycle test using the TGAI (Guidelines 850.1300 and 850.1350) are required. The preferred test species for the invertebrate life cycle test is *Daphnia magna*. Without these data, the Agency cannot preclude chronic risks to aquatic organisms.

Avian reproductive studies (Guideline 850.2300) using the TGAI are required for cycloate because the pesticide is stable in the environment to the extent that potentially toxic amounts may persist in animal feed, especially preceding or during the breeding season and information derived from mammalian reproduction studies indicates reproduction in terrestrial vertebrates may be adversely affected by the anticipated use of the product. In the absence of data, potential chronic risk to birds must be presumed. The value of having the avian reproduction study done is very high.

Terrestrial plant testing is necessary since cycloate is an herbicide with nonresidential terrestrial use patterns. Tier 1 terrestrial plant testing is required on cycloate (TEP formulation), consisting of seedling emergence and vegetative vigor tests with ten crop species (Guidelines 850.4100 and 850.4150). Tier 2 tests (Guidelines 850.4225 and 850.4250) will be required for any test species that shows a reduction in response equal to or greater than 25% in the Tier 1 tests. Therefore, Tier 2 tests are held in reserve, pending the outcome of the Tier 1 tests.

Aquatic plant growth testing (Guideline 850.4400) is required for the cycloate TEP because it is an herbicide that has outdoor nonresidential terrestrial uses. The following species should be tested at Tier 2: *Kirchneria subcapitata*, *Lemna gibba*, *Skeletonema costatum*, *Anabaena flos-aquae* and a freshwater diatom. Without the above data, the Agency must preclude acute and chronic risk to nontarget terrestrial and aquatic plants.

As mentioned in the ecological effects section, there are outstanding data needs for cycloate sulfoxide. There is uncertainty regarding potential risk to aquatic and terrestrial organisms from cycloate sulfoxide. In order to ascertain toxicity to the environment, an avian subacute dietary toxicity test on cycloate sulfoxide (Guideline 850.2200) is held in reserve, pending the review of submitted data on parent cycloate.

d. Residue Chemistry Data

The registrant has submitted a new residue analytical method (GC/NPD) for cycloate and its plant metabolites which need to be included in the tolerance expression. The new GC/NPD method, must be radiovalidated.

The reregistration requirements for multiresidue methods data are not yet fulfilled. Multiresidue methods data (Guideline 860.1360) are required to provide recovery data through the PAM I protocol for cycloate's 3HC and 4HC metabolites. The registrant should follow the directions for the protocols found in PAM Volume I, Appendix II, starting with the decision tree for multiresidue methods testing (i.e., decisions on what protocols to follow and proper applications of the methods).

e. Toxicological Data

There is concern for developmental neurotoxicity resulting from exposure to cycloate. A developmental neurotoxicity study (including cholinesterase measures) in the rat has been identified as a data gap.

2. Labeling for Manufacturing-Use Products

To remain in compliance with FIFRA, manufacturing-use product (MUP) labeling should be revised to comply with all current EPA regulations, PR Notices and applicable policies. The MUP labeling should bear the labeling contained in the table at the end of this section. The MUP label will explicitly prohibit use of products that do not conform to Section V.B.2 of this document.

B. End-Use Products

1. 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.

2. Labeling for End-Use Products

Labeling changes are necessary to implement measures outlined in Section V above. Specific language to implement these changes is specified in Table 16 at the end of this section.

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 16) describes how language on the labels should be amended.

Table 16. Summary of Required Labeling Changes for Cycloate

Description	Amended Labeling Language	Placement on Label
	Manufacturing Use Products	
For all Manufacturing Use Products	"Only for formulation into an herbicide for the following use(s) [fill blank only with those uses that are being supported by MP registrant]."	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 MP 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 MP label if the formulator, user group, or grower has complied with U.S. EPA submission requirements regarding support of such use(s)."	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 Pollution Discharge Elimination 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 EPA."	Precautionary Statements
	End-Use Products Intended for Occupational Use (WPS)	
PPE Requirements Established by the RED[1] for Liquid Formulations	"Personal Protective Equipment (PPE)" "Some materials that are chemical-resistant to this product are" (*registrant inserts correct chemical-resistant material*). "If you want more options, follow the instructions for category" *[registrant inserts A,B,C,D,E,F,G,or H]* "on an EPA chemical-resistance category selection chart." "Engineering controls are required for all mixers, loaders and applicators (see Engineering Controls for additional requirements)." "All mixers, loaders, applicators, and other handlers must wear at a minumum: – Long-sleeved shirt and long pants, – Shoes plus socks, and – Chemical-resistant gloves and chemical-resistant apron when mixing and loading."	Immediately following/below Precautionary Statements: Hazards to Humans and Domestic Animals

Description	Amended Labeling Language	Placement on Label
PPE Requirements Established by the RED[1] for Liquid Formulations, continued	"Handlers performing tasks, such as spill clean-up or cleaning equipment, for which engineering controls are not feasible must wear: – Long-sleeved shirt and long pants, – Shoes plus socks, – Chemical-resistant gloves, – Chemical-resistant apron, and – A NIOSH-approved respirator with -- an organic-vapor removing cartridge with a prefilter approved for pesticides (MSHA/NIOSH approval number prefix TC-23C), or -- a canister approved for pesticides (MSHA/NIOSH approval number prefix TC-14G), or -- an organic-vapor cartridge or canister with any N[2], R or P or He prefilter."	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 and 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)
Engineering Controls: Liquid Formulations	"Engineering Controls" "**Mixers and loaders** must use a closed system that meets the requirements listed in the Worker Protection Standard (WPS) for agricultural pesticides [40 CFR 170.240(d)(4)] for dermal protection, and must: – Wear the personal protective equipment required in the PPE section of this labeling for mixers and loaders, – Wear protective eyewear, if the system operates under pressure, – *Either* use a closed system that also meets the requirements in the WPS for inhalation protection *or* wear the type of respirator specified in the personal protective equipment sections of the labeling, and – Be provided and have immediately available for use in an emergency, such as a spill or equipment breakdown: chemical-resistant footwear, and, if using a closed system cab that provides respiratory protection, a respirator of the type specified in the PPE section of this labeling."	Precautionary Statements: Hazards to Humans and Domestic Animals (Immediately following PPE and User Safety Requirements)

Description	Amended Labeling Language	Placement on Label
Engineering Controls: Liquid Formulations, continued	"**Applicators** must use motorized ground equipment that is equipped with an enclosed cab that meets the definition in the Worker Protection Standard for Agricultural Pesticides [40 CFR 170.240(d)(5)] for dermal protection. In addition, applicators must: – Wear the personal protective equipment required in the PPE section of this labeling for applicators, – *Either* wear the type of respirator specified in the PPE section of this labeling *or* use an enclosed cab with a properly functioning ventilation system that is used and maintained according to the manufacturer's written operating instructions and that is declared in writing by the manufacturer or by a government agency to provide at least as much respiratory protection as the type of respirator specified in the PPE section of this labeling, – Be provided and have immediately available for use in an emergency for when they must exit the cab in the treated area: chemical-resistant gloves, and, if using an enclosed cab that provides respiratory protection, a respirator of the type specified in the PPE section of this labeling, – Take off any PPE that was worn in the treated area before reentering the cab, and – Store all such PPE in a chemical-resistant container, such as a plastic bag, to prevent contamination of the inside of the cab."	Precautionary Statements: Hazards to Humans and Domestic Animals (Immediately following PPE and User Safety Requirements)
Additional Mitigation Measures for Handlers and Applicators in California	Remove all of the language from the current label under the heading "Additional Mitigation Measures for Handlers and Applicators in California." Add the following section: "Additional Use Limitations for California Only: Mixers, loaders, applicators, and other handlers are prohibited from handling more than 93 gallons (560 pounds active ingredient) in any 21-day period. Property operators must include in their Pesticide Use Records the name of the person(s) who handled the product for each application."	Precautionary Statements: Hazards to Humans and Domestic Animals (Immediately following the PPE requirements)
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 immediately following Engineering Controls (Must be placed in a box)
Environmental Hazards	"Do not apply directly to water, to areas where surface water is present or to intertidal areas below the mean high water mark. Do not apply when weather conditions favor drift from the target area. Do not contaminate water when disposing of equipment wash water or rinsate."	Precautionary Statements immediately following the User Safety Recommendations

Description	Amended Labeling Language	Placement on Label
Entry Prohibition Period for all end-use products with uses within the scope of the Worker Protection Standard for Agricultural Pesticides	"Entry (including early entry that would otherwise be permitted under the WPS) by any person -- other than a correctly trained and equipped handler who is performing a handling task permitted by the WPS -- is PROHIBITED for 48 hours following application. Do not allow entry by unprotected persons into the treated area until 48-hour period is expired and the warning signs are removed."	Directions for Use under Agricultural Use Requirements Box
Notification Requirements	"NOTIFICATION: Before the start of the application, notify workers of the application by warning them orally and by posting warning signs at entrances to the treated area. The signs must bear the skull and crossbones symbol and state: (1) "DANGER/PELIGRO," (2) "DO NOT ENTER/NO ENTRE," (3) the date and time of treatment, (4) "Cycloate {or use other brand name} in use," and (5) name, address, and telephone number of the applicator. Post the warning sign instead of the WPS sign for this application, but follow all WPS requirements pertaining to location, legibility, size, and timing of posting and removal."	Directions for Use under Agricultural Use Requirements Box
Special Early Entry Exception	"Special Early Entry Exception: Workers may enter the treated area during the first 48 hours following application to plant crops, provided all of the following conditions are met: (1) The special early entry workers must use motorized ground equipment that is equipped with an enclosed cab that meets the definition in the Worker Protection Standard for Agricultural Pesticides [40 CFR 170.240(d)(5)] for dermal protection. In addition, these workers must: – Wear the personal protective equipment required in the PPE section of this labeling for applicators, – *Either* wear the type of respirator specified in the PPE section of this labeling *or* use an enclosed cab with a properly functioning ventilation system that is used and maintained according to the manufacturer's written operating instructions and that is declared in writing by the manufacturer or by a government agency to provide at least as much respiratory protection as the type of respirator specified in the PPE section of this labeling, – Be provided and have immediately available for use in an emergency when they must exit the cab in the treated area: chemical-resistant gloves, and, if using an enclosed cab that provides respiratory protection, a respirator of the type specified in the PPE section of this labeling, – Take off any PPE that was worn in the treated area before reentering the cab, and – Store all such PPE in a chemical-resistant container, such as a plastic bag, to prevent contamination of the inside of the cab. (2) Employers of the special early entry workers must make sure that these workers: – Have received training equivalent to WPS pesticide handler training before entering the treated area, – Are provided with the specified type of respirator, and the respirator fits them correctly and is maintained as required in the WPS for handlers, and – Are provided all of the WPS protections for early entry workers, including PPE instructions, labeling information and instructions, decontamination sites, and duties related to providing, cleaning, and maintaining the PPE for early-entry workers."	Directions for Use under Agricultural Use Requirements Box

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 Direction for Use directly above the Agricultural Use Box.
General Application Restrictions	"Chemigation is prohibited."	Place near the beginning of the Direction for Use section.
Application Restrictions for garden beets, spinach, and sugarbeets	"Garden Beets, Spinach, and Sugar Beets:" "Maximum of 2/3 gallon (4 pounds active ingredient) per application and one application per crop cycle."	Directions for Use associated with each crop listed
Application Restrictions for dry bulk fertilizer	"Impregnation of dry bulk fertilizer is permitted in commercial settings only. On-farm impregnation of dry bulk fertilizer is prohibited. All persons involved in the impregnation process are considered pesticide handlers and must wear the handler personal protective equipment and follow the engineering control requirements specified on this labeling. If at any time during the impregnation process, including loading of the impregnated fertilizer into the trucks for transporting, the system does not provide inhalation protection equivalent to an organic-vapor removing respirator, all persons at the impregnation site must wear the respirator required on this labeling for handlers."	Directions for Use associated with the dry bulk fertilizer instructions

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

[2] ***Instruction to Registrant****:* Drop the "N" type prefilter from the respirator statement if the pesticide product contains, or is used with, oil.

D. Existing Stocks

Registrants may generally distribute and sell products bearing old labels/labeling for 26 months from the date of the issuance of this Reregistration Eligibility Decision (RED) for cycloate. Persons other than the registrants may generally distribute or sell such products for 50 months from the date of issuance of this RED. However, existing stocks time frames will be established case-by-case, depending on the number of products involved, the number of label changes and other factors. Refer to "Existing Stocks of Pesticide Products; Statement of Policy," as prescribed in the *Federal Register* of June 26, 1991 (56 FR 29362) (FRL-3846-4).

The Agency has determined that registrants may distribute and sell cycloate products bearing old labels/labeling for 26 months from the date of issuance of this RED. Persons other than the registrants may generally distribute or sell such products for 50 months from the date of issuance of this RED. Registrants and persons other than the registrants remain obligated to meet pre-existing label requirements and existing stocks requirements applicable to products they sell or distribute.

VI. APPENDICES

Appendix A. CYCLOATE (Case No. 2125): Table of Use Patterns Eligible for Reregistration

Site Application Type Application Timing Application Equipment	Formulation [EPA Reg. No.]	Maximum Single Application Rate (lbs. a.i./acre)	Maximum No. of Applications Per Season	Maximum Seasonal Rate (lbs. a.i./acre)	Preharvest Interval (Days)	Use Directions and Limitations
Beets, Garden						
Soil broadcast or band[1] Pre-plant, or at-planting, or immediately post-planting Ground	6 lbs./gal. EC [73637-5]	3.0-4.0	One	Not specified (NS)[6]	Not specified (NS)[7]	Use on mineral soils only. Use lower rate on sandy soils and higher rate on heavier soils. When the product is applied in combination with fluid fertilizers, do not apply over 150 lbs. of actual nitrogen per acre.
Beets, Sugar						
Soil broadcast or band[1] Pre-plant, or at-planting, or immediately post-planting Ground	6 lbs./gal. EC [73637-5]	3.0-4.0	One[2]	NS[6]	NS[7]	Use on mineral soils only. Use lower rate on sandy soils and higher rate on heavier soils. Injury may result in highly saline or alkaline soils. May be tanked mixed with the herbicide EPTC for pre-plant use on sugarbeets grown in MI, MN, OH, and the Red River Valley area of ND.
Soil broadcast or band[1] Fall Ground	6 lbs./gal. EC [73637-5]	4.0	One[2]	NS[6]	NS[7]	Recommended only in the states of ID, MN, MT, ND, OR, and WY. Apply and incorporate in late fall before ground freezes.
Soil incorporated Post-emergence Irrigation	6 lbs./gal. EC [ID010015][3] [OR010022][3] [WA010023][3]	4.0	NS	NS[6]	NS[7]	Incorporate to a maximum depth of 3 inches and minimum depth of 2 inches.
Spinach						
Soil broadcast or band[1] Pre-plant, or at-planting, or immediately post-planting Ground	6 lbs./gal. EC [73637-5]	3.0[4] 4.0[5]	One	NS[6]	NS[7]	Use on mineral soils only.
Soil broadcast Pre-plant Ground	6 lbs./gal. EC [OR010023][3] [WA010021][3] [WA010022][3]	3.24	NS	NS[6]	NS[7]	Incorporate to a maximum depth of 3 inches and minimum depth of 2 inches.

Site Application Type Application Timing Application Equipment	Formulation [EPA Reg. No.]	Maximum Single Application Rate (lbs. a.i./acre)	Maximum No. of Applications Per Season	Maximum Seasonal Rate (lbs. a.i./acre)	Preharvest Interval (Days)	Use Directions and Limitations
Spinach seed soil incorporated	6 lbs./gal. EC [WA020003]	3.0	NS	NS[6]	NS[7]	

EC = Emulsifiable Concentrate

[1] For band treatment, reduce the amount of product proportional to the row spacing and band width to be treated.

[2] If the product is applied to sugarbeets in the fall, it should not be re-applied the following spring.

[3] Use directions were extracted from a LUIS Report dated 10/15/01.

[4] Dose rate recommended in AR, CO, CT, DE, IL, MA, MD, ME, MS, NH, NJ, NY, NC, OH, OK, PA, SC, TX, VT, VA and western TN.

[5] Dose rate recommended in CA only.

[6] Maximum seasonal rate must be specified on the label.

[7] PHI must be specified on the label.

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

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 Cycloate

New Guideline Number	Old Guideline Number	Requirement	Use Pattern	Bibliographical Citation(s)
PRODUCT USE CHEMISTRY				
830.1600	61-2A	Starting Materials and Manufacturing Process	**All**	41614702
830.1620	61-2B	Description of Production Process		
830.1670		Discussion of Formation of Impurities		
830.1700	62-1	Preliminary Analysis		41614701
830.6302	63-2	Color	A, B	41582401
830.6303	63-3	Physical State		
830.6304	63-4	Odor		
830.7220	63-6	Boiling Point/Boiling Range		
830.7300	63-7	Density, Relative Density, Bulk Density	**All**	
830.7840 830.7860	63-8	Solubility on TGAI	**All**	41582401 (Upgradable), Data Gap
830.7950	63-9	Vapor Pressure	**All**	41582401
830.7370	63-10	Dissociation Constant in Water	**All**	
830.7550	63-11	Octanol/Water Partition Coefficient	**All**	41920603
830.7000	63-12	pH of Water Solutions or Suspensions	**All**	41582401
830.7050	None	Ultraviolet/Visible Absorption		Data Gap
830.6313	63-13	Stability on TGAI	**All**	41582401 (Upgradable), Data Gap
ECOLOGICAL EFFECTS				
850.2100	71-1A	Avian Acute Oral Toxicity, Bobwhite Quail on TGAI	A, B	00132798, Acc. 072166 & 073005
850.2200	71-2A/2B	Avian Subacute Dietary Toxicity, Bobwhite Quail on TGAI	A, B	00145554, Acc. 072166
		Avian Subacute Dietary Toxicity, Mallard Duck on TGAI		42090306, Acc. 072166
		Avian Subacute Dietary Toxicity, Bobwhite Quail or Mallard Duck on Cycloate Sulfoxide		Reserved
850.2300	71-4A	Avian Reproduction, Bobwhite Quail on TGAI	A, B	Data Gap
	71-4B	Avian Reproduction, Mallard Duck on TGAI		Data Gap
850.1075	72-1A	Fish Acute Toxicity, Bluegill Sunfish	A, B	00084743, 00143654, 41614703, 45608401, Acc. 072166 & 090620
	72-1C	Fish Acute Toxicity, Rainbow Trout		
850.1010	72-2A	Invertebrate Acute Toxicity	A, B	00143655, 05001497

New Guideline Number	Old Guideline Number	Requirement	Use Pattern	Bibliographical Citation(s)
850.1035	72-3A	Estuarine/Marine Fish Acute Toxicity on TGAI	A, B	Data Gap
	72-3C	Estuarine/Marine Invertebrate Acute Toxicity on TGAI	A, B	Data Gap
850.1300	72-4A	Fish-Early Life Stage on TGAI	A, B	Data Gap
850.1350	72-4B	Aquatic Invertebrate Life Cycle on TGAI	A, B	05001497, Data Gap
850.1730	72-6B	Fish BCF (Aquatic Organism Accumulation)	A, B	Reserved
850.4100	122-1A	Seedling Germination/Seedling Emergence, Tier 1 (10 most sensitive species from testing with parent compound) on TEP	A, B	Data Gap
850.4150	122-1B	Vegetative Vigor, Tier 1 (10 most sensitive species from testing with parent compound) on TEP	A, B	Data Gap
850.4225	123-1A	Seedling Germination/Seedling Emergence, Tier 2 (10 most sensitive species from testing with parent compound) on TEP	A, B	Reserved
850.4250	123-1B	Vegetative Vigor, Tier 2 (10 most sensitive species from testing with parent compound) on TEP	A, B	43889101, Reserved
850.4400	123-2	Aquatic Plant Growth, Tier 2 (5 most sensitive species from testing with parent compound) on TEP	A, B	Data Gap
850.3020	141-1	Honey Bee Acute Contact Toxicity on TGAI	A, B	00036935
TOXICOLOGY				
870.1100	81-1	Acute Oral Toxicity, Rat	A, B	00132271, 00132791, 13279091, Acc. 073004
870.1200	81-2	Acute Dermal Toxicity, Rabbit		
870.1300	81-3	Acute Inhalation Toxicity, Rat	A, B	00132792, 41589203, 42237001, 42868601
870.2400	81-4	Primary Eye Irritation, Rabbit	A, B	00132791, 13279091
870.2500	81-5	Primary Skin Irritation		
870.2600	81-6	Dermal Sensitization, Guinea Pig	A, B	41708101, 41729901
870.6100	81-7	Acute Delayed Neurotoxicity, Rat	A, B	42854001, 42921701, 42985701
870.6200A	81-8	Acute Neurotoxicity Screening Battery, Rat	A, B	42921701, 43968001
870.3100	82-1A	90-Day Subchronic Feeding, Rodent	A, B	40458401
870.3150	82-1B	90-Day Subchronic Feeding, Nonrodent (Dog)		
870.3200	82-2	21-Day Dermal, Rat	A, B	42090305, 43323801
None	None	21-Day Inhalation, Rat	A, B	43552101
870.3465	82-4	90-Day Inhalation, Rat	A, B	40049601-2, 42237001, 42985701

New Guideline Number	Old Guideline Number	Requirement	Use Pattern	Bibliographical Citation(s)
870.6200B	82-7	Subchronic Neurotoxicity Study	A, B	42921701, 42985701, 43967801
870.4100	83-1A	Chronic Feeding Toxicity, Rodent	A, B	00077787, 00137735, 92025028
	83-1B	Chronic Feeding Toxicity, Nonrodent (Dog)		40458401
870.4200	83-2A	Chronic Carcinogenicity (Feeding), Rat	A, B	00077787, 00077789, 00137735, 92025028
	83-2B	Chronic Carcinogenicity (Feeding), Mouse		00031592, 41920604
870.3700	83-3A	Prenatal Developmental Toxicity, Rat	A, B	00146659
	83-3B	Prenatal Developmental Toxicity, Rabbit		42694901
870.3800	83-4	2-Generation Reproduction, Rat	A, B	00132795, 41333402, 41589203, 41691901
None	None	3-Generation Reproduction, Rat	A, B	00132795
870.4300	83-5	Combined Chronic Toxicity/ Carcinogenicity Study, Rat	A, B	00077787, 00137735
870.6300	83-6	Developmental Neurotoxicity Study, Rat	A, B	Data Gap
870.5140	84-2A	Gene Mutation (Ames Test)	A, B	40825201, 41582401-2
870.5375	84-2B	Structural Chromosomal Aberration	A, B	41614704-5, 41629901
870.5500	84-4	Other Genotoxic Effects	A, B	40825201, 41614705, 41629901
870.7485	85-1	General Metabolism, Rat/Mouse/Monkey	A, B	00132796, 00138177, 42090303-5, 42169101, 43043401, 92025034
None	None	14-Day Oral Metabolism	A, B	42090303-5
870.7600	85-2	Dermal Absorption (Penetration), Rat	A, B	00164351, 40229701, 43712502
OCCUPATIONAL/RESIDENTIAL EXPOSURE				
875.1100	231	Estimation of Dermal Exposure at Outdoor Sites	A, B	43712501-3, 43739701, Reserved
875.1300	232	Estimation of Inhalation Exposure at Outdoor Sites	A, B	43712501-3, 43739701, Reserved
ENVIRONMENTAL FATE				
835.2120	161-1	Hydrolysis	A, B	00149662
835.2240	161-2	Photodegradation, Water	A, B	42249701
835.2410	161-3	Photodegradation, Soil on Cycloate Sulfoxide	A, B	Reserved
835.2370	161-4	Photodegradation, Air	A, B	42541101 (Supplemental)
835.4100	162-1	Aerobic Soil Metabolism Study	A, B	41582403, 42812901
835.4200	162-2	Anaerobic Soil Metabolism Study	A, B	00162652 (Supplemental)
835.4400	162-3	Anaerobic Aquatic Metabolism Study	A, B	42997901

New Guideline Number	Old Guideline Number	Requirement	Use Pattern	Bibliographical Citation(s)
835.1230 835.1240 835.4240	163-1	Leaching and Adsorption/Desorption	A, B	41920603
835.1410	163-2	Laboratory Volatilization from Soil	A, B	41920602
835.6100	164-1	Terrestrial Field Dissipation Study #1	A, B	41582404-5 (Upgradable)
		Terrestrial Field Dissipation Study #2		Data Gap
835.1850	165-1	Confined Accumulation in Rotational Crops	A, B	42409001
835.1900	165-2	Field Accumulation in Rotational Crops	A, B	Data Gap
835.1950	165-4	Bioaccumulation in Fish, Bluegill Sunfish	A, B	41920601
None	166-2	Small Scale Retrospective Ground Water	A, B	Reserved
None	166-3	Large Scale Retrospective Ground Water	A, B	Reserved
None	167-1	Field Runoff	A, B	Reserved
None	167-2	Surface Water Monitoring	A, B	Reserved
RESIDUE CHEMISTRY				
860.1300	171-4A	Nature of the Residue, Plants	A, B	00093480, 42090301-2
	171-4B	Nature of the Residue, Livestock		43273101, 43392701
860.1340	171-4C	Residue Analytical Method, Plants	A, B	00115084, 00115097, 43523801, 44489501
	171-4D	Residue Analytical Method, Animals		00145578, 43392701
860.1380	171-4E	Storage Stability	A, B	41582402, 41582406, 43501601, 44051801, 44551001
860.1480	171-4J	Magnitude of Residues in Meat, Milk, Poultry and Eggs	A, B	43392701
860.1500	171-4K	Crop Field Trials, Garden Beet	A, B	42919703, 42939701, 92025031
		Crop Field Trials, Spinach		41640301, 42919703
		Crop Field Trials, Sugarbeet		41640303, 42919702, 92025030
		Crop Field Trials, Swiss Chard		45679801
860.1520	171-4L	Processed Food, Sugarbeet (refined sugar, dried pulp and molasses)	A, B	42939701-2
860.1360	171-4M	Multiresidue Methods (3- and 4-hydroxycycloate metabolites)	A, B	Data Gap

Appendix C. Technical Support Documents

Additional documentation in support of this RED is maintained in the OPP Public Regulatory Docket, located in Room 119, Crystal Mall #2, 1801 S. Bell Street, Arlington, VA 22202-4501. It is open Monday through Friday, excluding legal holidays, from 8:30 AM to 4 PM.

The cycloate docket initially contained preliminary risk assessments and related documents as of May 12, 2004. Sixty days later, the comment period closed. The Agency then considered comments and added the formal "Response to Comments" documents to the docket. All documents, in hard copy form, may be viewed in the OPP docket room or downloaded or viewed via the Agency's website at *http://www.epa.gov/pesticides/reregistration/status.htm*. In addition, the technical support documents for cycloate are available through EPA Dockets, under docket ID number OPP-2004-0234. The public may access EPA Dockets at *http://www.epa.gov/edockets*. These documents include:

BEAD Documents:

1. Evaluation of Cycloate Chemigation (David Donaldson & William Phillips, September 8, 2004); and
2. Preliminary Analysis of Cycloate Mitigation for Extension of the Re-Entry Interval in Spinach and Dry Bulk Fertilizer Impregnation in Sugar Beets (David Donaldson, Nicole Zinn & William Phillips, October 12, 2004).

HED Documents:

1. HED Response to Helm Agro US, Inc. on Inhalation Occupational Exposure Assessment (John Liccione, October 2, 2004).

EFED Documents:

1. Comparison of Cycloate Estimated Environmental Concentrations in Wildlife Food Items with Expanded Suite of Mammalian Reproduction Endpoints (Michael Davy, September 21, 2004).

Other Documents:

1. Response #1 to EPA Final Cycloate Inquiries from American Sugarbeet Growers Association (Luther Markwart, September 22, 2004);
2. Response #2 to EPA Final Cycloate Inquiries from American Sugarbeet Growers Association (Luther Markwart, October 12, 2004);
3. Response #1 to EPA Final Cycloate Inquiries from Washington State University (Jane Thomas, September 7, 2004); and
4. Response #2 to EPA Final Cycloate Inquiries from Washington State University (Jane Thomas, September 24, 2004).

Appendix D. Citations Considered to Be Part of the Data Base Supporting the Reregistration Eligibility 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 (????), 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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92025034	Chin, T.; Clement, R. (1990) ICI Americas Inc. Phase 3 Reformat of MRID 00132796. Cycloate: Metabolism Study in the Rat: EHC Report No. and Study No T-10424. Prepared by Environmental Health Centre. 95 p.
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ACC 090620 / MRID 20540	Johnston, C.D. (1963) Acute Eye Irritation Test of Six Experimental Compounds: R-1910, R-2063-B, R-4572, N-2404, N-2790 and N-3684. (Unpublished study received Nov 29, 1965 under 7F0522; prepared by Woodard Research Corp., submitted by Stauffer Chemical Co., Richmond, CA; CDL:097555-C)

Appendix E. EPA's Batching of Cycloate 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 cycloate, the primary active ingredient, the Agency has batched products which can be considered similar for purposes of acute toxicity. Factors considered in the sorting process include each product's active and inert ingredients (identity, percent composition and biological activity), type of formulation (e.g., emulsifiable concentrate, aerosol, wettable powder, granular, etc.) and labeling (e.g., signal word, use classification, precautionary labeling, etc.). Note: The Agency is not describing batched products as "substantially similar," since some products 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 that 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, only their own products within in a batch or to generate all the required acute toxicological studies for each of their own products. If the registrant chooses to generate the data for a batch, he/she must use one of the products within the batch as the test material. If the registrant chooses to rely upon previously submitted acute toxicity data, he/she may do so provided that the data base is complete and valid by 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, the registrants must clearly identify the test material by EPA Registration Number. If more than one confidential statement of formula (CSF) exists for a product, the registrant must indicate the formulation actually tested by identifying the corresponding CSF.

In deciding how to meet the product-specific data requirements, registrants must follow the directions given in the Data Call-In Notice and its attachments appended to the RED. The DCI Notice contains two response forms which are to be completed and submitted to the Agency within 90 days of receipt. The first form, "Data Call-in Response," asks whether the registrant will meet the data requirements for each product. The second form, "Requirements Status and Registrant's Response," lists the product-specific data required for each product, including the standard six acute toxicity tests. A registrant who wishes to participate in a batch must decide whether he/she will provide the data or depend on someone else to do so. If the registrant supplies the data to support a batch of products, he/she must select the one of the following options: Developing Data (Option 1), Submitting an Existing Study (Option 4), Upgrading an Existing Study (Option 5) or Citing an Existing Study (Option 6). If a registrant depends on another's data, he/she must choose among: Cost Sharing (Option 2), Offers to Cost Share (Option 3) or Citing an Existing Study (Option 6). If a registrant does not want to participate in a batch, the choices are Options 1, 4, 5 or 6. However, a registrant should know that choosing not to participate in a batch does not preclude other registrants in the batch from citing his/her studies and offering to cost share (Option 3) those studies.

Two products were found which contain cycloate as the active ingredient. These products have been placed into one batch in accordance with the active and inert ingredients and type of formulation. Products with state registration are not included in the list.

Batch 1	EPA Reg. No.	Percent Cycloate	Formulation Type
	62719-403	73.9	Liquid
	71085-21	73.9	Liquid

Appendix F. List of Available Related Documents and Electronically Available Forms

Pesticide Registration Forms are available via the Agency's website at *http://www.epa.gov/opprd001/forms/*. These forms are in PDF format and require the Acrobat reader.

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 hard copy 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 Notice 98-1)	*http://www.epa.gov/opppmsd1/PR_Notices/pr98-1.pdf*

Pesticide Registration Kit *http://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 §156, Labeling Requirements for Pesticides and Devices (PDF format)
   f. 40 CFR §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 22161-0002

Telephone: (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 Information Center (NPIC) can provide information on active ingredients, uses, toxicology and chemistry of pesticides. You can contact NPIC by telephone at (800) 858-7378 or through their website at *http://www.ncis.orst.edu*.

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:

- Date of receipt;
- EPA identifying number; and
- 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.

Appendix G. Generic Data Call-In

See the following table for a list of generic data requirements. Note that a complete Data Call-In (DCI), with all pertinent instructions, is being sent to registrants under separate cover.

Appendix H. Product Specific Data Call-In

See attached table for a list of product-specific data requirements. Note that a complete Data Call-In (DCI), with all pertinent instructions, is being sent to registrants under separate cover.

Appendix I. **List of Registrants Sent this Data Call-In**