SERA TR 06-52-07-01a

Control/Eradication Agents for the Gypsy Moth -

Human Health and Ecological Risk Assessment for Disparlure (a.i.) and Disrupt II formulation – REVISED DRAFT

Prepared for:

USDA, Forest Service

Forest Health Protection

USDA Forest Service Contract No: **AG-3187-C-06-0010**
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Submitted to:
Paul Mistretta, COR
Kay A. Matthews, Contracting Officer
USDA/Forest Service, Southern Region
1720 Peachtree RD, NW
Atlanta, Georgia 30309

Prepared by Patrick Durkin

Submitted by:
Syracuse Environmental Research Associates, Inc.
5100 Highbridge St., 42C
Fayetteville, New York 13066-0950
Telephone: (315) 637-9560
Fax: (315) 637-0445
E-Mail: SERA_INC@msn.com
Home Page: www.sera-inc.com

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PREFACE

This document is a revision to a risk assessment that was originally prepared by Syracuse Environmental Research Associates, Inc. (SERA Inc.) under GSA Contract No. GS-10F-0082F, USDA Forest Service BPA: WO-01-3187-0150, USDA Purchase Order No.: 43-3187-1-0269. The SERA documented was prepared by Drs. Patrick R. Durkin (SERA Inc.) and Julie Klotzbach (currently with Syracuse Research Corporation). The SERA document was submitted to the USDA Forest Service as Control/Eradication Agents for the Gypsy Moth - Human Health and Ecological Risk Assessment for Disparlure (a.i.) - FINAL REPORT, SERA TR 04-43-05-04b, reported dated August 27, 2004. As indicated in the title, SERA TR 04-43-05-04b covered only the active ingredient – i.e., disparlure – and did not address the formulation of disparlure in Disrupt II flakes. The original SERA document was reviewed by Dr. Rolf Hartung (Univ. Michigan, retired) and by USDA/Forest Service personnel: Dr. Paul Mistretta, Mr. Joseph Cook, and Ms. Donna Leonard.

Under USDA Order No. AG-43ZP-D-06-0015, USDA Forest Service Contract No: AG-3187-C-06-0010, SERA revised the above report to include Disrupt II flakes. The subsequent revision (SERA TR 06-52-02-01a) was submitted to the USDA on June 30, 2006). This revision was based on new information provided by the USDA/Forest Service. The listing below indicates the specific references that were added to the June 30, 2006 revised risk assessment concerning Disrupt II:

Hercon Environmental. 2006a. Hercon Disrupt II Product Label. Copy courtesy of Donna Leonard, USDA Forest Service, Forest Health Protection, PO Box 2680, Asheville, NC 28802. e-mail: dleonard@fs.fed.us. Received June 27, 2006.

Hercon Environmental. 2006b. Hercon Disrupt II Material Safety Data Sheet. Copy courtesy of Priscilla MacLean, Product Development Manager, Hercon Environmental, P.O. Box 435, Emigsville PA, 17318. e-mail: pmaclean@herconenviron.com. Received June 27, 2006.

Leonard D. 2006a. Comments on Application Rates for Disparlure in STS (Slow-The-Spread) Programs. Comments by Donna Leonard, USDA Forest Service, Forest Health Protection, Asheville, NC. Comments received via email from dleonard@fs.fed.us on June 27, 2006.

Leonard D. 2006b. Comments on The Use of Disparlure in STS (Slow-The-Spread) Programs. Comments by Donna Leonard, USDA Forest Service, Forest Health Protection, Asheville, NC. Comments received via email from dleonard@fs.fed.us on June 27, 2006.

MacLean P. 2006. Comments on Inerts in Disrupt II, Product Development Manager, Hercon Environmental, P.O. Box 435, Emigsville PA, 17318. e-mail: pmaclean@herconenviron.com. Received June 27, 2006.

Palmer SJ; Krueger HO. 2006a. SF 2003 and SF 2005: A 48-Hour Static-Renewal Acute Toxicity Test with the Cladoceran (*Daphnia magna*). Wildlife International, Ltd. Project Number: 6 L4a- 102. Study completion date: Jan. 12, 2006. Copy courtesy of Paul Mistretta, USDA/FS.

Palmer SJ; Krueger HO. 2006b. MF 2003 and MF 2005: A 48-Hour Static-Renewal Acute Toxicity Test with the Cladoceran (*Daphnia magna*). Wildlife International, Ltd. Project Number: 6 L4a- 101. Study completion date: Jan. 12, 2006. Copy courtesy of Paul Mistretta, USDA/FS.

Because of limitations in the available toxicity data on disparlure and Disrupt II, more extensive use has been made of quantitative structure activity relationships (QSAR) and the following additional references (not specific to disparlure) have been added:

Bintein S, Devillers J, and Karcher W. 1993. Nonlinear dependence of fish bioconcentration on n-octanol/water partition coefficient. SAR QSAR Environ Res. 1(1):29-39.

Clements RG, Nabholz JV, and Zeeman M. 1996. Estimating Toxicity of Industrial Chemicals to Aquatic Organisms Using Structure-activity Relationships. Environmental Effects Branch, Health and Environmental Review Division, Office of Pollution Prevention and Toxics, U.S. Environmental Protection Agency. Report dated August 30, 1996.

Jeppsson R. 1975. Parabolic Relationship between Lipophilicity and Biological Activity of Aliphatic Hydrocarbons, Ethers and Ketones after Intravenous Injections of Emulsion Formulations into Mice. Acta Pharmacol. Et Toxicol. 37: 56-64.

U.S. EPA/OPPT (U.S. Environmental Protection Agency/Office of Pollution Prevention and Toxics). 2000. On-Line EPI Suite User's Guide, Version 3.12. Developed by the EPA's Office of Pollution Prevention Toxics and Syracuse Research Corporation (SRC). Available at: http://www.epa.gov/opptintr/exposure/docs/episuite.htm

The current risk assessment has been revised based on comments from Forest Service and APHIS personnel. A consolidation of comments was prepared by Joe Cook (USDA/FS). This was the primary source for the current revisions. Comments from various Forest Service personnel were provided and consulted as needed, including comments from Hank Appleton, Jesus Cota, John Kyhl, and Donna Leonard. A PDF copy of the risk assessment with annotations from APHIS personnel was also consulted. Lastly, an unpublished synopsis of the following study was provided by Donna Leonard, reviewed and incorporated into this risk assessment as appropriate:

Thwaits BF; Sorensen PW. 2005. Olfactory sensitivity of rainbow trout to racemic disparlure. Unpublished synopsis dated April 1, 2005. Copy courtesy of Donna Leonard, USDA/Forest Service. 2 pp.

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LIST OF APPENDICES

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Workbook
Disparlure: Simplified EXCEL Worksheets for Calculating Risks to Small Aquatic Invertebrates SERA EXWS 06-52-07-01a. Worksheet dated August 25, 2006.

ACRONYMS, ABBREVIATIONS, AND SYMBOLS

AEL	adverse-effect level
AGM	Asian Gypsy Moth
a.i.	active ingredient
BCF	bioconcentration factor
bw	body weight
CBI	confidential business information
cm	centimeter
CNS	central nervous system
EC_x	concentration causing X% inhibition of a process
EC_{25}	concentration causing 25% inhibition of a process
EC_{50}	concentration causing 50% inhibition of a process
F	female
FH	Forest Health
FIFRA	Federal Insecticide, Fungicide and Rodenticide Act
FQPA	Food Quality Protection Act
g	gram
ha	hectare
HQ	hazard quotient
IARC	International Agency for Research on Cancer
IRIS	Integrated Risk Information System
k_a	absorption coefficient
k_e	elimination coefficient
kg	kilogram
$K_{o/c}$	organic carbon partition coefficient
$K_{o/w}$	octanol-water partition coefficient
K_p	skin permeability coefficient
L	liter
lb	pound
LC_{50}	lethal concentration, 50% kill
LD_{50}	lethal dose, 50% kill
LOAEL	lowest-observed-adverse-effect level
m	meter
M	male

ACRONYMS, ABBREVIATIONS, AND SYMBOLS (*continued*)

mg	milligram
mg/kg/day	milligrams of agent per kilogram of body weight per day
mL	milliliter
mM	millimole
MRID	Master Record Identification Number
MSDS	material safety data sheet
MW	molecular weight
NAGM	North American Gypsy Moth
NOAEL	no-observed-adverse-effect level
NOEC	no-observed-effect concentration
NOEL	no-observed-effect level
NOS	not otherwise specified
NRC	National Research Council
NTP	National Toxicology Program
OPP	Office of Pesticide Programs
OPPTS	Office of Pesticide Planning and Toxic Substances
ppm	parts per million (used in expressing dietary concentrations only)
QSAR	quantitative structure activity relationship
RfD	reference dose
SERA	Syracuse Environmental Research Associates
SRC	Syracuse Research Corporation
UF	uncertainty factor
U.S.	United States
USDA	U.S. Department of Agriculture
U.S. EPA	U.S. Environmental Protection Agency
WHO	World Health Organization
µ	micron
▸	greater than
≥	greater than or equal to
<	less than
≤	less than or equal to
=	equal to
≃	approximately equal to
~	approximately

COMMON UNIT CONVERSIONS AND ABBREVIATIONS

To convert ...	Into ...	Multiply by ...
acres	hectares (ha)	0.4047
acres	square meters (m^2)	4,047
atmospheres	millimeters of mercury	760
centigrade	Fahrenheit	1.8 °C + 32
centimeters	inches	0.3937
cubic meters (m^3)	liters (L)	1,000
Fahrenheit	centigrade	5/9 (°F-32)
feet per second (ft/sec)	miles/hour (mi/hr)	0.6818
gallons (gal)	liters (L)	3.785
gallons per acre (gal/acre)	liters per hectare (L/ha)	9.34
grams (g)	ounces, (oz)	0.03527
grams (g)	pounds, (oz)	0.002205
hectares (ha)	acres	2.471
inches (in)	centimeters (cm)	2.540
kilograms (kg)	ounces, (oz)	35.274
kilograms (kg)	pounds, (lb)	2.2046
kilograms per hectare (hg/ha)	pounds per acre (lb/acre)	0.892
kilometers (km)	miles (mi)	0.6214
liters (L)	cubic centimeters (cm^3)	1,000
liters (L)	gallons (gal)	0.2642
liters (L)	ounces, fluid (oz)	33.814
miles (mi)	kilometers (km)	1.609
miles per hour (mi/hr)	cm/sec	44.70
milligrams (mg)	ounces (oz)	0.000035
meters (m)	feet	3.281
ounces (oz)	grams (g)	28.3495
ounces per acre (oz/acre)	grams per hectare (g/ha)	70.1
ounces per acre (oz/acre)	kilograms per hectare (kg/ha)	0.0701
ounces fluid	cubic centimeters (cm^3)	29.5735
pounds (lb)	grams (g)	453.6
pounds (lb)	kilograms (kg)	0.4536
pounds per acre (lb/acre)	kilograms per hectare (kg/ha)	1.121
pounds per acre (lb/acre)	mg/square meter (mg/m^2)	112.1
pounds per acre (lb/acre)	µg/square centimeter ($µg/cm^2$)	11.21
pounds per gallon (lb/gal)	grams per liter (g/L)	119.8
square centimeters (cm^2)	square inches (in^2)	0.155
square centimeters (cm^2)	square meters (m^2)	0.0001
square meters (m^2)	square centimeters (cm^2)	10,000
yards	meters	0.9144

Note: All references to pounds and ounces refer to avoirdupois weights unless otherwise specified.

CONVERSION OF SCIENTIFIC NOTATION

Scientific Notation	Decimal Equivalent	Verbal Expression
$1 \cdot 10^{-10}$	0.0000000001	One in ten billion
$1 \cdot 10^{-9}$	0.000000001	One in one billion
$1 \cdot 10^{-8}$	0.00000001	One in one hundred million
$1 \cdot 10^{-7}$	0.0000001	One in ten million
$1 \cdot 10^{-6}$	0.000001	One in one million
$1 \cdot 10^{-5}$	0.00001	One in one hundred thousand
$1 \cdot 10^{-4}$	0.0001	One in ten thousand
$1 \cdot 10^{-3}$	0.001	One in one thousand
$1 \cdot 10^{-2}$	0.01	One in one hundred
$1 \cdot 10^{-1}$	0.1	One in ten
$1 \cdot 10^{0}$	1	One
$1 \cdot 10^{1}$	10	Ten
$1 \cdot 10^{2}$	100	One hundred
$1 \cdot 10^{3}$	1,000	One thousand
$1 \cdot 10^{4}$	10,000	Ten thousand
$1 \cdot 10^{5}$	100,000	One hundred thousand
$1 \cdot 10^{6}$	1,000,000	One million
$1 \cdot 10^{7}$	10,000,000	Ten million
$1 \cdot 10^{8}$	100,000,000	One hundred million
$1 \cdot 10^{9}$	1,000,000,000	One billion
$1 \cdot 10^{10}$	10,000,000,000	Ten billion

EXECUTIVE SUMMARY

OVERVIEW

Disparlure is a naturally occurring insect pheromone used to disrupt mating of gypsy moths by confusing male moths. Disparlure is also used as a attractant in traps. There are limited data available on the toxicity of disparlure. Only a small number of acute exposure studies have been conducted; no chronic exposure studies in any species were identified in the available literature. Based on the results of the available data, the toxicity profile of disparlure in terrestrial animals does not suggest that disparlure is likely to cause adverse effects at plausible levels of exposure. Similarly, disparlure is not likely to cause any toxic effects in aquatic species at the limit of solubility of disparlure in water. Thus, under normal conditions of exposure, no hazard to aquatic species can be identified. In cases of an accidental application of disparlure to a small body of standing water, such as pond, no effects are likely in fish. An accidental application or some other similar event such as an accidental spill could lead to an insoluble film of disparlure at the air-water interface of a standing body of water. This could result in some small invertebrates becoming trapped in the film of disparlure. While the entrapment of daphnids has been observed in laboratory studies of both disparlure and Disrupt II formulations, the likelihood of this occurring in the field to an extent that detectable effects would be observed is difficult to determine. The formation of a film that could trap small invertebrates in rapidly moving bodies of water does not seem plausible.

PROGRAM DESCRIPTION

Disparlure is a naturally occurring insect pheromone (attractant) synthesized by the female gypsy moth to attract the male gypsy moth. Disparlure can take two enantiomer forms, referred to as (+)disparlure and (-)disparlure. Enantiomers are mirror-image molecules with identical gross structures. The (+)enantiomer is the form produced by the female gypsy moth and is the only form that is biologically active as an attractant. In gypsy moth programs, two forms of disparlure are used: the (+)enantiomer and the racemic mixture, a 50:50 blend of the (+)enantiomer and (-)enantiomer. Racemic disparlure is used as a control agent. It is broadcast over relatively large areas and disrupts mating by confusing male moths – i.e., the male moth has difficulty in locating the female moth.

Disparlure is always formulated in a slow release matrix and several different formulations have been tested including polyvinyl chloride flakes, microcapsules, and polyvinyl chloride twine. Disrupt II, a formulation of disparlure in polyvinylchloride flakes, has been used by the USDA Forest Service for many years. The specific formulation has evolved over time. This risk assessment considers the available information both on the current and some previous Disrupt II formulations.

Since 1995, the use of disparlure in programs intended to slow the spread of gypsy moths has increased over 250-fold, from 2,448 acres treated in 1995 to a maximum of 647,394 acres treated in 2003. The (+)enantiomer of disparlure is used as an attractant or bait in two types of traps:

milk carton traps that also contain DDVP and delta traps that do not contain an insecticide. These traps are used to monitor existing (endemic) populations and detect new infestations.

HUMAN HEALTH RISK ASSESSMENT

Hazard Identification – Insect pheromones are generally regarded as nontoxic to mammals and these pheromones are commonly employed in very low environmental concentrations. Consequently, U.S. EPA requires less rigorous testing of these products than is required of insecticides. Except for some standard acute toxicity studies in laboratory mammals, few data are available regarding the toxicity of disparlure to terrestrial species. Results of acute exposure studies for oral, dermal, ocular and inhalation exposure to disparlure show no indication of adverse effects. The LD_{50} of a single dose administered to rats by gavage exceeds 34,600 mg/kg. With the exception of one acute gavage study in rats using the 50:50 racemic mix, none of the toxicity studies specified whether the 50:50 racemic mix or the (+)enantiomer was tested. Based on the results of studies on disparlure itself (i.e., the active ingredient), acute exposure to disparlure has very low toxicity in mammals. No studies investigating the effects of chronic exposure of mammals to disparlure or studies investigating the effects of disparlure on the nervous system, immune system, reproductive system or endocrine system were identified. The carcinogenic potential of disparlure has not been assessed. In a single study on mutagenicity, there was no indication that disparlure is mutagenic. There is no information available regarding the kinetics and metabolism of disparlure in mammals. The kinetics of absorption of disparlure following dermal, oral or inhalation exposure are not documented in the available literature. A case report of an accidental exposure indicates that disparlure may persist in humans for years.

Exposure Assessment – For both occupational exposure of workers and accidental exposure of the general public, exposure to disparlure may involve multiple routes of exposure (i.e., oral, dermal, and inhalation). Nonetheless, dermal exposure is generally most likely to be the predominant route. While exposure scenarios can be developed and exposures quantified for each potential exposure route based on application rates of disparlure and limited monitoring data, given the low toxicity of disparlure to laboratory mammals and the lack of chronic exposure studies, detailed quantitative estimates of exposure will not significantly add to the assessment of risk associated with disparlure.

Dose-Response Assessment – The toxicity data on disparlure are not adequate for making a standard dose-response assessment. The limited available data indicate that disparlure has a low order of acute toxicity based on mortality as follows: oral LD_{50} >34,600 mg/kg, dermal LD_{50} >2,025 mg/kg, and inhalation LC_{50} >5 mg/L · 1 hour. Data regarding the toxicity of disparlure to animals or humans after subchronic or chronic exposures were not located. Moreover, the acute toxicity of this compound for endpoints other than mortality is poorly characterized. Thus, due to insufficient data, the U.S. EPA has not derived either an RfD for acute or chronic exposure.

Risk Characterization – Although studies on the acute toxicity of disparlure have been conducted in laboratory animals, the lack of subchronic or chronic toxicity data precludes a

quantitative characterization of risk. The available data regarding the acute toxicity of disparlure indicate that the potential hazard from exposure to the compound is low.

The reliance on acute toxicity data introduces uncertainties into the risk assessment that cannot be quantified. Other uncertainties in this analysis are associated with the exposure assessment and involve environmental transport and dermal absorption. These uncertainties are relatively minor compared to the lack of subchronic or chronic toxicity data. Thus, while there is no reason to believe that longer-term exposure to disparlure will produce adverse effects, this assumption can not be substantiated due to the lack of chronic toxicity data. The significance of this uncertainty is at least partially offset by the very low exposures that are plausible given the low application rates and the nature of plausible exposures of humans to disparlure.

ECOLOGICAL RISK ASSESSMENT

Hazard Identification – There is very little information regarding the toxicity of disparlure to nontarget wildlife species. As discussed above, rigorous toxicity testing of disparlure has not been required by the U.S. EPA. Thus, the only studies available are acute toxicity studies in bobwhite quail, mallard ducks, rainbow trout, bluegill sunfish, *Daphnia magna* and Eastern oysters. No chronic toxicity studies were identified in the literature or in the studies submitted to the U.S. EPA.

Results of acute gavage and dietary toxicity studies in mallard ducks and bobwhite quail show that disparlure has very low toxicity in these species, with no mortalities observed following exposure to up to 2510 mg/kg bw in bobwhite quail.

Limited data are available regarding the toxicity of disparlure to aquatic animals. A major issue in the interpretation of the aquatic toxicity data on disparlure involves the solubility of disparlure in water. While no measured values for the solubility of disparlure in water are available, estimates based on quantitative structure-activity relationships developed by the U.S. EPA suggest that the solubility of disparlure in water is in the range of 0.0019 to 0.0028 mg/L. The bioassays that have been conducted on disparlure and Disrupt II formulations of disparlure have not measured concentrations of disparlure in the test water but report nominal concentrations of disparlure that exceed the water solubility of disparlure by factors of about 10 [0.028 mg/L] to over 150,000 [300 mg/L]. Based on the results of the available bioassays and considerations of water solubility, disparlure does not appear to present any toxic hazards to aquatic species. In toxicity tests of small aquatic invertebrates (i.e., daphnids), trapping of the organism at the surface of the water has been noted in bioassays of both technical grade disparlure and Disrupt II formulations. The trapping of small invertebrates at surface of the water can present a physical hazard to the organism. The significance of this physical hazard observed in bioassays to potential hazards in field applications is unclear.

Exposure Assessment – Disparlure appears to be essentially nontoxic to mammals and birds. While this assessment is limited by the lack of chronic toxicity data in terrestrial species, it is not expected that acute or chronic exposure of terrestrial mammals or birds to disparlure would result

in the development of significant adverse effects. Given the low toxicity of disparlure and limited available data, an exposure assessment for terrestrial species would not add to the assessment of risk for terrestrial species. Thus, an exposure assessment for terrestrial species is not included in this risk assessment. For aquatic species, the range of plausible nominal concentrations of disparlure in water are calculated at 0.0015 mg/L to 0.0037 mg/L over the range of applications rates considered in this risk assessment. These concentrations apply to a 1 meter deep body of water. The lower end of this range is within the estimated solubility of disparlure in water – i.e., 0.0019 to 0.0028 mg/L.

Dose-Response Assessment – Given the low toxicity of disparlure to terrestrial animals coupled with the limitations imposed due to lack of chronic exposure data, no standard dose-response can be made for disparlure for terrestrial species. Disparlure is produced by other species in the genus *Lymantria* that are closely related to the gypsy moth (http://www.pherobase.com) such as the nun moth (*Lymantria monacha*), a Eurasian pest of conifers that is considered a serious risk for introduction into North America (http://www.na.fs.fed.us/spfo/pubs/pest_al/nunmoth/nun_moth.shtm). However, since there are no quantitative data available regarding the efficacy of disparlure in nontarget moths, a dose-response assessment for this effect in a nontarget species cannot be made. Similarly, no explicit dose-response relationship is proposed for fish. There is no basis for asserting that adverse effects in fish are plausible under any foreseeable conditions. For aquatic invertebrates, there is no basis for asserting that toxic effects are likely at the limit of the solubility of disparlure in water. At nominal concentrations that exceed the solubility of disparlure in water (e.g., as the result of an accidental spill or application to water), small invertebrates that may interact with the water-surface interface could become trapped in this interface due to a layer of undissolved disparlure at the air-water interface.

Risk Characterization – There is little data available on terrestrial and aquatic animals to allow for a quantitative characterization of risk. Furthermore, the lack of chronic toxicity data in any species adds significant uncertainty to any risk characterization. Thus, for both terrestrial and aquatic species, the potential for the development of toxicity from long-term exposure to disparlure cannot be assessed. Nonetheless, given the low toxicity of disparlure based on acute toxicity studies, it is unlikely that exposure to disparlure will result in the development of serious adverse effects in terrestrial and aquatic species. Regarding potential effects on terrestrial invertebrates, disparlure is able to disrupt mating of some other closely related species of moths other than the gypsy moth. These other closely related species, however, are all are Asian or Eurasian species and are not known to exist in North America. Thus, there is no basis for asserting that mating disruption is plausible in nontarget species in North America.

Under normal conditions, aquatic species will not be exposed to substantial levels of disparlure. At the limit of the solubility of disparlure in water, there is no indication that toxic effects are likely in any aquatic species. If Disrupt II flakes are accidently applied to water, the amount of disparlure in the water could result in the formation of an insoluble layer of disparlure at the air-water interface. There is no indication that this would impact fish. Based on toxicity studies conducted in the laboratory, small invertebrates that come into contact with the air-water

interface might become trapped in an insoluble film of disparlure. The likelihood of this occurring and the likelihood of this causing any detectable impact in a body of water is difficult to determine and would vary with the quantity of flakes applied to the body of water and the depth of the body of water. Based on variability in the experimental data as well as the range of application rates used in the USDA programs, hazard quotients would vary from about 0.15 to about 0.37 below the level of concern by factors of about 3 to 10. This risk characterization applies to accidental application of disparlure to a 1 meter deep body of water.

1. INTRODUCTION

The USDA Forest Service uses disparlure and the formulation of disparlure as Disrupt II in programs to control or eradicate gypsy moth populations. This document is an update to a risk assessment prepared in 1995 (USDA 1995) and provides risk assessments for human-health effects and ecological effects to support an assessment of the environmental consequences of these uses.

This document has four chapters, including the introduction, program description, risk assessment for human health effects, and risk assessment for ecological effects or effects on wildlife species. Each of the two risk assessment chapters has four major sections, including an identification of the hazards associated with disparlure, an assessment of potential exposure to the product, an assessment of the dose-response relationships, and a characterization of the risks associated with plausible levels of exposure. These are the basic steps recommended by the National Research Council of the National Academy of Sciences (NRC 1983) for conducting and organizing risk assessments.

Although this is a technical support document and addresses some specialized technical areas, an effort was made to ensure that the document can be understood by individuals who do not have specialized training in the chemical and biological sciences. Certain technical concepts, methods, and terms common to all parts of the risk assessment are described in plain language in a separate document (SERA 2006).

The human health and ecological risk assessments presented in this document are not, and are not intended to be, comprehensive summaries of all of the available information. No published reviews regarding human health or ecological effects of disparlure have been encountered. Moreover, almost all of the mammalian toxicology studies and most of the ecotoxicology studies are unpublished reports submitted to the U.S. EPA as part of the registration process for disparlure.

Because of the lack of a detailed, recent review concerning disparlure and the preponderance of unpublished relevant data in U.S. EPA files, a complete search of the U.S. EPA FIFRA/CBI files was conducted. Full text copies of relevant studies were kindly provided by the U.S. EPA Office of Pesticide Programs. These studies were reviewed, discussed in Sections 3 and 4 as necessary, and synopses of the most relevant studies are provided in the appendices to this document.

The Forest Service will update this and other similar risk assessments on a periodic basis and welcomes input from the general public on the selection of studies included in the risk assessment. This input is helpful, however, only if recommendations for including additional studies specify why and/or how the new or not previously included information would be likely to alter the conclusions reached in the risk assessments.

2. PROGRAM DESCRIPTION

2.1. OVERVIEW

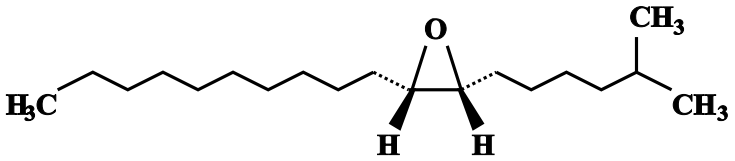
Disparlure is a naturally occurring insect pheromone (attractant) synthesized by the female gypsy moth to attract the male gypsy moth. Disparlure can take two enantiomer forms, referred to as (+)disparlure and (-)disparlure. Enantiomers are mirror-image molecules with identical gross structures. The (+)enantiomer is the form produced by the female gypsy moth and is the only form that is biologically active as an attractant. In gypsy moth programs two forms of disparlure are used: the (+) enantiomer that is used as an attractant or bait in traps and the racemic mixture, a 50:50 blend of the (+) and (-) enantiomers that is used as a control agent. When it is used as a control agent, racemic disparlure is broadcast over relatively large areas to disrupt mating by confusing the male moths.

Disparlure is always formulated in a slow release matrix and several different formulations have been tested including polyvinyl chloride flakes, microcapsules, and polyvinyl chloride twine. Disrupt II, a formulation of disparlure in polyvinylchloride flakes, has been used by the USDA Forest Service for many years. The specific formulation has evolved over time. This risk assessment considers the available information both on the current and some previous Disrupt II formulations.

Since 1995, the use of disparlure in programs intended to slow the spread of gypsy moths has increased over 250-fold, from 2,448 acres treated in 1995 to 647,394 acres treated in 2003. (+)disparlure is used as an attractant or bait in two types of traps: milk carton traps that also contain DDVP and delta traps that do not contain an insecticide. These traps are used to monitor existing (endemic) populations and detect new infestations.

2.2. CHEMICAL DESCRIPTION

Disparlure is the common name for cis-7,8-epoxy-2-methyloctadecane:



Disparlure can take two enantiomer forms, referred to as (+)disparlure and (-)disparlure. The term *enantiomer* refers to molecules that are structurally identical except for differences in the 3-dimensional configuration such that one form is the mirror image of the other.

(+)Disparlure is a naturally occurring insect pheromone (attractant) synthesized by the female gypsy moth to attract the male gypsy moth. (+)Disparlure is also a natural constituent of and is a pheromone for other species including the nun moth (*Lymantria monacha*, Morewood et al. 1999, 2000) and *Lymantria fumida* [the pink gypsy moth which is a species native to Japan]

(Schaefer et al. 1999). As with the gypsy moth, both of these *Lymantria* species are forest pests and adverse effects on these species are not a substantial concern for this risk assessment.

Selected chemical and physical properties of disparlure are summarized in Table 2-1. Due to the lack of experimental data, most of the values given in Table 2-1 are estimated from EPI Suite, an estimation program developed by Meylan and Howard (2000) in conjunction with the U.S. EPA (U.S. EPA/OPPT 2000). For convenience, the specific estimates for disparlure that were obtained from EPI Suite are referenced in this document as EPI Suite (2006) and a full copy of this run is included as Appendix 4.

In gypsy moth programs, two forms of disparlure are used: the (+)enantiomer and the racemic mixture, a 50:50 blend of the (+)enantiomer and (-)enantiomer. For disparlure, the (+)enantiomer is the biologically active form (that is, the form that attracts the male gypsy moth). Racemic disparlure is used as a control agent. It is broadcast over relatively large areas and disrupts mating by confusing male moths. This product is typically aerially applied in a single application just before the emergence of adult gypsy moths. Although the label for Disrupt II allows a second application later in the season, operational programs never use a second application.

As discussed in Section 3 and Section 4, most toxicity studies conducted on disparlure do not specify whether the racemic mix or the (+)enantiomer of disparlure was tested. Except for the attractant effects of (+)disparlure, there is no clear indication that toxicity profiles differ between the (+)enantiomer of disparlure and the 50:50 racemic mix. For the purposes of this risk assessment, no distinction is made between (+)disparlure and the racemic mix. All references to the active ingredient (a.i.) refer to disparlure and do not distinguish between (+)disparlure and the 50:50 racemic mix.

When used as a control agent, disparlure is formulated in a slow release matrix and several different formulations have been tested including polyvinyl chloride flakes, microcapsules, and twine (Caro et al. 1977, 1981; Taylor 1982). In recent programs, the USDA used Disrupt II (Leonhardt et al. 1996) and this formulation is currently registered by U.S. EPA (Hercon Environmental 1993). This formulation contains 17.9% disparlure and 82.1% carrier flakes. Disrupt II flakes are about 1/32 inch by 3/32 inch and consist of polyvinyl chloride films, polyvinyl chloride resin and a plasticizer (Hercon Environmental 2004). The USDA has participated in the development of new formulations of disparlure in either new flake formulations developed by Hercon or new microcapsule formulation being developed by 3M (Leonard 2004).

Currently, the USDA has elected to use a new Disrupt II flake formulation (Leonard 2006a,b). As with past formulations of Disrupt II, this flake formulation contains 17.9% disparlure and 82.1% polyvinylchloride carrier flakes and other inerts (Hercon 2006a,b). As detailed further in Section 4.1.3.3, toxicity data are available on the current formulation of Disrupt II as well as a

previous formulation. Available information on the inerts in Disrupt II is discussed in Section 3.1.14.

2.3. APPLICATION METHODS AND RATES

The application rates recommended on the label of Disrupt II (Hercon 2006a), range from 6 grams a.i./acre to 30 grams a.i./acre, corresponding to about 0.0132 lb a.i./acre to 0.066 lb a.i./acre[1 gram = 0.0022 lb (avdp)].

The USDA uses disparlure in two different types of programs: slow the spread and eradication. Slow the spread programs involve the control of the North American Gypsy Moth (NAGM), a species that is already established in the US. Slow the spread programs are typically administered by the USDA/Forest Service using application rates of 6 grams a.i./acre and occasionally using an application rate of 15 g a.i./acre. Tobin and Leonard (2006) have estimated that this range of application rates will result in the release of disparlure that is substantially greater than the amounts released by female gypsy moths during a major outbreak.

Eradication efforts are administered by USDA/APHIS (Animal and Plant Health Inspection Service). Eradication efforts are focused on the Asian strain of the gypsy moth (AGM) that is not known to be established in the United States as well as small and isolated infestations of the NAGM that could be eradicated. For purposes of exclusion and eradication, APHIS considers AGM to be a separate species from NAGM. With NAGM, eradication uses applications of up to 15 g a.i./acre. The maximum labeled application rate of 30 g a.i./acre has only been used once for AGM eradication. This application involved only 600 acres out of a total of approximately 2.5 million acres treated between 1995 and 2005 – i.e., less than 0.03% of the total acres treated.

Because the application rate of 30 g a.i./acre is used only rarely, the current risk assessment will explicitly consider application rates in the range of 6 grams a.i./acre and 15 g a.i./acre. If other application rates need to be considered in certain applications, the Worksheet A02 of the EXCEL workbook that accompany this risk assessment may be modified. This workbook is described in Section 4.4.2 of this risk assessment.

(+)Disparlure is used as an attractant or bait in two types of traps: milk carton traps that also contain DDVP and delta traps that do not contain an insecticide. These traps are used to monitor existing (endemic) populations and detect new infestations. Since the early 1980s, (+)disparlure has been formulated as 3 x 25 mm plastic laminates (two outer layers of 50 μm PVC with an inner polymeric layer containing 500 μg (+)disparlure).

2.4. USE STATISTICS

Use statistics for the number of acres treated with disparlure according to type of use are summarized in Table 2-2 (USDA/FS 2005). From 1995 to 2003, the use of disparlure to slow the spread of gypsy moths increased substantially. In 1995, 2,448 acres were treated with disparlure flakes and in 2003, 647,394 acres were treated; this is an increase in acres treated of over 250-fold. It is anticipated that slow the spread applications will typically entail about 500,000 acres

per year and that these applications will account for 99.9% of all mating disruption applications (Leonard 2005a).

3. HUMAN HEALTH RISK ASSESSMENT

3.1 HAZARD IDENTIFICATION

3.1.1 Overview.

Insect pheromones are generally regarded as nontoxic to mammals (Jacobson 1976) and, as with disparlure, application rates of insect pheromone are generally very low – i.e., pheromones are active a very low concentrations. Consequently, U.S. EPA requires less rigorous testing of these products than is required of insecticides (U.S. EPA 1994). Except for some standard acute toxicity studies in laboratory mammals, little information is available regarding the biological activity of disparlure. The USDA has funded acute toxicity studies on disparlure during its development for use in the gypsy moth control program. The studies were conducted by Industrial Bio-test and were submitted to the U.S. EPA by Hercon Environmental Company as part of the registration package (Kretchmar 1972). Summaries of these studies are published in the open literature (Beroza et al. 1975).

Results of acute toxicity studies for oral, dermal, ocular and inhalation exposure to disparlure are summarized in Table 3-1. With the exception of one acute gavage study in rats using the 50:50 racemic mix (Coleman 2000), none of the toxicity studies specified whether the 50:50 racemic mix or the (+)enantiomer was tested. Based on the results of studies on disparlure, acute exposure to disparlure appears to pose a very low risk to mammals. No studies investigating the effects of chronic exposure of mammals to disparlure or studies investigating the effects of disparlure on the nervous system, immune system, reproductive system or endocrine system were identified. The carcinogenic potential of disparlure has not been assessed. The results of a single study show that disparlure is not mutagenic.

3.1.2 Mechanism of Action

As discussed in Section 4.1.2.3, the mechanism of action for the efficacy of disparlure as an attractant for male gypsy moths has been well characterized. However, since disparlure has very low toxicity to mammals, studies on the mechanism of action for toxicity of disparlure in mammals have not been conducted. Thus, there is no information available in the FIFRA files or in the open literature regarding the mechanism of toxicity (if any) of disparlure in mammals.

3.1.3 Kinetics and Metabolism

No studies designed specifically to obtain information on the kinetics or metabolism of disparlure were identified. The kinetics of absorption of disparlure following dermal, oral or inhalation exposure are not documented in the available literature. Disparlure appears to persist in humans for long periods of time. This supposition is based on a case report of an individual who had direct dermal contact with disparlure in 1977 (Cameron 1981, 1983, 1995). This individual appears to have attracted male gypsy moths for a period of over 15 years. It is estimated that the exposure level of this individual to disparlure was very low, although no quantitative estimates of exposure were reported.

Assays have been conducted using disparlure and several natural and xenobiotic epoxides to determine the ability of each to induce epoxide metabolizing enzymes (Moody et al. 1991). Male mice were given 500 mg a.i./kg/day disparlure by intraperitoneal injection for 3 days. This was the maximum dose tested in preliminary range finding studies. Exposure to the compound had no effect on relative liver weight, using matched controls, or microsomal protein. Relative cytosolic protein was significantly ($p<0.05$) increased by 18% over control values. Disparlure also caused a moderate but statistically significant ($p<0.05$) increase in microsomal cholesterol epoxide hydrolase activity. This study suggests that very high doses of disparlure may induce enzymes involved in the metabolism of disparlure. Given the very low levels of exposure to disparlure that are likely in the use of this agent in gypsy moth control programs, this study has no direct relevance to this risk assessment.

3.1.4 Acute Oral Toxicity

Other than standard bioassays for acute toxicity that were conducted as part of the registration process, no information regarding the acute toxicity of disparlure was identified. The most common measure of acute oral toxicity is the LD_{50}, the estimate of a dose that causes 50% mortality in the test species. As summarized in Appendix 1, there are two studies investigating the acute oral toxicity of high doses of disparlure in rats (Coleman 2000; Kretchmar 1972). Acute oral exposure to 10,250–34,600 mg a.i./kg body weight was not lethal to rats (LD_{50} greater than 34,600 mg a.i./kg) (Kretchmar 1972). Disparlure was administered, undiluted, by gavage, and the rats were observed for 14 days following exposure. This report does not specify whether the test material used was the 50:50 racemic mix or the (+)enantiomer. Necropsy revealed no pathological alterations in any of the treated rats. At all dose levels, however, the animals exhibited hypoactivity, ruffed fur, and diuresis. The significance of these observations cannot be assessed because no control group was used. The apparent NOAEL for mortality and serious clinical toxicity is 34,600 mg a.i./kg, the highest dose tested.

In a more recent study in which rats were administered 5000 mg a.i./kg of a racemic preparation of disparlure, no deaths or pathological abnormalities were observed (Coleman 2000). Clinical signs of toxicity, including piloerection, hunched posture and ungroomed appearance were observed during the first three days following exposure; however, no clinical signs of toxicity were noted during the remaining 11 days of the observation period. As in the study by Kretchmar (1972), no control group was used in the Coleman (2000) study. In this study the LC_{50} is > 5000 mg a.i./kg and the NOAEL is 5000 mg a.i./kg. Thus, with the acute oral LD_{50} exceeding 5,000mg a.i./kg, disparlure would be classified as practically non-toxic using the scheme adopted by U.S. EPA (2003).

3.1.5 Subchronic and Chronic Systemic Toxic Effects

No studies investigating the subchronic or chronic effects of disparlure in mammals were identified. As discussed in Section 8.1.1, studies investigating subchronic and chronic exposures were not required for registration of disparlure (Jacobson 1976; U.S. EPA 1994).

3.1.6 Effects on Nervous System

As discussed in Durkin and Diamond (2002), a *neurotoxicant* is a chemical that disrupts the function of nerves, either by interacting with nerves directly or by interacting with supporting cells in the nervous system. This definition of *neurotoxicant* is critical because it distinguishes agents that act directly on the nervous system *(direct neurotoxicants*) from those agents that might produce neurologic effects that are secondary to other forms of toxicity (*indirect neurotoxicants*). Virtually any chemical will cause signs of neurotoxicity in severely poisoned animals and thus can be classified as an indirect neurotoxicant.

By this definition, disparlure may be classified as an indirect neurotoxicant. As noted in Section 3.1.4, hypoactivity and piloerection were observed following acute oral exposure to very high doses of disparlure (Coleman 2000; Kretchmar 1972). These observations, however, do not implicate disparlure as a direct neurotoxicant. No studies designed specifically to detect impairments in motor, sensory, or cognitive functions in animals or humans exposed to disparlure were identified. No evidence for disparlure producing direct effects on the nervous system was found.

3.1.7 Effects on Immune System

No studies investigating the effects of disparlure on immune system function in mammals were identified.

3.1.8 Effects on Endocrine System

No studies investigating the effects of disparlure on endocrine system function in mammals were identified.

3.1.9. Reproductive and Teratogenic Effects

No studies investigating the reproductive or teratogenic effects of disparlure in mammals were identified.

3.1.10. Carcinogenicity and Mutagenicity

No studies investigating the carcinogenic activity of disparlure in mammals were identified. A single study investigated the mutagenicity of disparlure with and without metabolic activation in *Salmonella typhimurium* and *Escherichia coli* (Oguma 1998). There was no evidence of mutagenic activity under any of the experimental conditions of this study. This report does not specify whether the test material used was the 50:50 racemic mix or the (+)enantiomer.

3.1.11. Irritation and Sensitization (Effects on Skin and Eyes)

The primary skin irritation of disparlure was evaluated in a single study using young albino New Zealand rabbits (Kretchmar 1972). Details are provided in Appendix 1. The test sites, located lateral to the midline of the shaved back, were approximately 10 cm apart from one another, and one site was abraded while the other remained intact. The sites were occluded with gauze patches for the duration of the 24-hour exposure period, after which the intact and abraded test sites were examined. The sites were examined and scored again after 72 hours. Signs of mild

skin irritation, including erythema and edema, were noted at 24 and 72 hours after application of disparlure. Based on the results of this single study, dermal exposure to a high dose of disparlure appears only mildly irritating to skin and is not a primary skin irritant.

Eye irritation was assayed in a single study in six young New Zealand rabbits exposed to 0.1 mL disparlure (Kretchmar 1972). Details of this study are provided in Appendix 1. Disparlure was instilled into the right eye of each rabbit (the left eye served as a control) to determine the extent of irritation or damage to cornea, iris, and conjunctiva. The severity of ocular lesions was monitored at intervals of 24, 48, and 72 hours. Three of the six rabbits had redness of the conjunctiva at 24 hours, but no effects were observed in any of the rabbits at the later observation periods. No effects were observed 7 days after exposure. Based on the results of this study, disparlure would be classified as a non-irritant for eyes using the scheme proposed by U.S. EPA (2003).

3.1.12. Systemic Toxic Effects from Dermal Exposure

The acute dermal toxicity of disparlure was tested using four young adult New Zealand rabbits (Kretchmar 1972). Study details are provided in Appendix 1. When applied, undiluted, to the shaved backs of the rabbits, 2,025 mg a.i./kg caused local skin reactions after 24 hours of contact with the epidermis. No other dose levels were tested. The rabbits were observed for 14 days after exposure, and the effects observed during this period included dryness (escharosis), skin flaking (desquamation), hemorrhaging, and fissures after 7 days and desquamation, fissures, and pustules after 14 days. Necropsy revealed no pathological alterations other than the effects on the skin. None of the rabbits died as a result of treatment (dermal LD_{50} greater than 2,025mg a.i./kg).

3.1.13. Inhalation Exposure

The acute toxicity of inhalation exposure to disparlure was assessed in rats (Grapenthien 1972). Study details are provided in Appendix 1. Rats were exposed to an aerosol of disparlure for 1 hour, with a calculated average concentration of the aerosol was 5.0 mg a.i./L air. The rats were observed for 14 days after exposure. None of the rats died as a result of exposure. No clinical signs of toxicity were reported. The LC_{50} for inhalation exposure is > 5.0 mg a.i./L air.

3.1.14. Inerts and Adjuvants

As discussed in Section 2, disparlure is typically applied in a slow release polyvinyl chloride formulation and various formulations have been test and used in USDA programs. As also discussed in Section 2, the USDA uses Disrupt II, a formulation of polyvinyl chloride flakes.

The precise composition of the flake formulation is considered proprietary by Hercon. In the preparation of the current risk assessment, the product manager at Hercon for Disrupt II was contacted and some information on the inerts has been disclosed. The new formulation of Disrupt II contains 5 inert ingredients. Two of the inerts, one of which is identified as diatomaceous earth, are on the U.S. EPA List 4A list and another is on List 4B. A new inert is

listed on the exemptions from requiring tolerances 40 CFR 180.910 and 180.930. Polyvinylchloride itself is exempt from tolerance under 40 CFR 180.960 (MacLean 2006).

The reference to the U.S. EPA *List 4* refers to the U.S. EPA method for classifying inert ingredients that are used in pesticide formulations. U.S. EPA classifies inerts into four lists based on the available toxicity information: toxic (List 1), potentially toxic (List 2), unclassifiable (List 3), and non-toxic (List 4). These lists as well as other updated information on pesticide inerts are maintained by the U.S. EPA at the following web site: http://www.epa.gov/opprd001/inerts/. Any compound classified by U.S. EPA as toxic or potentially toxic must be identified on the product label if the compound is present at a level of 1% or greater in the formulation. If the compounds are not classified toxic, all information on the inert ingredients in pesticide formulations is considered proprietary under Section 10(a) of the Federal Insecticide, Fungicide, and Rodenticide Act (FIFRA). In that case, the formulators of the pesticide need not and typically do not disclose the identity of the inert or adjuvant. List 4A is classified as minimal risk inert ingredients. List 4B is defined by the U.S. EPA as follows:

> Other ingredients for which EPA has sufficient information to reasonably conclude that the current use pattern in pesticide products will not adversely affect public health or the environment (http://www.epa.gov/opprd001/inerts/lists.html)

As discussed further in Section 4.1.3.3, some information is available on the toxicity of disparlure, the Disrupt II formulation of disparlure, and Disrupt II flakes that contain only the PVC flakes and other inerts (i.e., no disparlure). While limited, this information suggests that the PVC flakes and other inerts do not contribute to the toxicity of Disrupt II.

3.1.15. Impurities and Metabolites

3.1.15.1. Impurities **–**Virtually no chemical synthesis yields a totally pure product. Technical grade disparlure does contain low concentrations of four compounds that are structurally related to disparlure – i.e., three octadecenes (all at less than 1%) and one octadecyne (at less than 0.5%) (MTM Chemicals 1991). Additional data regarding impurities in disparlure been identified in the FIFRA/CBI files (Shin-Etsu Chemical Company 2002; Oguma 2000). The specific information contained in these files is protected under FIFRA Section 12(a)(2)(D) and this information cannot be disclosed in this risk assessment. Nonetheless, concern for impurities is reduced by the fact that the toxicity of impurities should be encompassed in the acute toxicity studies conducted on technical grade disparlure – i.e., disparlure that contains these impurities.

3.1.15.2. Metabolites **–** No studies on the metabolism of disparlure in mammals were identified in the open literature or the FIFRA/CBI files. Acute toxicity studies, however, typically involve a single exposure followed by a period of observation, most often a 14-day post-dosing period (e.g., U.S. EPA/OPPTS 2003). Because of this, the effects of metabolites formed during the observation period should be encompassed in the acute toxicity studies conducted on disparlure.

3.1.16. Toxicological Interactions.

DDVP pest strips (Vaprotape II strip) are contained in the milk carton trap together with a carrier containing disparlure. These milk carton traps are placed in selected areas to monitor gypsy moth infestations. No published literature or information in the FIFRA files permit an assessment of potential toxicological interactions between disparlure and DDVP or any other compounds. As separate risk assessment on DDVP has been prepared as part of the series of risk assessments on the control/eradication agents used for the gypsy moth.

3.2. EXPOSURE ASSESSMENT

3.2.1. Overview.

For both workers and the general public, exposures to disparlure may involve multiple routes of exposure (i.e., oral, dermal, and inhalation). Because of the limited toxicity data on disparlure – i.e., no chronic toxicity data are available – no chronic exposure scenarios are developed.

3.2.2. Dermal Exposure

Dermal exposure is most likely to be the predominant route for occupational exposure to disparlure and is also a possible route of exposure for the general public. As discussed in Section 3.1.3, a case report of an accidental exposure of a worker to disparlure show that no signs of toxicity developed; the only notable effect of disparlure exposure in this worker was the persistent attraction of gypsy moths (Cameron 1981, 1983, 1995). Exposure of this worker was most likely by the dermal route, although the possibility of inhalation exposure cannot be ruled out (Cameron 1995). Since the systemic toxicity of disparlure in mammals is very low, the absence of dermal absorption data does not add significant uncertainty to this risk assessment since no systemic toxicity is would be expected to occur, even at very high exposure levels of disparlure. While dermal exposure of workers is expected to be non-toxic, dermal exposure is likely to cause the persistent attraction of gypsy moths.

3.2.3. Inhalation Exposure

Both workers and the public may be exposed to disparlure by inhalation and the magnitude of the exposure can be estimated from available monitoring studies. In these studies, high application rates, relative to the projected rates used in program activities (29.1 g acre, Section 2.3), were used in order to be able to detect disparlure in air.

Caro et al. (1981) investigated the distribution and persistence of three disparlure formulations including gelatin microcapsules, laminated plastic flakes, and hollow fibers. Each formulation was applied at a rate of 500 g a.i./hectare (approximately 0.45 lb a.i./acre). Release of disparlure from these formulations was most rapid during the first 2 days after application. Initially, air concentrations ranged from approximately 22 to 30 ng/m^3 (nanograms per meter cubed) for microcapsules and fibers and from 7.3 to 8.2 ng/m^3 for flakes. Other investigators using the same application rate reported similar initial concentrations of disparlure in air, approximately 28-30 ng/m^3 for gelatin microcapsules and laminated plastic flakes (Taylor 1982). At a lower application rate (250 g hectare), there were somewhat higher levels, 44.5-99.3 ng/m^3, using gelatin microcapsules (Plimmer et al. 1977).

Over time, the concentrations of disparlure in air will decrease as the disparlure dissipates. After 30 days, air concentrations ranged from approximately 0.4 to 2.5 ng/m^3 for all formulations (Caro et al. 1981). Flakes that originally contained 7.1% disparlure (w/w) contained 6.0% (w/w) disparlure (85% of the original level) by 30 days after treatment. Results of a study using a disparlure gelatin microcapsule formulation show that release rates increase with increasing temperature (Caro et al. 1977).

The highest reported air concentration after aerial application of 250 g hectare racemic disparlure on flakes is slightly less than 100 ng/m^3 (Taylor 1982). At an application rate of nearly 30 g acre, concentrations of approximately 30 ng/m^3 can be expected. Since this estimate is based on the highest levels of disparlure in air, which occur within the first 5 days after application (Caro et al. 1981, Taylor 1982), actual levels of exposure could be lower.

Air concentrations resulting from the release of disparlure from traps are expected to be low relative to air concentrations resulting from aerial application of disparlure. Traps contain only 0.5 mg disparlure/trap. The rate of dissipation of disparlure from traps is dependent upon many factors, including dispenser design, lure type, and air temperature and flow (Bierl 1977, Bierl-Leonbardt 1979, Leonhardt et al. 1990). Thus, air concentrations results from volatilization of disparlure from traps are expected to be very low and highly variable.

Over a 120-day period, 38 to 68% of disparlure was lost from lures in laminated plastic dispensers, with loss varying over a variety of experimental conditions (Bierl-Leonbardt 1979). Loss of (+)disparlure was reduced with the use of thicker plastic dispensers and increased with increasing air flow rate and increasing temperature. Greenhouse studies have shown that approximately 50%–80% of (+)disparlure is released from PVC twine or laminates during a 16-week aging process (Kolodny-Hirsch and Webb 1993). Release rates 30 to 40 ng/hr were noted from cotton wicks containing 100 µg (+)disparlure 30 to 40 ng/hr, with increased rates observed at higher temperatures.

3.2.4. Oral Exposure

Although the efficacy of disparlure depends on its volatility, the studies summarized above demonstrate that 70%–85% of disparlure may remain in the carrier matrix after prolonged periods of time. Consequently, oral exposure may occur from consumption of disparlure flakes or tape. At an application rate of approximately 30 g acre, an individual would have to consume all of the flakes in a 1 m^2 area to receive a dose of 7.4 mg. If this were done by a 10 kg child, the dose would be 0.74 mg/kg.

3.3. DOSE-RESPONSE ASSESSMENT

The toxicity data on disparlure are not adequate for making a standard dose-response assessment. As detailed in Section 3.1, the limited available data indicate that disparlure has a low order of acute toxicity, based on mortality as the endpoint:

Oral LD_{50} >34,600 mg/kg
Dermal LD_{50} >2,025 mg/kg
Inhalation LC_{50} >5 mg/L · 1 hour

Data regarding the toxicity of disparlure to animals or humans after subchronic or chronic exposures were not located in the available literature. Moreover, the acute toxicity of this compound for endpoints other than mortality is poorly characterized.

3.4. RISK CHARACTERIZATION

3.4.1 Overview

Although studies on the acute toxicity of disparlure have been conducted in laboratory animals, the lack of subchronic or chronic toxicity data precludes a quantitative assessment of risk for longer-term exposures. The available data regarding the acute toxicity of disparlure indicate that the potential hazard from exposure to the compound is low.

The reliance on acute toxicity data introduces uncertainties into the risk assessment that cannot be quantified. Other uncertainties in this analysis are associated with the exposure assessment and involve environmental transport and dermal absorption. Thus, while there is no reason to believe that longer-term exposure to disparlure will produce adverse effects, this assumption can not be substantiated due to the lack of chronic exposure data. The significance of this uncertainty is at least partially offset by the very low exposures that are plausible given the low doses of disparlure used in programs to control the gypsy moth.

3.4.2. Workers and the General Public

It is not possible to develop a reference dose (RfD); therefore, the calculation of a hazard quotient (level of exposure divided by the RfD) and a standard risk characterization cannot be developed. Nonetheless, the limited information that is available regarding the use and toxicity of disparlure gives no clear indication of hazard. For example, the plausible level of oral exposure to a small child is less than 1 mg/kg (Section 3.1.4). This is a factor of 10,000–35,000 less than the exposure levels that were not lethal to rats (Kretchmar 1972, Section 3.1.4). Empirical relationships between acute exposure levels that are lethal to experimental mammals and subchronic or chronic NOAELs in experimental mammals (for example, Dourson and Stara, 1983) do not suggest that the use of disparlure to control of the gypsy moth is likely to pose a substantial hazard to humans.

The only clear and unequivocal biological activity of disparlure is its ability to attract the male gypsy moth. Because disparlure appears to be highly persistent in humans, dermal contact with the compound might make an individual an attractant to male moths over a period of many years. Although this is not likely to cause adverse health effects, it is likely to be a nuisance.

3.4.3. Sensitive Subgroups

The toxic effects of disparlure, if any, have not been identified. Consequently, groups at special risk, if any, cannot be characterized. Because disparlure attracts the male gypsy moth, individuals who have an aversion to insects might be considered to be a sensitive subgroup. Nonetheless, this aversion and sensitivity would not be related to any frank health effect.

3.4.4. Cumulative Effects

Very little information is available on the toxicity of disparlure. As noted above, the ability to attract the male gypsy moth is the only clear biological activity of this compound. Since this compound seems to persist in humans for prolonged periods, repeated exposures are more likely than single exposures to transfer sufficient quantities of disparlure to the individual to attract the moth.

3.4.5. Connected Actions

No information is available on the interaction of disparlure with other control agents or other chemicals usually found in the environment. There is an obvious and substantial interaction of disparlure with the adult male gypsy moth. Individuals who are exposed to sufficient quantities of disparlure and who live in an area in which male gypsy moths reside will attract the moth. The definition of a sufficient quantity of disparlure, however, cannot be characterized from the available data.

4. ECOLOGICAL RISK ASSESSMENT

4.1. HAZARD IDENTIFICATION

4.1.1. Overview

There is very little information regarding the toxicity of disparlure to nontarget wildlife species. As discussed in Section 3.1, rigorous toxicity testing of disparlure was not required by the U.S. EPA (U.S. EPA 1994). Thus, the only studies identified in the available literature are acute toxicity studies in bobwhite quail, mallard ducks, rainbow trout, bluegill sunfish, *Daphnia magna* and Eastern oysters. No chronic toxicity studies were identified in the available literature.

Results of acute gavage and dietary toxicity studies in mallard ducks and bobwhite quail show that disparlure has very low toxicity in these species, with no mortalities observed following exposure to up to 2510 mg/kg bw in bobwhite quail.

Limited data are available regarding the toxicity of disparlure to aquatic animals. A major issue in the interpretation of the aquatic toxicity data on disparlure involves the solubility of disparlure in water. While no measured values for the solubility of disparlure in water are available, estimates based on quantitative structure-activity relationships developed by the U.S. EPA suggest that the solubility of disparlure in water is in the range of 0.0019 to 0.0028 mg/L. The bioassays that have been conducted on disparlure and Disrupt II formulations of disparlure have not measured concentrations of disparlure in the test water but report nominal concentrations of disparlure that exceed the water solubility of disparlure by factors of about 10 [0.028 mg/L] to over 150,000 [300 mg/L]. Based on the results of the available bioassays and considerations of water solubility, disparlure does not appear to present any toxic hazards to aquatic species. In toxicity tests of small aquatic invertebrates (i.e., daphnids), trapping of the organism at the surface of the water has been noted in bioassays and this can present a physical hazard to the organism. The significance of this physical hazard observed in bioassays to potential hazards in field applications is unclear.

4.1.2. Toxicity to Terrestrial Organisms

4.1.2.1. Mammals– As discussed in Section 3.1, there is very little information on the toxicity of disparlure in mammalian species. Results of acute toxicity studies for oral, dermal, ocular and inhalation exposure to disparlure show that disparlure has very low toxicity to mammals. Other than some minor clinical signs of toxicity (i.e., piloerection, hunched posture and ungroomed appearance in rats), acute oral exposure of rats to very high doses of disparlure (up to 34,600 mg a.i./kg bw) did not result in death or signs of systemic toxicity in rats (Kretchmar 1972). Thus, acute exposure to disparlure does not appear to exhibit any organ-specific toxicity. There is no information available regarding chronic exposure of mammals to disparlure. No field studies are available in which the impact of disparlure were assessed on mammalian wildlife communities.

4.1.2.2. Birds– As summarized in Appendix 2, the acute toxicity of disparlure administered by gavage has been studied in bobwhite quail (Fink et al. 1980) and acute exposure to dietary disparlure has been studied in bobwhite quail chicks and mallard ducklings (Hudson 1975). In adult bobwhite quail administered single doses of disparlure ranging from 398 to 2510 mg a.i./kg by gavage, no mortalities were observed at any dose level (Fink et al. 1980). In the highest dose group, lethargy was observed in 3 of 10 birds; it is unclear if this observation was treatment related. In quail chick and mallard ducklings exposed to 313 to 5000 ppm disparlure in the diet for 5 days, no mortalities were observed and no clinical signs of toxicity were reported during the 14-day observation period. Based on the results of these studies, the LD_{50} for a single dose of disparlure administered by gavage to bobwhite quail is > 2510 mg a.i./kg bw and the corresponding value for 5-day dietary exposure to quail chicks and mallard ducklings is > 5000 ppm.

4.1.2.3. Terrestrial Invertebrates– As discussed in Section 2, disparlure is a naturally occurring insect pheromone. The mechanism of action of disparlure in disrupting gypsy moth mating is well characterized. The (+)disparlure enantiomer, which is produced and released by female gypsy moths, is a powerful attractant to male gypsy moths. Male gypsy moths detect disparlure through highly specific detectors located on antennae (Murlis et al. 2000, Plettner et al. 2000). The (–)disparlure enantiomer is a receptor antagonist to (+)disparlure and has slight repellent activity (Plettner et al. 2000). When sprayed over a large area, disparlure disrupts mating by confusing male moths. There are a large number of greenhouse and field studies showing that disparlure is an effective agent in decreasing gypsy moth populations (Beroza et al, 1975, Campbell 1983, Herculite Products Inc., 1978, Kolodny-Hirsch and Webb 1993, Leonhardt et al. 1990, Leonhardt et al. 1993, Leonhardt et al. 1996, Plimmer et al. 1977, Schwalbe et al. 1978, Schwalbe et al. 1979, Sharov et al. 2002, Thorpe et al. 1993, US Department of Agriculture 1973).

Although disparlure is considered highly selective for gypsy moths, there is some evidence showing that disparlure may have effects on the mating of other species of moths. As part of the reproductive communication between male and female nun moths, female nun moths produce a blend of pheromones that contains disparlure (Gries et al. 2001). Studies show that lures containing disparlure are effective in attracting male nun moths (Gries et al. 2001, Morewood et al. 1999, Morewood et al. 1999). The potency of disparlure in attracting male gypsy moths relative to nun moths has not been assessed. Disparlure is also produced by *L. fumida* [a species native to Japan] (Schaefer et al. 1999). Thus, based on the results of these studies, it appears that disparlure is not completely selective for the gypsy moth. Although studies have not been conducted, it is possible that other closely related species of moths could also respond to disparlure.

No laboratory or field studies on the effects of acute or chronic exposure of disparlure to other terrestrial invertebrates were identified in the available literature.

4.1.2.4. Terrestrial Plants (Macrophytes)–Neither the published literature nor the U.S. EPA files include data regarding the toxicity of disparlure to terrestrial plants.

4.1.2.5. Terrestrial Microorganisms– Neither the published literature nor the U.S. EPA files include data regarding the toxicity of disparlure to terrestrial microorganisms.

4.1.3. Aquatic Organisms.

4.1.3.1. Fish – As summarized in Appendix 3, acute toxicity studies of disparlure were conducted in rainbow trout and bluegill sunfish (Knapp and Terrell 1980, Rausina no date). No effect on survival was observed in bluegill sunfish exposed to disparlure at a nominal concentration of 100 mg/L (Rausina no date) or 300 mg/L (Knapp and Terrell 1980) for up to 96 hours. The 96-hour LC_{50} for bluegill sunfish is >300 mg/L. In rainbow trout, no effect on survival was observed following exposure to 100 mg/L disparlure for 48 hours (Rausina no date). However, after 72 hours of exposure to 100 mg/L disparlure, only 8 of 10 trout survived. Survival of trout was not affected at disparlure concentrations of 0.1 to 10 mg/L. Under these experimental conditions, the NOEC for mortality in rainbow trout is 10 mg/L.

Based on current standard for toxicity studies in fish, neither of these studies would be considered acceptable by current standards (e.g., U.S. EPA/OPPTS 2006). For example, the U.S. EPA guidelines for acute toxicity studies in fish require information on the solubility of test compound in water and require that the test substance not be tested as concentrations in excess of the solubility of the compound in water.

As noted above and detailed further in Appendix 3, neither Rausina (no date) nor Knapp and Terrell (1980) measured the concentration of disparlure in the test water. As noted in Section 2, no measured values are available for the solubility of the disparlure in water. Based on quantitative structure activity relationships (QSAR), however, it is likely that the solubility of disparlure in water is very low. As indicated in Table 2-1, the QSAR package developed by the U.S. EPA estimates a water solubility for disparlure of 0.0019 to 0.0028 mg/L (EPI Suite 2006). In the preparation of this risk assessment, Hercon (the company that manufactures the Disrupt II flakes) was contacted and the chemists at Hercon indicated that they were not aware of any measured water solubility values for disparlure but, consistent with the estimates from EPI Suite (2006), the chemists at Hercon indicated that the water solubility is likely to be very low.

The importance of considering water solubility in the assessment of a chemicals toxicity to aquatic species is discussed by Clements et al. (1996), the individuals who developed the toxic estimation algorithms used in EPI Suite. Essentially, if a compound is non-toxic at the limit of water solubility, then the compound can be classified as presenting no plausible toxic risk to the organism. Physical hazards may still be plausible. This is discussed further in Section 4.1.3.3 (Aquatic Invertebrates).

The toxicity values estimated by EPI Suite (2006) using algorithms of Clements et al. (1996) are summarized in Table 4-2. The algorithms used to estimate the toxicity values were developed by Clements et al. (1996) and are based on regression equations which take the general form of:

$$Log_{10}(TV) = m Log_{10}(Kow) + b$$

where *TV* is the toxicity value in units of millimoles/liter (mM/L), Kow is the octanol/water partition coefficient, and *m* and *b* are model parameters (slope and intercept, respectively). While the algorithms are based on molar concentrations, EPI Suite converts these concentrations to units of mg/L for the output files. The specific model parameters are summarized in Table 4-2 and are based on QSAR estimates for mono-epoxides – i.e., compounds structurally similar to disparlure.

A very important feature of these estimates concern the limiting values for the Kow of the compound. As discussed by Clements et al. (1996), this recommended limiting value is based on the range of Kow values on which the QSAR estimates are based. For mono-epoxides, the limit recommended by Clements et al. (1996) is 5. As noted in Table 2-1, the estimated log Low value for disparlure is 8.08 – i.e., higher than the recommended cut off value by a factor of about 1000.

This cutoff value is very important in the interpretation of the estimated toxicity values. As indicated in Table 4-2, the estimated toxicity values for fish range from about 0.12 to 0.14 mg/L based on the Kow. Although the studies by Knapp and Terrell (1980) as well as Rausina (no date) have serious limitations, they clearly indicate no mortality at the nominal concentrations. It is likely, however, that the actual concentrations would not have exceeded the water solubility of disparlure – i.e., 0.0019 to 0.0028 mg/L (Table 2-1). The simple interpretation is that the water solubility of disparlure is so low that the maximum possible concentration in water is below the estimated toxicity values by a factor of about 43 [0.12 mg/L ÷ 0.0028 mg/L] to 74 [0.14 mg/L ÷ 0.0019 mg/L]. This is the basis for asserting that disparlure is not likely to pose a risk of toxicity to fish.

Thwaits and Sorensen (2005) have recently submitted a brief summary of a study using rainbow trout in which disparlure was assayed for olfactory stimulation. At nominal concentrations of either 0.028 mg/L or 0.28 mg/L, with or without the presence of methanol (used to enhance the solubility of disparlure in water), disparlure evidenced no activity relative to negative controls (well water or well water with methanol) or L-serine as a positive control.

***4.1.3.2. Amphibians*–** Neither the published literature nor the U.S. EPA files include data regarding the toxicity of disparlure to amphibian species.

***4.1.3.3. Aquatic Invertebrates* –** As with fish, the data on the toxicity of disparlure itself to aquatic invertebrates is relatively old (LeBlanc et al. 1980; Ward 1981) and these studies would not meet the current requirements of the U.S. EPA (e.g., U.S. EPA/OPPTS 2006) because of the same limitations discussed in Section 4.1.3.1 (Fish). The acute toxicity of disparlure to *Daphnia*

was evaluated in a single study (LeBlanc et al. 1980). Details of this study are provided in Appendix 3. A dose-related increase in mortality was observed following 48 hours of exposure, with 7% mortality at 0.028 mg/L and 100% mortality at a 0.22 mg/L. The LC_{50} value was calculated at 0.098 mg/L and the NOEC for mortality was 0.017 mg/L. In Eastern oysters exposed to 1.25 to 20 mg/L disparlure for 96 hours, there was no effect on new shell growth (Ward 1981). Again, all of these toxicity values refer to nominal concentrations rather than measured concentrations and all of these toxicity values exceed the plausible range of the solubility of disparlure in water – i.e., 0.0019 to 0.0028 mg/L (Table 2-1).

The major difference, however, between the data on fish and data on daphnids involves the mortality. As detailed in Appendix 3, LeBlanc et al. (1980) report a clear dose-response relationship for daphnids. The important detail, however, is that this mortality was associated with organisms being trapped at the air-water interface. While not discussed by LeBlanc et al. (1980), it is likely that the entrapment of the daphnids at the air-water interface was attributable to the undissolved disparlure in the test solution. Based on the highest estimate of the solubility of disparlure in water (i.e., 0.0028 mg/L) the nominal test concentrations used by LeBlanc et al. (1980) exceed the solubility of disparlure in water by factors of 10 [0.028 mg/L ÷ 0.0028 mg/L] to about 78 [0.22 mg/L ÷ 0.0028 mg/L].

The supposition that daphnid mortality in the study by LeBlanc et al. (1980) is due to the physical trapping of the organisms at the water surface by undissolved disparlure is supported by the more recent studies by Palmer and Krueger (2006a,b) on various formulations of Disrupt II flakes. The studies were sponsored by concerns with the quality of the data on disparlure, the preliminary risk assessment on disparlure (SERA 2004), as well as a desire to better characterize the potential hazards of the inerts used in Disrupt II formulations.

The studies by Palmer and Krueger (2006a,b) involved Disrupt II formulations that were designated as *Standard Flakes* and *Modified Flakes*. This nomenclature is somewhat awkward but will be maintained because these terms are used in the reports by Palmer and Krueger (2006a,b) and these terms are also used (at least currently) by individuals in the USDA who are involved in applications of Disrupt II (e.g., Leonard 2006b). *Standard flakes* refer to an older formulation that was the only formulation used operationally in USDA programs up through 2003. Hercon modified their Disrupt II formulation by changing one of the inert ingredients and these modified flakes were first tested by USDA in 2002. By 2004 the modified formulation of Disrupt II had replaced the standard formulation in most operational applications (Leonard 2006d). As noted in Section 2, the USDA has been involved in the refinement of various formulations of disparlure for many years and it seems likely that new formulations will be developed in the future.

Standard Flakes were tested in the study by Palmer and Krueger (2006a) and *Modified Flakes* were tested in the study by Palmer and Krueger (2006b). Both of these studies involved identical experimental designs, the details of which are given in Appendix 3. Both studies involved three set of flakes: blank flakes that contained no disparlure (i.e., only the inerts), fully formulated

flakes that were manufactured in 2003, and fully formulated flakes that were manufactured in 2005.

In each study, the daphnids were exposed to a series of six water accommodated fractions (WAF) at nominal concentrations of 0.18, 0.54, 1.8, 5.4, 18, and 54 mg a.i./L. The technique using water accommodated fractions is a method specifically designed for water insoluble compounds (e.g., French-McCay 2002; Pelletier et al. 1997). As implemented by Palmer and Krueger (2006a,b), the application of this method involved mixing the flakes (formulated or blank) into 12 L of dilution water and stirring the mixture for approximately 24 hours. The test water (without flakes) was then decanted into the test chambers into which the daphnids were placed.

As with the studies in fish and the earlier studies with invertebrates, the concentration of disparlure in the test water was not measured. Consequently, the "concentrations" of disparlure are reported as *nominal concentrations* rather than *measured concentrations*. As detailed in U.S. EPA guidelines for the conduct of acute bioassays in *Daphnia* (U.S. EPA 1996), the U.S. EPA guidelines for toxicity studies in *Daphnia* require measurements of the concentrations of the test substance in water. The rationale for this requirement is simple: if the concentration is not measured, there may be substantial uncertainty in attempting to characterize the exposure. The distinction between *nominal concentrations* and *measured concentrations* is particularly important for compounds such as disparlure which have a very low solubility in water. As detailed further below, the *nominal concentrations* of disparlure in the toxicity studies of disparlure and Disrupt II flakes substantially exceed the water solubility. This leads, in turn, to the development of a film on the surface of the water and this film traps the daphnids. Thus, the effect, while adverse, appears to be a physical rather than toxic effect.

As detailed in Appendix 3, the blank flakes – i.e., the flakes without disparlure – did not result in any mortality in any of the test groups for either the *Standard Flakes* (Palmer and Krueger 2006a) or the *Modified Flakes* (Palmer and Krueger 2006b). The flakes from 2003 – both standard and modified – resulted in very low rates of mortality and immobility and the estimated LC_{50} values in both of these bioassays were >300 mg formulation/L, equivalent to >53 mg a.i./L.

The new flakes from 2005 – again both standard and modified – yielded much lower estimates of the 48 hour-LC_{50}: 69 mg formulation/ L (12.3 mg a.i./L) for standard flakes (Palmer and Krueger 2006a) and 48 mg formulation/L (8.6 mg a.i./L) for modified flakes (Palmer and Krueger 2006b). The reason or reasons for the differences between on the 2003 flakes and the 2005 flakes is unclear and this issue is not addressed in the report by Palmer and Krueger (2006a,b) other than to note the differences in toxicities. For the standard flakes, Palmer and Krueger (2006a) note only the following differences in physical appearance:

> *The SF 2003 and SF 2005 test solutions and the blank solution appeared clear and colorless in the test chambers at test initiation. At test termination, all of the solutions, with the exception of the*

> *300 mg/L SF 2005 solution, appeared clear and colorless. The 300 mg/L SF 2005 test solution appeared clear and colorless with white particulates on the bottom of the test chamber.* (Palmer and Krueger (2006a, p. 12.)

For the modified flakes, Palmer and Krueger (2006b) note differences in appearance between the 2003 and 2005 flakes that are somewhat more striking than those for the standard flakes:

> *Prior to decanting, the MF 2003 and MF 2005 WAF solutions, and the blank solution, appeared clear and colorless, with white particles on the surface of the water and green and white particles settled on the bottom of the WAF bottles, increasing in amount with increasing concentration. The MF 2003 and MF 2005 test solutions and the blank solution appeared clear and colorless in the test chambers at test initiation and termination.* (Palmer and Krueger (2006b, p. 12.)

During the period when these bioassays were being conducted, the testing facility was visited by a toxicologist with the USDA Forest Service who reported striking differences in the appearance of the 2003 and 2005 flakes, both standard and modified, prior to mixing the flakes with water (Appleton 2006).

As detailed in Appendix 3, the recent bioassays on the flake formulations using daphnids (Palmer and Krueger 2006a,b) are similar to the earlier bioassay on technical grade disparlure using daphnids (LeBlanc et al. 1980) in that all of these studies observed daphnids trapped at the surface of the water. While LeBlanc et al. (1980) did not report the numbers of daphnids that were trapped at various nominal concentrations, the data reported by Palmer and Krueger (2006a,b) clearly indicate an association between the nominal concentrations, number of organisms trapped at the water surface, and subsequent mortality or immobility.

The observations in these studies and the QSAR estimate of the very low water solubility of disparlure (Table 2-1) suggest that the trapping of the daphnids at the surface of the water was due to a layer of insoluble disparlure at the surface of the test water. Because no daphnids were trapped at the water surface in the bioassays on the blank flakes, both standard and modified, it is not plausible to assert that any of the inerts in either the standard or modified flakes contributed to the entrapment of the organisms at the water surface.

When daphnids are trapped at the surface of the water, the organisms are under substantial stress and, if they remain trapped for a prolonged period, the animals may die for reasons that are not directly related to the systemic toxicity of the disparlure – e.g., impaired respiration. This is noted by Palmer and Krueger (2006a,b) in both sets of bioassays:

> *Due to the nature of the test substance, mortality/immobility among daphnids in the Disrupt II formulation treatment groups*

> *may have been due, in part, to a physical effect, rather than only to toxicity.* (Palmer and Krueger (2006a,b p. 15)

As with fish, the weight of the evidence suggest that disparlure will not pose any risk to daphnids in terms of toxicity. Unlike fish, however, the available data clearly indicated that disparlure could pose a physical hazard to daphnids and possibly other aquatic invertebrates if the amount of disparlure in the water is sufficient to create an insoluble film of disparlure on the surface of the water.

While the hazard during a laboratory bioassay is clearly documented, the likelihood of this physical hazard occurring in the field after a normal application of disparlure is more difficult to assess. Disrupt II is not intentionally applied to water. While no microcosm or mesocosm studies have been conducted, Disrupt II as well as other experimental formulations of disparlure have been used by the USDA for over a decade. In that period, no incidents or field observations have been made that would suggest any adverse effects on aquatic invertebrates (Leonard 2006c). The potential for a physical hazard to aquatic invertebrates is considered further in Section 4.4.4 (risk characterization for aquatic invertebrates).

4.1.3.4. Aquatic Plants– Neither the published literature nor the U.S. EPA files include data regarding the toxicity of disparlure to aquatic plants.

4.1.3.5. Other Aquatic Microorganisms– Neither the published literature nor the U.S. EPA files include data regarding the toxicity of disparlure to aquatic microorganisms.

4.2. EXPOSURE ASSESSMENT

4.2.1. Overview.

As discussed in Sections 3.1 and 4.1, disparlure appears to be essentially nontoxic to mammals and birds. While this assessment is limited by the lack of chronic toxicity data in terrestrial species, it is not expected that acute or chronic exposure of terrestrial mammals or birds to disparlure would result in the development of significant adverse effects. Given the low toxicity of disparlure and limited available data, an exposure assessment for terrestrial species would not add to the assessment of risk for terrestrial species. Thus, an exposure assessment for terrestrial species is not included in this risk assessment. For aquatic species, the range of plausible nominal concentrations of disparlure in water are calculated at 0.0015 mg/L to 0.0037 mg/L over the range of applications rates considered in this risk assessment – i.e., 6 g a.i./acre to 15 g a.i./acre. These concentrations apply to a 1 meter deep body of water. The lower end of this range is within the estimated solubility of disparlure in water – i.e., 0.0019 to 0.0028 mg/L – and the upper end of this range slightly exceeds the estimated solubility of disparlure in water.

4.2.2. Exposure of Aquatic Animals.

Disparlure is not intentionally applied to bodies of water (Hercon 2006a; Leonard 2006b). Thus, under normal conditions, aquatic organisms are not likely to be exposed to substantial amounts of disparlure. Accidental applications to surface water have been reported (Leonard 2006c) and these can be considered.

Disrupt II flakes could be accidentally applied to either standing bodies of water (e.g., ponds or lakes) or moving bodies of water (e.g., streams or rivers). As discussed in Section 4.1.3, there is no basis for asserting that disparlure will pose any risk of toxic effects to aquatic organisms at the limit of estimated solubility of disparlure in water. The only risk that can be identified is the entrapment of small aquatic invertebrates in a surface film of disparlure (Section 4.1.3.3). A surface film of disparlure could occur if Disrupt II flakes were accidentally applied to a standing body of water, such as a lake or pond, in a sufficient amount to exceed the solubility of disparlure in the water. The development of a film in a flowing body of water, such as a stream or river, does not appear to be plausible. Consequently, for this risk assessment, exposure scenarios are developed only for standing bodies of water and these scenarios are used to assess potential effects only on small aquatic invertebrates that might interact with the surface of the water – i.e., benthic species are not considered to be at any risk.

If Disrupt II flakes are applied to a standing body of water, some disparlure will volatilize into the air and some disparlure will leach from the flakes into the water. The disparlure in the water will diffuse through the water and a film of disparlure on the surface of the water will form if the water becomes saturated. The film on the surface of the water with then volatilize over time. The kinetics of these processes cannot be characterized. Nonetheless, the bioassays conducted by Palmer and Krueger (2006a,b) suggest that this general scenario is plausible. Thus, in the exposure assessment for small aquatic invertebrates, instantaneous leaching will be assumed and the impact of volatilization will not be considered. These are conservative assumptions in that

they will tend to overestimate exposure. This is considered further in Section 4.4.4 (risk characterization for aquatic invertebrates).

As discussed in Section 2.3, this risk assessment considers application rates in the range of 6 grams a.i./acre to 15 grams a.i./acre. This range corresponds to application rates of about 1.5 mg/m^2 [6 grams a.i./acre × 1000 mg/g ×1 acre/4047 m^2 = 1.4826 mg/m^2] to 3.7 mg/m^2 [15 grams a.i./acre × 1000 mg/g ×1 acre/4047 m^2 = 3.7064 mg/m^2]. If these amounts of disparlure are applied accidentally to a 1 meter deep body of water, nominal concentrations – i.e., assuming complete mixing and ignoring solubility limitations – would be in the range of 0.0015 mg/L to 0.0037 mg/L [1000 liters per m^3]. Details of these calculations are given in Worksheet A01of the EXCEL workbook that accompanies this risk assessment.

As noted in Table 2-1 and discussed in Section 4.1.3, no measured values for the solubility of disparlure in water are available but estimates based on quantitative structure-activity relationships developed by the U.S. EPA (EPI Suite 2006) suggest that the solubility of disparlure in water is in the range of 0.0019 to 0.0028 mg/L. Thus, the nominal concentrations that might occur in a 1 meter deep body of water after an accidental direct application are within the estimated water solubility of disparlure at the lower bound of the application rate (i.e., an application rate of 6 g a.i./acre) [0.0015 mg/L < 0.0028 mg/L] but modestly exceed the estimates of the solubility of disparlure in water at the upper bound of the application rate by a factor of about 1.3 [0.0037 mg/L ÷ 0.0028 mg/L].

Deeper bodies of water will result in lower concentrations that are likely to be at or below the solubility of disparlure in water and shallower bodies of water would lead to nominal concentrations that would exceed the solubility of disparlure in water. This type of situational variability to difficult to encompass in a general risk assessment. As a tool for individuals who are involved in or wish to assess applications of disparlure under conditions other than those considered in this risk assessment, the workbook that accompanies this risk assessment includes a worksheet (named A02) that can be used to calculate nominal concentrations of disparlure based on specified application rates, fractional deposition (i.e., drift), and average depth of the water body. Worksheet A02 also calculates hazard quotients based on the dose-response assessment for daphnids (Section 4.3.3).

Note that Worksheet A02 applies only to the accidental application of disparlure to a standing body of water. No exposure scenarios are developed for accidents that involve the dumping of large amount of Disrupt II into a standing body of water. While such accidents are possible, none have been documented. In addition, the calculation of nominal concentrations is trivial under the assumption of instantaneous mixing – i.e., the amount of disparlure that is deposited in the water divided by the volume of the water. Given the available information on the toxicity of disparlure to aquatic species (Section 4.1.3), no further elaboration of this exposure assessment is warranted. Potential consequences for aquatic species are discussed in Section 4.4.3 (risk characterization for fish) and Section 4.4.4 (risk characterization for aquatic invertebrates).

4.3. DOSE-RESPONSE ASSESSMENT

4.3.1 Overview

Given the low toxicity of disparlure to terrestrial animals coupled with the limitations imposed by the lack of chronic toxicity data, no standard dose-response assessment can be made or is warranted for disparlure in terms of effects on terrestrial species. As reviewed in Section 4.1.2.3, disparlure is produced by other species of moths and has the ability to attract nun moths (Gries et al. 2001, Morewood et al. 1999, Morewood et al. 1999, Schaefer et al. 1999). However, since there are no quantitative data available regarding the efficacy of disparlure in nun moths, a dose-response assessment for this effect in a nontarget species cannot be made. Similarly, no explicit dose-response relationship is proposed for fish. There is no basis for asserting that adverse effects in fish are plausible under any foreseeable conditions. For aquatic invertebrates, there is no basis for asserting that toxic effects are likely at the limit of the solubility of disparlure in water. At nominal concentrations that exceed the solubility of disparlure in water, small invertebrates that may interact with the water-surface interface could become trapped in this interface due to a layer of undissolved disparlure at the air-water interface.

4.3.2. Fish

As discussed in Section 4.1.3.1, the available information on the toxicity of disparlure to fish are extremely limited. Nonetheless, there is no basis for asserting that disparlure is likely to pose a risk to fish at the limits of water solubility – i.e., in the range of 0.0019 to 0.0028 mg/L (Table 2-1) – or at nominal concentrations that are substantially in excess of the solubility of disparlure in water. Consequently, no formal dose-response relationship for fish is proposed. Nonetheless, it is noted that a nominal concentration of 10 mg/L from the study by Rausina (no date) is a clear NOEC – see Appendix 3 for details and the discussion in Section 4.1.3.1. This nominal concentration is a factor of about 3,500 to over 5,000 above the estimated values for the concentration of disparlure in water. The implications of this range of values are discussed further in Section 4.4.3.

4.3.3. Aquatic invertebrates

The risk characterization for aquatic invertebrates is somewhat more complicated than that for fish. As with fish, there is not basis for asserting that toxic effects are likely in daphnids at the limit of water solubility. However, as discussed in Section 4.1.3.3, information is available from toxicity tests with daphnids of both technical grade disparlure (LeBlanc et al. 1980) as well as Disrupt II formulations of disparlure (Palmer and Krueger 2006a,b) that exposures to disparlure that exceed the solubility of disparlure in water will result in a film (presumably composed of undissolved disparlure) at the water surface. While this may not pose a toxic risk to daphnids, the toxicity studies demonstrate that these organisms can become trapped at the water surface and this can result in the death of the animal.

The nominal concentrations at which entrapment is pronounced is in the range of the three higher nominal concentrations in the studies by Palmer and Krueger (2006a,b) using the Disrupt II formulations – i.e., a range of about 5.4 mg a.i./L to 54 mg a.i./L. The utility of these values are

limited because the amount of disparlure that leached from the flakes used in these bioassays was not determined. On the other hand, these nominal concentrations may better reflect conditions that could occur in the field – i.e., the processes of leaching from flakes to water as well as volatilization from the water surface to air.

Lower values can be identified from the study earlier study by LeBlanc et al. (1980) using technical grade disparlure. As indicated in Appendix 3, the minimum nominal concentration from the LeBlanc et al. (1980) at which any mortality was noted is 0.028 mg/L. At this concentration, mortality was 1/15. Using the Fischer Exact test (see Section 3.1.5.2. in SERA 2006), this incidence is not statistically significant ($p = 0.5$) and this concentration could be regarded as an NOEC. A similar case could be made for regarding higher concentrations from LeBlanc et al. (1980) as NOEC values: 0.048 mg/L (1/15 mortality, $p = 0.5$) and 0.079 mg/L (2/15 mortality, $p = 0.241379$). The clear LOAEL from the study by LeBlanc et al. (1980) is 0.13 mg/L (12/15 mortality, $p = 0.00000526$). The clear NOEC from this study is 0.01 mg/L at which no mortality was observed. The major limitation in the study by LeBlanc et al. (1980) is that trapping of the daphnids at the water surface is noted but details comparable to those given in Palmer and Krueger (2006a,b) are not provided.

For the current risk assessment, the NOEC value of 0.01 mg/L (nominal concentration) from the study by LeBlanc et al. (1980) will be used for characterizing risk. This is substantially above the estimated water solubility of disparlure – i.e., 0.0019 to 0.0028 mg/L from Table 2-1. As discussed above, the mortality observed in both the study by LeBlanc et al. (1980) as well as the studies by Palmer and Krueger (2006a,b) are probably due to the formation of a slick of disparlure at the surface of the water. Thus, the use of a nominal concentration is simply an index of exposure intended to suggest a slick that would be sufficiently minimal to cause no adverse effect even to small aquatic invertebrates.

No dose-response assessment is proposed for larger aquatic invertebrates or benthic invertebrates. These aquatic invertebrates would not likely be trapped in (large invertebrates) or interact with (benthic species) any slick of disparlure on the surface of the water that might be associated with the application of Disrupt II flakes for the control or eradication of the gypsy moth.

While the studies by Palmer and Krueger (2006a,b) are more recent and contain much more detailed information than is presented in the earlier study by LeBlanc et al. (1980), the Palmer and Krueger (2006a,b) studies are not used explicitly to derived toxicity values. The rationale for this approach is that the study by LeBlanc et al. (1980) does involve the application of known amount of disparlure to the test water. In the studies by Palmer and Krueger (2006a,b), detailed in Section 4.1.3.3, a known amount of Disrupt II flakes were applied to water and a fixed amount of time was allowed for the disparlure to leach from the flakes into the water. The amount of disparlure that actually leached from the flakes into the water, however, was not measured. In addition, the treated water was then decanted to arrive at the test water. The proportion of any leached disparlure that was decanted, however, cannot be determined. Thus, while both the

LeBlanc et al. (1980) study and the studies by Palmer and Krueger (2006a,b) involved nominal rather than measured concentrations, the uncertainties in the exposure to disparlure are greater in the studies by Palmer and Krueger (2006a,b). While it may be argued that the Palmer and Krueger (2006a,b) studies might better approximate the impact of an application of Disrupt II flakes, the Palmer and Krueger (2006a,b) studies did not involve actual exposures to the flakes. Thus, while the Palmer and Krueger (2006a,b) studies were well-designed and provide useful information, the earlier study by LeBlanc et al. (1980) involves fewer uncertainties in terms of the exposure of the daphnids to disparlure.

4.4. RISK CHARACTERIZATION

4.4.1. Overview

As discussed in Section 4.3.1, there is little data available on terrestrial and aquatic animals to allow for a quantitative characterization of risk in species other than rainbow trout and *Daphnia*. Furthermore, the lack of chronic toxicity data in any species adds significant uncertainty to any risk characterization. Thus, for both terrestrial and aquatic species, the potential for the development of toxicity from long-term exposure to disparlure cannot be assessed. Nonetheless, given the low toxicity of disparlure based on acute toxicity studies, it is unlikely that exposure to disparlure will result in the development of serious adverse effects in terrestrial and aquatic species. Regarding effects on terrestrial invertebrates, it is not likely that disparlure would disrupt mating of other species of moths that are native to North America (Section 4.1.2.3).

Under normal conditions, aquatic species will not be exposed to substantial levels of disparlure. At the limit of the solubility of disparlure in water, there is no indication that toxic effects are likely in any aquatic species. If Disrupt II flakes are accidently applied over water, the amount of disparlure in the water could result in the formation of an insoluble layer of disparlure at the air-water interface. This would occur only in standing bodies of water (ponds or lakes) and not in flowing bodies of water such as streams or rivers. There is no indication that the formation of disparlure film in a standing body of water would impact fish. Based on toxicity studies conducted in the laboratory, small invertebrates that come into contact with the air-water interface might become trapped in this insoluble film. The likelihood of this occurring and the likelihood of this causing any detectable impact in a body of water is difficult to determine and would vary with the quantity of flakes applied to the body of water and the depth of the body of water. Based on variability in the experimental data as well as the range of application rates used in the USDA programs, hazard quotients would vary from about 0.15 to about 0.37, assuming a 1 meter deep body of water, below the level of concern by factors of about 3 to 10.

4.4.2. Terrestrial Species

Based on the results of acute toxicity studies, the toxicity of disparlure to terrestrial mammals is very low (See Sections 3.1 and 4.1). However, the lack of chronic toxicity studies adds uncertainty to the risk characterization for all terrestrial species. Since results of acute toxicity studies in mammals and birds do not suggest that acute adverse effects are likely, it is not anticipated that exposure of these species to disparlure will results in the development of serious adverse effects in longer term exposures. However, since no chronic toxicity data are available, it is not possible to provide a characterization of risk for longer term exposure.

For terrestrial invertebrates, specifically other species of moths, exposure to disparlure has the potential to disrupt mating. However, due to the lack of data, it is not possible to quantify this risk.

4.4.3. Fish

As discussed in Section 4.1.3.1, the hazard identification for fish indicates that no toxic effects are plausible at the limit of the solubility of disparlure in water. In addition, toxicity studies in fish indicate no effects at nominal concentrations of disparlure in water that factors of about 3,500 to over 5,000 above the estimated values for the concentration of disparlure in water (Section 4.3.2). The reciprocals of these ratios could be taken as approximate hazard indices – i.e., 0.0002 to 0.0003 – and these could be useful in comparing the risks posed by disparlure to risks posed by other agents. A somewhat clearer articulation of the risk characterization, however, is that no risks to fish can be identified under any foreseeable circumstances.

4.4.4. Aquatic Invertebrates

As with fish, there is no indication that disparlure will be toxic to aquatic invertebrates at the limit of the solubility of disparlure in water. Also as with fish, the probability of substantial exposure to disparlure is remote except in the case of accidental misapplication of Disrupt flakes directly to water. Thus, under normal conditions, no risks to aquatic invertebrates can be identified.

The accidental application of Disrupt II flakes to water is plausible and, under some conditions, this could pose risks to aquatic invertebrates that interface with the water surface. This has been clearly demonstrated in laboratory studies with daphnids (Sections 4.1.3.3 and 4.3.3). As discussed in Section 4.2.2, accidental applications to surface water have been reported. If applied to rapidly moving water such as stream, there is no indication that adverse effects would be likely. If applied to standing water, however, concentrations calculated in Section 4.2.2 modestly exceed the estimate of the solubility of disparlure in water at the upper range by a factor of about 3 – i.e., a nominal concentration of 0.0074 mg/L. If the amount of disparlure deposited on the surface of standing water exceeds the solubility of disparlure in water, a surface film could form and some small aquatic invertebrates could be trapped at the air-water interface.

It seems unlikely, however, that this would lead to substantial or even detectable effects based on the clear NOEC value of 0.01 mg/L from the study by LeBlanc et al. (1980). As detailed in Worksheet A01 of the EXCEL workbook that accompanies this risk assessment, the highest calculated hazard quotient is 0.37 and is associated with the application of disparlure at a rate of 15 g a.i./acre to a body of water that is 1 meter deep. The hazard quotient will vary directly with the depth of the water. Since the calculations are based on a 1 meter deep body of water, the hazard quotients would be a factor of 10 lower in a 10 meter deep body of water and a factor of 10 higher in a 0.1 meter deep body of water.

Whether or not the accidental application of disparlure flakes to any body of water would lead to a detectable effect is unclear. As noted in Section 4.1.3.3, no incidents or field observations have been made that would suggest any adverse effects on aquatic invertebrates (Leonard 2006c). However, the only report of an accidental application to water involves application to a river. As noted above, applications to flowing bodies of water would not be expected to result in any adverse effects. Nonetheless, based on the application rates used in vast majority of program

activities (Section 2.3), hazard quotients for small aquatic invertebrates would exceed unity only in very shallow bodies of water.

The duration of any exposure to disparlure accidentally applied to water cannot be well characterized. As indicated in Appendix 4, the halftime of disparlure in water is estimated at 360 hours (15 days) based on algorithms used in Epi Suite EPI Suite (Meylan and Howard 2000; U.S. EPA/OPPT 2000). These algorithms, however, relay on estimates of water solubility and Henrys Law constant. As also indicated in Appendix 4, experimental values for the water solubility and Henrys Law constant of disparlure are not available and are themselves estimated by EPI Suite based on molecular structure. This adds uncertainty to the estimated halftime in water. The halftime in water will also be influenced by site-specific conditions as well as the formulation of disparlure in the Disrupt II flakes, increasing the uncertainty in estimates from EPI Suite.

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Table 2-1. Identification and Physical/Chemical Properties of Disparlure.

Property	Value [a]	Reference
CAS Number	029804-22-6	EPI Suite (2006)
Smiles Notation	O(C1CCCCCCCCCC)C1CCCCC(C)C	EPI Suite (2006)
U.S. EPA Registration Number	8730-55	Hercon Environmental, 2004
MW	282.51	EPI Suite (2006)
Henry's Law Constant (atm m^3/mole)	0.015 to 0.061	EPI Suite (2006)
Vapor pressure (mm Hg)	0.00021 to 0.00034	EPI Suite (2006)
Water solubility (mg/L)	0.0019 to 0.0028	EPI Suite (2006)
log $K_{o/w}$	8.08	EPI Suite (2006)
$K_{o/c}$ (acid, ml/g)	3.44×10^4	EPI Suite (2006)
Halftimes in water (days)	0.074 (river) 6.9 (lake)	EPI Suite (2006)
Halftimes in other media (days)	0.5 (air) 15 (water) 30 (soil) 135 (sediment)	EPI Suite (2006)

[a] For many estimates, EPI Suite provides more than one estimate based on different estimation methods. When more than one estimate is provided, the range of values are given. Estimates from EPI Suite are often present out to several decimal places. Except for molecular weight, all values in this table are rounded to two significant places.

Table 2-2: Use of Disparlure by the USDA to control the North American Gypsy Moth from 1995 to 2005 by Type of Use (USDA/FS 2005)

Year	Acres Treated for Eradication	Acres Treated to Slow the Spread
1995	0	2,448
1996	5,352	16,621
1997	0	10,808
1998	7,120	21,418
1999	38,980	19,360
2000	7,988	93,625
2001	0	212,925
2002	650	542,600
2003	0	647,394
2004	250	588,256
2005	0	287,890

Table 3-1: Summary of acute toxicity data of Disparlure in mammals (all values are expressed in terms of a.i.)

Species	Exposure/Dose	Effect	Reference
rat	single oral doses ranging from 10,250 – 34,600 mg/kg	LD_{50} > 34,600 mg/kg NOAEL (mortality) = 34,600 mg/kg	Kretchmar 1972
rat	single oral dose of 5000 mg/kg	LD_{50} > 5,000 mg/kg NOAEL (mortality) = 5,000 mg/kg	Coleman 2000
rat	inhalation exposure, 5.0 mg/L in air for 1 hour	LD_{50} > 5 mg/L air NOAEL (mortality) = 5.0 mg/L air	Grapenthien 1972
rabbit	dermal toxicity testing a single dose of 2,025 mg/kg	LD_{50} > 5,000 mg /kg NOAEL (mortality) = 5,000 mg/kg	Kretchmar 1972
rabbit	primary skin irritation testing a single dose of 0.5 g	Not a skin irritant (only very mild skin irritation)	Kretchmar 1972
rabbit	primary eye irritation testing a single dose of 0.1 g/eye	not an eye irritant	Kretchmar 1972

Table 4-1: Summary of acute toxicity data of Disparlure in avian and aquatic species (all values are expressed in terms of a.i.)

Species	Exposure/Dose	Effect	Reference
bobwhite quail	single oral doses ranging from 398 to 2510 mg/kg (by gavage)	LD_{50} > 2510 mg/kg	Fink et al. 1980
bobwhite quail chicks	313 to 5000 in diet for 5 days	LD_{50} > 5000 ppm	Hudson 1975
mallard ducklings	313 to 5000 in diet for 5 days	LD_{50} > 5000 ppm	Hudson 1975
bluegill sunfish [a]	300 mg/L for 96 hours	LC_{50} > 300 mg/L	Knapp and Terrell 1980
bluegill sunfish [a]	0.1 to 100 pm for 96 hours	LC_{50} > 100 mg/L	Rausina 1949
rainbow trout [a]	0.1 to 100 pm for 96 hours	LC_{50} > 100 mg/L NOEC = 10 mg/L	Rausina 1949
Daphnia [a, b]	0.01 to 0.22 mg/L for 96 hours	LC_{50} > 0.098 mg/L NOEC = 0.017 mg/L	LeBlanc et al. 1980
Eastern oysters [a]	1.25 to 20 mg/L for 96 hours	NOEC (new shell growth) = 20 mg/L	Ward 1981

[a] All values expressed a nominal rather than measured concentrations. See Section 4.1.3.3 for a discussion of the significance of nominal versus measured concentrations.
[b] Additional studies in *Daphnia* using water accommodated fractions of Disrupt II formulations have been conducted by Palmer and Krueger (2006a,b). The nominal concentrations reported in this study are not comparable to those reported above. See Section 4.3.3 for a more detailed discussion.

Table 4-2. Summary of QSAR Toxicity Estimates for Disparlure to Aquatic Species and Algorithms for Estimating the Toxicity of Mono-Epoxide Compounds to Aquatic Species Developed by Clements et Al. (1996).

Type of Estimate (Species)	Slope	Inter-cept	r^2 (n) [a]	Limiting Log_{10} Kow [b]	Estimated LC^{50} mg/L
Freshwater Acute					
Fish, 96h-LC_{50} (Fathead minnow)	0.382	-0.29	0.92 (4)	5	0.119
Fish, 16 day (Guppy)	0.246	-0.5	0.87 (9)	5	0.144
Invertebrate, 48h-LC_{50} (*Daphnia*)	-0.567	0.036	1.0 (2)	5	0.008

[a] Squared correlation coefficient and number of data points in analysis.
[b] These values are reported in the output of EPI Suite Version 3.12. Slightly different values are reported in Clements et al. (1996).

LIST OF APPENDICES

Appendix 1: Toxicity of disparlure to experimental mammals **(Unless otherwise specified, all concentrations are expressed as a.i.)**

Animal	Dose/Exposure	Response	Reference
ORAL - ACUTE			
rats, Sprague-Dawley 5 males, 5 females	single dose of 5000 mg a.i./kg (racemic preparation) by gavage. Animals observed for 15 days. No control group.	No mortalities. No microscopic abnormalities observed. Clinical signs of toxicity were piloerection, hunched posture and ungroomed appearance appearing on Day 1 of treatment. All signs were resolved by Day 4 of the observation period. **LD_{50} > 5000 mg a.i./kg**	Coleman 2000 MRID 45529801
rats, Sprague-Dawley albino	single dose of test material administered at several dose levels (10250, 15380, 23070, 34600 mg/kg) by gavage. Rats observed for 14 days following administration. No control group.	No mortality at any dose level. No gross pathological lesions at any dose level. At all dose levels, hypoactivity, ruffed fur, and diuresis were observed, **LD_{50} > 34600 mg a.i./kg**	Beroza et al. 1975 Hercon 1978 Kretchmar 1972 MRID 00128026
DERMAL			
rabbits, New Zealand	2025 mg/kg test material applied to shaved skin and occluded for 24 hours. Animals observed for 14 days for systemic toxcity	No mortalities. No gross pathologic lesions on necropsy. Local skin irritation after 24 hours (erythema and edema). 7 days after dosing, escharosis, desquamation, hemorrhaging and fissures. After 14 days, desquamation, fissures and pustules **LD_{50} > 2025 mg a.i./kg**	Beroza et al. 1975 Hercon 1978 Kretchman 1972 MRID 00128026

Appendix 1: Toxicity of disparlure to experimental mammals **(Unless otherwise specified, all concentrations are expressed as a.i.)**

Animal	Dose/Exposure	Response	Reference
rabbits, New Zealand	0.5 mL of undiluted test material (0.5 g) applied to shaved skin and occluded for 24 hours. Animals were observed for 72 hours	Primary dermal irritation study. Mild skin irritation (erythema and edema) was noted at 24 and 72 hours after application of test material	Beroza et al. 1975 Hercon 1978 Kretchman 1972 MRID 00128026
EYES			
6 young rabbits, New Zealand	0.1 mL undiluted sample (0.1 g) applied to conjunctival sac. Eye was not washed. Severity of ocular lesions was monitored at intervals of 24, 48, and 72 hours. Rabbits observed for 7 days.	3/6 rabbits had conjunctival redness at 24 hours. No effects observed in any rabbits at later times of the observation period	Beroza et al.1975 Hercon 1978 Kretchman 1972 MRID 00128026
INHALATION			
Albino rats (10)	Inhalation chamber study. Disparlure concentration 5.0 mg/L in air for 1 hour	No deaths were observed in this study. No assessment of sublethal toxicity was made **LC_{50}>5.0 mg a.i./L air**	Grapenthien 1972 MRID 00059821

Appendix 2: Toxicity of disparlure to birds **(unless otherwise specified, all doses and concentrations are expressed in terms of a.i.)**

Animal	Dose/Exposure	Response	Reference
bobwhite quail (5 months old)	Single oral doses of 398, 631, 1590, and 2510 mg/kg bw. Birds observed for 7 days after dosing	No mortalities at any dose level. No signs of toxicity associated with test material. At the highest dose, lethargy was observed in 3/10 birds on days 1-2 after dosing. Unclear if lethargy was related to test material. LD_{50} > 2510 mg/kg	Fink et al. 1980 MRID 00083102
bobwhite quail (12 day old chicks) mallard ducks (15 day old ducklings)	Dietary exposure to 313, 625, 1250,2500, 5000 ppm for 5 days. Birds observed for 3 days after end of dosing period	No mortalities in at any dose level for either species No signs of toxicity reported LC_{50} > 5000 ppm in diet for both quail and ducks	Hudson 1975 MRID 00105981 same data reported in MRID 00047225

Appendix 3: Toxicity of disparlure to aquatic species **(unless otherwise specified, all concentrations are expressed in terms of a.i.)**

Animal	Dose/Exposure	Response	Reference
FISH			
Rainbow trout Bluegills, 10 fish per concentration	0.1, 1.0, 10.0, 100.0 ppm (mg a.i./L) for 96 hours. Survival assessed at 1-6, 24, 48, 72, and 96 hours. Note: Very poor quality fiche. Dissolved oxygen was measured in the test water only when mortality was observed. The measurement itself cannot be read from the fiche.	No effect on dissolved oxygen. In bluegills, no affect on survivors at any concentration up to 96 hr exposure. **LC_{50}>100 ppm** In Rainbow trout, for all concentrations, no affect on survivors up to 48 hours. At the 100 ppm concentration, the number of survivors decreased to 8/10 after 72 hours of exposure. **LC_{50}>100 ppm**	Rausina 1949 MRID 00059735
Bluegill sunfish, 30 fish in each group	Nominal concentration of 0 ppm (untreated control) and 300 ppm for 96 hours. No aeration during the study. No description of how the test water was prepared. No discussion of any observations concerning a surface film on the water.	No mortalities observed and no signs of altered behavior. Dissolved oxygen in test water and control water were comparable: Day 1 11.0 ppm (control) 10.4 ppm (test water) Day 4: 3.4 ppm (control) 3.4 ppm (test water) pH constant in test and control water (pH 6.4) of the duration of testing. **LC_{50}>300 ppm**	Knapp and Terrell 1980 MRID 00127869
AQUATIC INVERTEBRATES			
	Technical Grade Disparlure		
Eastern oysters (*Crassostrea virginica*)	96 hour exposure to concentrations ranging from 1.25 to 20 ppm 92% disparlure Acetone concentrations ranged up to 10%	No affect on new shell growth at any concentration **NOEC > 20 ppm**	Ward 1981 MRID 00074291

Appendix 3: Toxicity of disparlure to aquatic species **(unless otherwise specified, all concentrations are expressed in terms of a.i.)**

Animal	Dose/Exposure	Response	Reference
Daphnia magna, <24 hours old, 15 daphnids/concentration.	Disparlure TGAI 48-hour exposure to 0.010 - 0.22 mg/L [0.22, 0.13, 0.079, 0.048, 0.028, 0.017, and 0.01 mg/L nominal]. The concentration of disparlure in the test media was not measured. Static conditions in 500 mL test solution. Mortalities were recorded after 24 and 48 hours.	No mortalities or sublethal effects occurred at concentrations of 0.010 and 0.017 mg/L. Mortality rates at higher doses: 0.22 mg/L 15/15 0.13 mg/L 12/15 0.079 mg/L 2/15 0.048 mg/L 1/15 0.028 mg/L 1/15	LeBlanc et al. 1980 MRID 00127868

Additional notes on LeBlanc et al. 1980: Some organisms (number not specified) were trapped in the air-water interface at concentrations of 0.028 mg/L and higher. **EC_{50} = 0.098 (0.019-0.12) mg/L**.
NOEC = 0.017 mg/L

Appendix 3: Toxicity of disparlure to aquatic species **(unless otherwise specified, all concentrations are expressed in terms of a.i.)**

Animal	Dose/Exposure	Response	Reference
Standard Disrupt II Flakes (SF) – i.e., flakes previously used by FS			
Daphnia magna, <24 hours old, 20 daphnids	Disrupt II, SF (**blank standard flakes, no disparlure**) 300 mg/L for 48 hours. 200 ml test solution volume	No mortality or immobility.	Palmer and Krueger 2006a
Daphnia magna, <24 hours old, 20 daphnids per concentration in 2 replicates with 10 organisms/replicate.	Disrupt II, SF 2003 (**standard flakes from 2003**, 17.9% disparlure) 0, 1, 3, 10, 30, 100, and 300 mg preparation/L. Preparations based on flakes mixed in water for 24 hours prior to the preparation of filtered test solutions (i.e., no flakes in the test solutions). Disparlure concentrations not monitored. The nominal formulation concentrations correspond to nominal concentrations of disparlure of: 0, 0.18, 0.54, 1.8, 5.4, 18, and 54 mg a.i./L.	No effects at any concentrations after 4 or 24 hours. At 48 hours, no effects at 1, 3, 30, and 100 mg formulation/L. At 10 mg/L, 1/20 organisms appeared lethargic. At 300 mg/L, 3/10 organisms in one replicate were trapped at the water surface but appeared normal after gentle submersion. 1/10 organisms did not appear normal (NOS) after being trapped on the water surface. EC_{50}: > 300 mg/L (53.7 mg a.i./L based on nominal concentrations)	Palmer and Krueger 2006a
Daphnia magna, <24 hours old, 20 daphnids per concentration in 2 replicates with 10 organisms/replicate.	Disrupt II, SF 2005 (**standard flakes from 2005**, 17.9% disparlure) 0, 1, 3, 10, 30, 100, and 300 mg preparation/L. Preparations based on flakes mixed in water for 24 hours prior to the preparation of filtered test solutions (i.e., no flakes in the test solutions). Disparlure concentrations not monitored. The nominal formulation concentrations correspond to nominal concentrations of disparlure of: 0, 0.18, 0.54, 1.8, 5.4, 18, and 54 mg a.i./L.	No effects at any concentrations after 4 hours. At 24 hours, 20 of 20 daphnids were either dead (n=3) or immobile (n=17) in the 300 mg/L group. No effects at lower concentrations. At 48-hours, no effects in the 1, 3, or 10 mg/L groups. At 30 mg/L, 9/20 organisms appeared to be lethargic. At 100 mg/L, 16/20 organisms were immobile. At 300 mg/L, 14/20 organisms were dead and the remaining 4 were immobile.	Palmer and Krueger 2006a

Additional Notes on Palmer and Krueger 2006a, (**standard flakes from 2005**): At 48 hours, no effects at 1, 3, 30, and 100 mg formulation/L. At 10 mg/L, 1/20 organisms appeared lethargic. At 300 mg/L, 3/10 organisms in one replicate were trapped at the water surface but appeared normal after gentle submersion. 1/10 organisms did not appear normal (NOS) after being trapped on the water surface.

24 hr LC_{50}: 173 (100-300 mg/L)

48 hr LC_{50}: 69 (30-100 mg/L)

Appendix 3: Toxicity of disparlure to aquatic species **(unless otherwise specified, all concentrations are expressed in terms of a.i.)**

Animal	Dose/Exposure	Response	Reference
Modified Disrupt II Flakes – i.e., flakes currently used by FS			
Daphnia magna, <24 hours old, 20 daphnids	Disrupt II, MF (blank modified flakes, no disparlure) 300 mg/L for 48 hours. 200 ml test solution volume.	No mortality or immobility.	Palmer and Krueger 2006b
Daphnia magna, <24 hours old, 20 daphnids per concentration in 2 replicates with 10 organisms/replicate.	Disrupt II, MF 2003 (**modified flakes from 2003**, 17.9% disparlure) 0, 1, 3, 10, 30, 100, and 300 mg preparation/L. Preparations based on flakes mixed in water for 24 hours prior to the preparation of filtered test solutions (i.e., no flakes in the test solutions). Disparlure concentrations not monitored. The nominal formulation concentrations correspond to nominal disparlure concentrations of disparlure of: 0, 0.18, 0.54, 1.8, 5.4, 18, and 54 mg a.i./L.	At 4 hours, 1/20 daphnids in the 1 mg/L group trapped on the water surface but normal after gentle submersion. At 24 hours, no effects at any concentrations. At 48 hours, no effects at 3, 10, 30, and 100 mg formulation/L. At 1 mg/L and 300 mg/L, 2/20 daphnids in each group were trapped at the water surface but normal after gentle submersion. EC_{50}: > 300 mg/L	Palmer and Krueger 2006b
Daphnia magna, <24 hours old, 20 daphnids per concentration in 2 replicates with 10 organisms/replicate.	Disrupt II, MF 2005 (**modified flakes from 2005**, 17.9% disparlure) 0, 1, 3, 10, 30, 100, and 300 mg preparation/L. Preparations based on flakes mixed in water for 24 hours prior to the preparation of filtered test solutions (i.e., no flakes in the test solutions). Disparlure concentrations not monitored. The nominal formulation concentrations correspond to nominal concentrations of disparlure of: 0, 0.18, 0.54, 1.8, 5.4, 18, and 54 mg a.i./L.	At 4 hours, 17/20 daphnids in the 300 mg/L group trapped on the water surface but normal after gentle submersion. No effects at lower concentrations. At 24 hours: No effects in the 1, 3, 10, and 30 mg/L groups. At 100 mg/L, 14/20 dead and 6/20 trapped on the water surface. At 300 mg/L, 14/20 trapped on the water surface and lethargic after gentle submersion.	Palmer and Krueger 2006a

Additional Notes, Palmer and Krueger 2006a. **Modified flakes, 2005**: At 48-hours, no effects in the 1, 3, or 10 mg/L groups. At 30 mg/L, 1/20 organisms appeared to be lethargic and 1/20 trapped on the water surface. At 100 mg/L, 20/20 organisms were dead. At 300 mg/L, 13/20 organisms were dead, 1/20 was lethargic, 2 were trapped on the water surface.

24 hr LC_{50}: > 30 mg/L

48 hr LC_{50}: 48 (30-100 mg/L)

Appendix 4: EPI Suite Output for Disparlure

Run conducted on June 28, 2006 by Patrick Durkin using EPI-Suite Version 3.12.

```
SMILES : O(C1CCCCCCCCCC)C1CCCCC(C)C
CHEM   : Oxirane, 2-decyl-3-(5-methylhexyl)-, cis-
CAS NUM: 029804-22-6
MOL FOR: C19 H38 O1
MOL WT : 282.51
----------------------------- EPI SUMMARY (v3.12) -------------------------
 Physical Property Inputs:
    Water Solubility (mg/L):   ------
    Vapor Pressure (mm Hg) :   ------
    Henry LC (atm-m3/mole) :   ------
    Log Kow (octanol-water):   ------
    Boiling Point (deg C)  :   ------
    Melting Point (deg C)  :   ------

KOWWIN Program (v1.67) Results:
==============================

                  Log Kow(version 1.67 estimate): 8.08

SMILES : O(C1CCCCCCCCCC)C1CCCCC(C)C
CHEM   : Oxirane, 2-decyl-3-(5-methylhexyl)-, cis-
MOL FOR: C19 H38 O1
MOL WT : 282.51
-------+-----+-----------------------------------------+---------+--------
 TYPE  | NUM |        LOGKOW FRAGMENT DESCRIPTION      |  COEFF  |  VALUE
-------+-----+-----------------------------------------+---------+--------
 Frag  |  3  |  -CH3    [aliphatic carbon]             | 0.5473  |  1.6419
 Frag  | 13  |  -CH2-   [aliphatic carbon]             | 0.4911  |  6.3843
 Frag  |  3  |  -CH     [aliphatic carbon]             | 0.3614  |  1.0842
 Frag  |  1  |  -O-     [oxygen, aliphatic attach]     |-1.2566  | -1.2566
 Const |     |  Equation Constant                      |         |  0.2290
-------+-----+-----------------------------------------+---------+--------
                                                      Log Kow   =   8.0828



MPBPWIN (v1.41) Program Results:
================================
Experimental Database Structure Match:  no data

SMILES : O(C1CCCCCCCCCC)C1CCCCC(C)C
CHEM   : Oxirane, 2-decyl-3-(5-methylhexyl)-, cis-
MOL FOR: C19 H38 O1
MOL WT : 282.51
----------------------- SUMMARY MPBPWIN v1.41 --------------------


Boiling Point:  328.27 deg C (Adapted Stein and Brown Method)

Melting Point:   56.00 deg C (Adapted Joback Method)
Melting Point:   78.02 deg C (Gold and Ogle Method)
Mean Melt Pt :   67.01 deg C (Joback; Gold,Ogle Methods)
  Selected MP:   67.01 deg C (Mean Value)

Vapor Pressure Estimations (25 deg C):
  (Using BP: 328.27 deg C (estimated))
```

```
  (Using MP: 67.01 deg C (estimated))
    VP:  0.00021 mm Hg (Antoine Method)
    VP:  0.000342 mm Hg (Modified Grain Method)
    VP:  0.000321 mm Hg (Mackay Method)
  Selected VP:  0.000342 mm Hg (Modified Grain Method)


-------+-----+--------------------+----------+---------
 TYPE  | NUM |  BOIL DESCRIPTION  |  COEFF   |  VALUE
-------+-----+--------------------+----------+---------
 Group |  3  |  -CH3              |   21.98  |   65.94
 Group | 13  |  -CH2-             |   24.22  |  314.86
 Group |  1  |  >CH-              |   11.86  |   11.86
 Group |  2  |  >CH-  (ring)      |   21.66  |   43.32
 Group |  1  |  -O-   (ring)      |   32.98  |   32.98
   *   |     |  Equation Constant |          |  198.18
============+====================+==========+=========
RESULT-uncorr|  BOILING POINT in deg Kelvin  |  667.14
RESULT- corr |  BOILING POINT in deg Kelvin  |  601.43
             |  BOILING POINT in deg C       |  328.27
-------------------------------------------------------

-------+-----+--------------------+----------+---------
 TYPE  | NUM |  MELT DESCRIPTION  |  COEFF   |  VALUE
-------+-----+--------------------+----------+---------
 Group |  3  |  -CH3              |   -5.10  |  -15.30
 Group | 13  |  -CH2-             |   11.27  |  146.51
 Group |  1  |  >CH-              |   12.64  |   12.64
 Group |  2  |  >CH-  (ring)      |   19.88  |   39.76
 Group |  1  |  -O-   (ring)      |   23.05  |   23.05
   *   |     |  Equation Constant |          |  122.50
============+====================+==========+=========
   RESULT    |  MELTING POINT in deg Kelvin  |  329.16
             |  MELTING POINT in deg C       |   56.00
-------------------------------------------------------



Water Sol from Kow (WSKOW v1.41) Results:
=========================================

          Water Sol: 0.001939 mg/L

SMILES : O(C1CCCCCCCCCC)C1CCCCC(C)C
CHEM   : Oxirane, 2-decyl-3-(5-methylhexyl)-, cis-
MOL FOR: C19 H38 O1
MOL WT : 282.51
---------------------------------- WSKOW v1.41 Results
------------------------
Log Kow  (estimated)  :  8.08
Log Kow (experimental):  not available from database
Log Kow used by Water solubility estimates:  8.08

Equation Used to Make Water Sol estimate:
   Log S (mol/L) = 0.796 - 0.854 log Kow - 0.00728 MW + Correction
       (used when Melting Point NOT available)
```

```
      Correction(s):          Value
      --------------------    -----
       No Applicable Correction Factors
   Log Water Solubility  (in moles/L) :  -8.163
   Water Solubility at 25 deg C (mg/L):  0.001939


WATERNT Program (v1.01) Results:
================================

                  Water Sol (v1.01 est): 0.0027812 mg/L

SMILES : O(C1CCCCCCCCCC)C1CCCCC(C)C
CHEM   : Oxirane, 2-decyl-3-(5-methylhexyl)-, cis-
MOL FOR: C19 H38 O1
MOL WT : 282.51
-------+-----+-----------------------------------------+----------+--------
-
 TYPE  | NUM |    WATER SOLUBILITY FRAGMENT DESCRIPTION   |  COEFF   |  VALUE
-------+-----+-----------------------------------------+----------+--------
-
 Frag  |  3  |  -CH3    [aliphatic carbon]               |-0.3213   | -0.9638
 Frag  | 13  |  -CH2-   [aliphatic carbon]               |-0.5370   | -6.9812
 Frag  |  3  |  -CH     [aliphatic carbon]               |-0.5285   | -1.5856
 Frag  |  1  |  -O-     [oxygen, aliphatic attach]       | 1.2746   |  1.2746
 Const |     |  Equation Constant                        |          |  0.2492
-------+-----+-----------------------------------------+----------+--------
-
                            Log Water Sol (moles/L) at 25 dec C  =   -8.0068
                            Water Solubility (mg/L) at 25 dec C  =0.0027812
```

Appendix 4: EPI Suite Run for Disparlure (cont)

```
ECOSAR Program (v0.99h) Results:
================================
SMILES : O(C1CCCCCCCCCC)C1CCCCC(C)C
CHEM   : Oxirane, 2-decyl-3-(5-methylhexyl)-, cis-
CAS Num:
ChemID1:
ChemID2:
ChemID3:
MOL FOR: C19 H38 O1
MOL WT : 282.51
Log Kow: 8.08  (KowWin estimate)
Melt Pt:
Wat Sol: 0.0007897 mg/L  (calculated)
ECOSAR v0.99h Class(es) Found
-----------------------------
Epoxides
                                                                    Predicted
ECOSAR Class                    Organism            Duration  End Pt   mg/L (ppm)
============================  ==================  ========  ======   ==========
Neutral Organic SAR         : Fish                14-day    LC50      0.00192 *
(Baseline Toxicity)

Epoxides                    : Fish                96-hr     LC50        0.119 *
Epoxides                    : Fish                14-day    LC50        0.144 *
Epoxides                    : Daphnid             48-hr     LC50        0.008 *
 Note:  * = asterisk designates: Chemical may not be soluble
        enough to measure this predicted effect.
         Fish and daphnid acute toxicity log Kow cutoff: 5.0
         Green algal EC50 toxicity log Kow cutoff: 6.4
         Chronic toxicity log Kow cutoff: 8.0
         MW cutoff: 1000


HENRY (v3.10) Program Results:
==============================

       Bond Est :  1.49E-002 atm-m3/mole
       Group Est:  6.14E-002 atm-m3/mole

SMILES : O(C1CCCCCCCCCC)C1CCCCC(C)C
CHEM   : Oxirane, 2-decyl-3-(5-methylhexyl)-, cis-
MOL FOR: C19 H38 O1
MOL WT : 282.51
--------------------------- HENRYWIN v3.10 Results -------------------------
----------+-----------------------------------------+---------+----------
   CLASS  |     BOND CONTRIBUTION DESCRIPTION       | COMMENT |  VALUE
----------+-----------------------------------------+---------+----------
 HYDROGEN |  38  Hydrogen to Carbon (aliphatic) Bonds |         | -4.5477
 FRAGMENT |  18  C-C                                |         |  2.0935
 FRAGMENT |   2  C-O                                |         |  2.1709
 FACTOR   |   *  Epoxide                            |         |   .5000
----------+-----------------------------------------+---------+----------
 RESULT   |    BOND ESTIMATION METHOD for LWAPC VALUE |  TOTAL  |  0.217
----------+-----------------------------------------+---------+----------
HENRYs LAW CONSTANT at 25 deg C = 1.49E-002 atm-m3/mole
                               = 6.07E-001 unitless
```

	GROUP CONTRIBUTION DESCRIPTION	COMMENT	VALUE
	3 CH3 (X)		-1.86
	13 CH2 (C)(C)		-1.95
	1 CH (C)(C)(C)		0.24
	2 CH (C)(C)(O)		0.24
	1 O (C)(C)		2.93
RESULT	GROUP ESTIMATION METHOD for LOG GAMMA VALUE	TOTAL	-0.40

```
HENRYs LAW CONSTANT at 25 deg C = 6.14E-002 atm-m3/mole
                                = 2.51E+000 unitless


Henrys LC [VP/WSol estimate using EPI values]:
    HLC:  6.556E-002 atm-m3/mole
    VP:   0.000342 mm Hg
    WS:   0.00194 mg/L


BIOWIN (v4.02) Program Results:
==============================
SMILES : O(C1CCCCCCCCCC)C1CCCCC(C)C
CHEM   : Oxirane, 2-decyl-3-(5-methylhexyl)-, cis-
MOL FOR: C19 H38 O1
MOL WT : 282.51
-------------------------- BIOWIN v4.02 Results --------------------------

   Biowin1 (Linear Model Prediction)    :  Does Not Biodegrade Fast
   Biowin2 (Non-Linear Model Prediction):  Does Not Biodegrade Fast
   Biowin3 (Ultimate Biodegradation Timeframe):  Weeks
   Biowin4 (Primary  Biodegradation Timeframe):  Days-Weeks
   Biowin5 (MITI Linear Model Prediction)    :  Does Not Biodegrade Fast
   Biowin6 (MITI Non-Linear Model Prediction):  Does Not Biodegrade Fast
   Ready Biodegradability Prediction:  NO
```

TYPE	NUM	Biowin1 FRAGMENT DESCRIPTION	COEFF	VALUE
Frag	1	Linear C4 terminal chain [CCC-CH3]	0.1084	0.1084
Frag	1	Aliphatic ether [C-O-C]	-0.3474	-0.3474
MolWt	*	Molecular Weight Parameter		-0.1345
Const	*	Equation Constant		0.7475
RESULT		Biowin1 (Linear Biodeg Probability)		0.3741

TYPE	NUM	Biowin2 FRAGMENT DESCRIPTION	COEFF	VALUE
Frag	1	Linear C4 terminal chain [CCC-CH3]	1.8437	1.8437
Frag	1	Aliphatic ether [C-O-C]	-3.4294	-3.4294
MolWt	*	Molecular Weight Parameter		-4.0117
RESULT		Biowin2 (Non-Linear Biodeg Probability)		0.0699

```
 A Probability Greater Than or Equal to 0.5 indicates --> Biodegrades Fast
 A Probability Less Than 0.5 indicates --> Does NOT Biodegrade Fast
```

TYPE	NUM	Biowin3 FRAGMENT DESCRIPTION	COEFF	VALUE
Frag	1	Linear C4 terminal chain [CCC-CH3]	0.2983	0.2983
Frag	1	Aliphatic ether [C-O-C]	-0.0087	-0.0087
MolWt	*	Molecular Weight Parameter		-0.6243
Const	*	Equation Constant		3.1992
RESULT		Biowin3 (Survey Model - Ultimate Biodeg)		2.8645

TYPE	NUM	Biowin4 FRAGMENT DESCRIPTION	COEFF	VALUE
Frag	1	Linear C4 terminal chain [CCC-CH3]	0.2691	0.2691
Frag	1	Aliphatic ether [C-O-C]	-0.0097	-0.0097
MolWt	*	Molecular Weight Parameter		-0.4076
Const	*	Equation Constant		3.8477
RESULT		Biowin4 (Survey Model - Primary Biodeg)		3.6995

```
 Result Classification:   5.00 -> hours     4.00 -> days    3.00 -> weeks
  (Primary & Ultimate)    2.00 -> months    1.00 -> longer
```

TYPE	NUM	Biowin5 FRAGMENT DESCRIPTION	COEFF	VALUE
Frag	1	Aliphatic ether [C-O-C]	0.0015	0.0015
Frag	3	Methyl [-CH3]	0.0004	0.0012
Frag	13	-CH2- [linear]	0.0494	0.6424
Frag	1	-CH- [linear]	-0.0507	-0.0507
Frag	2	-CH - [cyclic]	0.0124	0.0249
MolWt	*	Molecular Weight Parameter		-0.8405
Const	*	Equation Constant		0.7121
RESULT		Biowin5 (MITI Linear Biodeg Probability)		0.4910

TYPE	NUM	Biowin6 FRAGMENT DESCRIPTION	COEFF	VALUE
Frag	1	Aliphatic ether [C-O-C]	-0.1071	-0.1071
Frag	3	Methyl [-CH3]	0.0194	0.0583
Frag	13	-CH2- [linear]	0.4295	5.5834
Frag	1	-CH- [linear]	-0.0998	-0.0998
Frag	2	-CH - [cyclic]	-0.1295	-0.2589
MolWt	*	Molecular Weight Parameter		-8.1558
RESULT		Biowin6 (MITI Non-Linear Biodeg Probability)		0.3883

```
 A Probability Greater Than or Equal to 0.5 indicates --> Biodegrades Fast
 A Probability Less Than 0.5 indicates --> Does NOT Biodegrade Fast
```

```
AOP Program (v1.91) Results:
============================
SMILES : O(C1CCCCCCCCCC)C1CCCCC(C)C
CHEM   : Oxirane, 2-decyl-3-(5-methylhexyl)-, cis-
MOL FOR: C19 H38 O1
MOL WT : 282.51
------------------- SUMMARY (AOP v1.91): HYDROXYL RADICALS -------------------
Hydrogen Abstraction       =  21.7096 E-12 cm3/molecule-sec
Reaction with N, S and -OH =   0.0000 E-12 cm3/molecule-sec
Addition to Triple Bonds   =   0.0000 E-12 cm3/molecule-sec
Addition to Olefinic Bonds =   0.0000 E-12 cm3/molecule-sec
Addition to Aromatic Rings =   0.0000 E-12 cm3/molecule-sec
Addition to Fused Rings    =   0.0000 E-12 cm3/molecule-sec

   OVERALL OH Rate Constant =  21.7096 E-12 cm3/molecule-sec
   HALF-LIFE =     0.493 Days (12-hr day; 1.5E6 OH/cm3)
   HALF-LIFE =     5.912 Hrs
------------------- SUMMARY (AOP v1.91): OZONE REACTION ----------------------

               ******  NO OZONE REACTION ESTIMATION ******
               (ONLY Olefins and Acetylenes are Estimated)

Experimental Database:  NO Structure Matches



PCKOC Program (v1.66) Results:
==============================

                  Koc (estimated): 3.44e+004


SMILES : O(C1CCCCCCCCCC)C1CCCCC(C)C
CHEM   : Oxirane, 2-decyl-3-(5-methylhexyl)-, cis-
MOL FOR: C19 H38 O1
MOL WT : 282.51
--------------------------- PCKOCWIN v1.66 Results ---------------------------

         First Order Molecular Connectivity Index  ..... :  9.736
         Non-Corrected Log Koc  ........................... :  5.8004
         Fragment Correction(s):
                  1   Ether, aliphatic  (-C-O-C-)  .....  : -1.2643
         Corrected Log Koc  ............................... :  4.5361

                        Estimated Koc:  3.437e+004



HYDROWIN Program (v1.67) Results:
=================================
SMILES : O(C1CCCCCCCCCC)C1CCCCC(C)C
CHEM   : Oxirane, 2-decyl-3-(5-methylhexyl)-, cis-
```

```
MOL FOR: C19 H38 O1
MOL WT : 282.51
--------------------------- HYDROWIN v1.67 Results ---------------------------

NOTE: Fragment(s) on this compound are NOT available from the fragment
    library. Substitute(s) have been used!!!  Substitute R1, R2, R3,
    or R4 fragments are marked with double astericks "**".

                  O
               R1  / \  R3
EPOXIDE:         >C - C<
               R2       R4
         ** R1: n-Octyl-                ** R3: n-Butyl-
            R2: -H                         R4: -H
 Ka hydrolysis at (epoxy O) atom #  1:  4.271E-001  L/mol-sec

 Total Ka (acid-catalyzed) at 25 deg C :  4.271E-001  L/mol-sec
 Ka Half-Life at pH 7:     187.803  days

   The rate constant estimated for the EPOXIDE DOES NOT
   include the neutral hydrolysis rate constant!!
   For some epoxides, the neutral rate constant is the
   dominant hydrolysis rate at environmental pHs!
   If the neutral rate constant is important, the HYDRO
   estimated rate will under-estimate the actual rate!



BCF Program (v2.15) Results:
============================
SMILES : O(C1CCCCCCCCCC)C1CCCCC(C)C
CHEM   : Oxirane, 2-decyl-3-(5-methylhexyl)-, cis-
MOL FOR: C19 H38 O1
MOL WT : 282.51
--------------------------------- Bcfwin v2.15
---------------------------------
Log Kow  (estimated)  :  8.08
Log Kow (experimental):  not available from database
Log Kow used by BCF estimates:  8.08

Equation Used to Make BCF estimate:
   Log BCF = -1.37 log Kow + 14.4 + Correction

      Correction(s):                    Value
       Alkyl chains (8+ -CH2- groups)  -1.500

   Estimated Log BCF =  1.827  (BCF = 67.08)



                           Volatilization From Water
                           =========================

Chemical Name: Oxirane, 2-decyl-3-(5-methylhexyl)-, cis-

Molecular Weight    :  282.51 g/mole
```

```
Water Solubility    :  -----
Vapor Pressure      :  -----
Henry's Law Constant:  0.0149 atm-m3/mole  (estimated by Bond SAR Method)

                            RIVER            LAKE
                          ---------        ---------
Water Depth     (meters):   1                1
Wind Velocity    (m/sec):   5                0.5
Current Velocity (m/sec):   1                0.05

      HALF-LIFE (hours) :   1.781            160.4
      HALF-LIFE (days ) :   0.07422          6.682


STP Fugacity Model:  Predicted Fate in a Wastewater Treatment Facility
=========================================================================
   (using 10000 hr Bio P,A,S)
PROPERTIES OF: Oxirane, 2-decyl-3-(5-methylhexyl)-, cis-
-------------
Molecular weight (g/mol)                                  282.51
Aqueous solubility (mg/l)                                 0
Vapour pressure (Pa)                                      0
                (atm)                                     0
                (mm Hg)                                   0
Henry 's law constant (Atm-m3/mol)                        0.0149
Air-water partition coefficient                           0.609366
Octanol-water partition coefficient (Kow)                 1.20226E+008
Log Kow                                                   8.08
Biomass to water partition coefficient                    2.40453E+007
Temperature [deg C]                                       25
Biodeg rate constants (h^-1),half life in biomass (h) and in 2000 mg/L MLSS
(h):
          -Primary tank        0.00      9999.79       10000.00
          -Aeration tank       0.00      9999.79       10000.00
          -Settling tank       0.00      9999.79       10000.00

 STP Overall Chemical Mass Balance:
 ---------------------------------
                              g/h               mol/h          percent

Influent                    1.00E+001         3.5E-002        100.00

Primary sludge              5.99E+000         2.1E-002        59.88
Waste sludge                3.33E+000         1.2E-002        33.28
Primary volatilization      2.72E-005         9.6E-008         0.00
Settling volatilization     6.01E-005         2.1E-007         0.00
Aeration off gas            9.17E-003         3.2E-005         0.09

Primary biodegradation      1.75E-002         6.2E-005         0.18
Settling biodegradation     4.25E-003         1.5E-005         0.04
Aeration biodegradation     5.60E-002         2.0E-004         0.56

Final water effluent        5.97E-001         2.1E-003         5.97

Total removal               9.40E+000         3.3E-002        94.03
Total biodegradation        7.77E-002         2.8E-004         0.78
```

```
STP Fugacity Model:  Predicted Fate in a Wastewater Treatment Facility
======================================================================
   (using Biowin/EPA draft method)
PROPERTIES OF: Oxirane, 2-decyl-3-(5-methylhexyl)-, cis-
-------------
Molecular weight (g/mol)                              282.51
Aqueous solubility (mg/l)                             0
Vapour pressure (Pa)                                  0
                (atm)                                 0
                (mm Hg)                               0
Henry 's law constant (Atm-m3/mol)                    0.0149
Air-water partition coefficient                       0.609366
Octanol-water partition coefficient (Kow)             1.20226E+008
Log Kow                                               8.08
Biomass to water partition coefficient                2.40453E+007
Temperature [deg C]                                   25
Biodeg rate constants (h^-1),half life in biomass (h) and in 2000 mg/L MLSS
(h):
          -Primary tank        0.02        30.00          30.00
          -Aeration tank       0.23         3.00           3.00
          -Settling tank       0.23         3.00           3.00

 STP Overall Chemical Mass Balance:
 ----------------------------------
                              g/h               mol/h          percent

Influent                    1.00E+001         3.5E-002        100.00

Primary sludge              3.78E+000         1.3E-002        37.84
Waste sludge                3.83E-002         1.4E-004         0.38
Primary volatilization      1.72E-005         6.1E-008         0.00
Settling volatilization     6.92E-007         2.4E-009         0.00
Aeration off gas            1.14E-004         4.0E-007         0.00

Primary biodegradation      3.69E+000         1.3E-002        36.91
Settling biodegradation     1.63E-001         5.8E-004         1.63
Aeration biodegradation     2.32E+000         8.2E-003        23.16

Final water effluent        6.87E-003         2.4E-005         0.07

Total removal               9.99E+000         3.5E-002        99.93
Total biodegradation        6.17E+000         2.2E-002        61.70
 (** Total removal recommended maximum is 99 percent)


Level III Fugacity Model (Full-Output):
=======================================
  Chem Name   : Oxirane, 2-decyl-3-(5-methylhexyl)-, cis-
  Molecular Wt: 282.51
  Henry's LC  : 0.0149 atm-m3/mole (Henrywin program)
  Vapor Press : 0.000342 mm Hg  (Mpbpwin program)
  Liquid VP   : 0.00089 mm Hg  (super-cooled)
  Melting Pt  : 67 deg C (Mpbpwin program)
  Log Kow     : 8.08  (Kowwin program)
  Soil Koc    : 4.93e+007  (calc by model)
```

```
          Mass Amount    Half-Life    Emissions
           (percent)        (hr)       (kg/hr)
Air        0.395           11.8         1000
Water      3.77            360          1000
Soil       28.1            720          1000
Sediment   67.8            3.24e+003    0

           Fugacity    Reaction    Advection   Reaction    Advection
            (atm)       (kg/hr)      (kg/hr)    (percent)   (percent)
Air        1.26e-011    857         146         28.6        4.88
Water      4.55e-010    269         140         8.96        4.66
Soil       2.57e-012    1e+003      0           33.4        0
Sediment   2.8e-010     537         50.2        17.9        1.67

Persistence Time: 1.24e+003 hr
Reaction Time:    1.39e+003 hr
Advection Time:   1.1e+004 hr
Percent Reacted:  88.8
Percent Advected: 11.2

Half-Lives (hr), (based upon Biowin (Ultimate) and Aopwin):
   Air:      11.82
   Water:    360
   Soil:     720
   Sediment: 3240
     Biowin estimate: 2.865  (weeks       )

Advection Times (hr):
   Air:      100
   Water:    1000
   Sediment: 5e+004
```
