US Environmental Protection Agency
Office of Pesticide Programs

Reregistration Eligibility Decision (RED) for Grotan (HHT)

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Agency

Office of Prevention, Pesticides
And Toxic Substances
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Reregistration Eligibility Decision for HHT

List C

Case No. 3074

Reregistration Eligibility Decision (RED) Document

for

HHT

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Glossary of Terms and Abbreviations

AGDCI	Agricultural Data Call-In
ai	Active Ingredient
aPAD	Acute Population Adjusted Dose
AR	Anticipated Residue
BCF	Bioconcentration Factor
CFR	Code of Federal Regulations
cPAD	Chronic Population Adjusted Dose
CSF	Confidential Statement of Formula
CSFII	USDA Continuing Surveys for Food Intake by Individuals
DCI	Data Call-In
DEEM	Dietary Exposure Evaluation Model
DFR	Dislodgeable Foliar Residue
EC	Emulsifiable Concentrate Formulation
EDWC	Estimated Drinking Water Concentration
EEC	Estimated Environmental Concentration
EPA	Environmental Protection Agency
EXAMS	Exposure Analysis Modeling System
EUP	End-Use Product
FCID	Food Commodity Intake Database
FDA	Food and Drug Administration
FIFRA	Federal Insecticide, Fungicide, and Rodenticide Act
FFDCA	Federal Food, Drug, and Cosmetic Act
FQPA	Food Quality Protection Act
FOB	Functional Observation Battery
G	Granular Formulation
GENEEC	Tier I Surface Water Computer Model
GLN	Guideline Number
HAFT	Highest Average Field Trial
IR	Index Reservoir
LC_{50}	Median Lethal Concentration. A statistically derived concentration of a substance that can be expected to cause death in 50% of test animals. It is usually expressed as the weight of substance per weight or volume of water, air or feed, e.g., mg/l, mg/kg or ppm.
LD_{50}	Median Lethal Dose. A statistically derived single dose that can be expected to cause death in 50% of the test animals when administered by the route indicated (oral, dermal, inhalation). It is expressed as a weight of substance per unit weight of animal, e.g., mg/kg.
LOC	Level of Concern
LOD	Limit of Detection
LOAEL	Lowest Observed Adverse Effect Level
µg/g	Micrograms Per Gram
µg/L	Micrograms Per Liter
mg/kg/day	Milligram Per Kilogram Per Day
mg/L	Milligrams Per Liter

MOE	Margin of Exposure
MRID	Master Record Identification (number). EPA's system of recording and tracking studies submitted.
MUP	Manufacturing-Use Product
NA	Not Applicable
NAWQA	USGS National Water Quality Assessment
NPDES	National Pollutant Discharge Elimination System
NR	Not Required
NOAEL	No Observed Adverse Effect Level
OP	Organophosphate
OPP	EPA Office of Pesticide Programs
OPPTS	EPA Office of Prevention, Pesticides and Toxic Substances
PAD	Population Adjusted Dose
PCA	Percent Crop Area
PDP	USDA Pesticide Data Program
PHED	Pesticide Handler's Exposure Data
PHI	Preharvest Interval
ppb	Parts Per Billion
PPE	Personal Protective Equipment
ppm	Parts Per Million
PRZM/EXAMS	Tier II Surface Water Computer Model
Q_1*	The Carcinogenic Potential of a Compound, Quantified by EPA's Cancer Risk Model
RAC	Raw Agriculture Commodity
RED	Reregistration Eligibility Decision
REI	Restricted Entry Interval
RfD	Reference Dose
RQ	Risk Quotient
SCI-GROW	Tier I Ground Water Computer Model
SAP	Science Advisory Panel
SF	Safety Factor
SLC	Single Layer Clothing
SLN	Special Local Need (Registrations Under Section 24(c) of FIFRA)
TGAI	Technical Grade Active Ingredient
TRR	Total Radioactive Residue
USDA	United States Department of Agriculture
USGS	United States Geological Survey
UF	Uncertainty Factor
UV	Ultraviolet
WPS	Worker Protection Standard

ABSTRACT

The Environmental Protection Agency (EPA or the Agency) has completed the human health and environmental risk assessments for hexahydro-1,3,5-tris(2-hydroxyethyl)-s-triazine (HHT) and is issuing its reregistration eligibility and risk management decisions. The risk assessments, which are summarized in this document, are based on review of registrant-submitted data supporting the use patterns of currently registered products, citations from the open literature, and additional information received through the public docket. The risk assessments have been revised, as needed, according to information received since they were first made available to the public in April 2008. After considering the risk assessments, available information about alternatives to HHT for specific uses, public comments, and risk mitigation options, the Agency developed its reregistration eligibility and risk management decisions for uses of HHT. As a result of this review, EPA has determined that some uses of HHT are eligible for reregistration, provided that the prescribed risk mitigation measures are adopted and labels are amended accordingly, and required data are submitted. Other uses are not eligible for reregistration, based on a combination of critical data gaps and unacceptable risks. The reregistration eligibility decision and the associated risk mitigation measures are discussed fully in this document.

I. Introduction

This document is the Environmental Protection Agency's (EPA or "the Agency") reregistration eligibility determination (RED) for all currently registered uses of hexahydro-1,3,5-tris(2-hydroxyethyl)-s-triazine (HHT). This document also summarizes the human health and environmental risks used to make the reregistration eligibility decision.

The Federal Insecticide, Fungicide, and Rodenticide Act (FIFRA) was amended in 1988 to accelerate the reregistration of products with active ingredients registered prior to November 1, 1984, and amended again by the Food Quality Protection Act of 1996 (FQPA) and the Pesticide Registration Improvement Act of 2003 (PRIA) to set time frames for the issuance of Reregistration Eligibility Decisions. FIFRA calls for the development and submission of data to support the reregistration of an active ingredient, as well as a review of all data submitted to the U.S. Environmental Protection Agency (EPA or "the Agency"). Reregistration involves a thorough review of the scientific database underlying a pesticide's registration. The purpose of the Agency's review is to reassess the potential hazards arising from the currently registered uses of a pesticide, to determine the need for additional data on health and environmental effects, and to determine whether or not the pesticide meets the "no unreasonable adverse effects" criteria of FIFRA.

The Agency made its reregistration eligibility determination for HHT based on the required data, the current guidelines for conducting acceptable studies to generate such data, and published scientific literature. The Agency has found that currently registered uses of HHT, with the exception of paints, stains, coatings, and industrial and household cleaning products, are eligible for reregistration provided the requirements for reregistration identified in this reregistration eligibility decision (RED) are implemented.

This document consists of six sections: Section I contains the regulatory framework for reregistration reassessment; Section II provides an overview of the chemical, including a profile of its use and usage; Section III gives an overview of the human health and ecological risk assessments; Section IV presents the Agency's reregistration eligibility and risk management decisions; Section V summarizes label changes necessary to implement the risk mitigation measures outlined in Section IV; and Section VI includes the appendices, related supporting documents, and Data Call-In (DCI) information. The revised risk assessment documents and related addenda are not included in this document, but are available in the Public Docket at http://www.regulations.gov in docket number EPA-HQ-OPP-2008-0193.

II. Chemical Overview

A. Case Overview

Case 3074, HHT, includes products containing Hexahydro-1,3,5-tris(2-hydroxyethyl)-s-triazine, an antimicrobial chemical that displays some fungicidal activity. HHT products are formulated as liquid concentrates and are registered for in-can preservation of adhesives and

to preserve a variety of metal working cutting fluids, indoor construction compounds (e.g., caulk), lubricants, slurries, paints, stains, coatings, solutions, and emulsions.

The actual antimicrobial agent in HHT is formaldehyde (HCHO); therefore, this RED also addresses potential risks associated with formaldehyde exposure from HHT uses only. EPA is preparing a separate formaldehyde RED to address potential risks associated with non-HHT uses of formaldehyde. This document will be available in the formaldehyde public docket at http://www.regulations.gov in docket number EPA-HQ-OPP-2008-0121.

The chemicals assessed in Case 3074 are presented in Table 1.

Table 1. Chemicals Assessed in the HHT RED[1]

Case Number	CAS Number	PC Code	Empirical Formula	Chemical Name	Names Used in RED Documents	Common Names
3074	4719-04-4	083301	$C_9H_{21}N_3O_3$	Hexahydro-1,3,5-tris(2-hydroxyethyl)-s-triazine	HHT	Grotan, Triadine, Proxel, Onyxide, Myacide, Nipacide, and Surcide-P
0556	50-00-0	043001	CH_2O (Gas or anhydrous form) $H_2C(OH)_2$ or $C_1H_4O_2$ (Formaldehyde monohydrate)	Formaldehyde (gas) Formaldehyde monohydrate (aqueous solution)	Formaldehyde, HCHO, HCOH	Formaldehyde, Formalin

[1] This RED addresses potential risks associated with formaldehyde exposure from HHT uses only. EPA is preparing a separate formaldehyde RED to address potential risks associated with non-HHT uses of formaldehyde.

No direct food use is associated with HHT; therefore, no tolerance or tolerance exemption has been established.

Prior to the reregistration program, EPA began reviewing chemicals under the registration standard program. Chemicals for which Registration Standard documents were written were referred to as "List A" chemicals in reregistration. HHT is a "List C" reregistration chemical; therefore, no Registration Standard was completed. Data Call-Ins (DCI) requiring chemical identity, toxicology, field trial, ecological, and other data were issued for HHT in December 1992 (GDCI-083301-17025) and September 1993 (GDCI-083301-17370). Data from submitted studies along with published scientific literature were used to characterize the risks associated with the uses described in this document. Additional data required as a result of reregistration are presented in Section V of this document.

B. Use and Usage

Since the early 1980s, HHT products have been used to control microbial agents and fungi. A detailed table of the uses of HHT eligible for reregistration can be found in Appendix A.

Type of Pesticide:	Fungicide, Bacteriostat
Use Sites:	Metal working cutting fluids; in-can preservation of adhesives; chain lubricants; aqueous mineral slurries; paints; stains; coatings; surfactant/detergent solutions and emulsions; chemical and clinical reagents; inks and dyes; fuel and oil in storage; indoor construction compounds such as caulks, spackling, grout, adhesives, foams; and in industrial processes such as oil field drilling muds, workover fluids, and completion fluids.
Target Pests:	Microbial agents, bacteria
Formulations:	HHT products are formulated as liquid concentrates.
Application Methods:	Products containing HHT can be applied in residential settings by brush/roller and airless sprayer (paints); mop, wipe, trigger pump/aerosol (cleaners); and in laundry detergents. Commercial/occupational applications include liquid pour/pump, brush/roller and airless sprayer (paints); and mop, wipe, trigger pump/aerosol (cleaners).

III. Summary of HHT Risk Assessments

The purpose of this section is to summarize EPA's human health and ecological risk conclusions for HHT to help the reader better understand EPA's risk management decisions. The human health and ecological risk assessment documents and supporting information listed in Appendix C were used to formulate the safety finding and regulatory decision for HHT. The full risk assessments and related supporting documents are available at http://www.regulations.gov in docket number EPA-HQ-OPP-2008-0193.

EPA developed this RED for HHT through a modified, 4–Phase public participation process. The Agency uses public participation processes to involve the public in developing pesticide reregistration decisions. EPA released its preliminary risk assessments for 60-day public comment in March 2008. Substantive comments were incorporated into the final risk assessments which were used to make this reregistration eligibility decision.

HHT is a formaldehyde releaser, meaning that the actual antimicrobial agent in HHT is formaldehyde. As mentioned previously, this RED also addresses potential risks associated with formaldehyde exposure from HHT uses only. EPA is preparing a separate

formaldehyde RED to address potential risks associated with non-HHT uses of formaldehyde.

The Agency's use of human studies in the HHT risk assessment is in accordance with the Agency's Final Rule promulgated on January 26, 2006, related to Protections for Subjects in Human Research, which is codified in 40 CFR Part 26.

A. Human Health Risk Assessment

EPA has conducted a human health risk assessment for HHT to support the reregistration eligibility decision. EPA evaluated the submitted toxicology, product and residue chemistry, and occupational/residential exposure studies as well as available open literature and determined that the data are adequate to support a reregistration eligibility decision. However, additional data for HHT are needed (see Section V). A summary of the human health risk assessment findings and conclusions is provided below.

1. Background on Assessing Human Health Risks to Formaldehyde

a. Formaldehyde Non-Cancer Assessment

On June 12, 2008, members of the Antimicrobials Division's Toxicity endpoint Selection Committee (ADTC) met to discuss the non-cancer inhalation toxicity endpoint for formaldehyde that had been previously selected by the committee for use in conducting inhalation toxicity risk assessments for the formaldehyde reregistration eligibility decision (RED) document.

The original endpoint of 100 ppb was selected from the published report of Horvath et al. [JAMA 259, no. 5: 701-707, 1988], who reported nasal and respiratory effects in 109 workers occupationally exposed to formaldehyde. The value of 100 ppb was selected as a NOAEL for use in occupational risk assessments, while for the general population, a value of 10 ppb was selected. This value was derived by application of a 10-fold uncertainty factor to the NOAEL value of 100 ppb to account for intraspecies variation in response in accordance with Agency policy.

During the public comment phase of the formaldehyde risk assessment, the Formaldehyde Council responded to the selection of the 100 ppb endpoint. They stated that the Agency should consider the results of a 2007 publication by Noisel et al. [Regulatory Toxicology and Pharmacology 48: 118-127), which reviewed some of the available scientific literature. This study, in the Council's opinion, "is based on human exposure rather than controlled human chamber studies and can be used for deriving a No-Observed-Adverse-Effect-Level (NOAEL) for the non-cancer endpoint for formaldehyde."

The ADTC noted both observational human exposure data as well as data compiled from exposure of human subjects under controlled conditions in the Noisel et al. publication. Notwithstanding the need for intentional exposure data to be presented to the Agency's Human Studies Review Board, the ADTC noted that irritant effects of formaldehyde have

been reported in other studies below the 0.75 ppm concentration recommended by Noisel et al. as a safe level. Further, this recommendation is for worker populations only.

The irritant effects of formaldehyde, including both eye and nasal irritation as well as respiratory symptoms (irritation, changes in pulmonary function), can be considered from a toxicological perspective to be composed of both physiological and adverse responses. Based on the available data, the ADTC was not compelled to select a value higher than that already proposed. With respect to the 10-fold uncertainty factor used for risk assessment to the general population, the ADTC concluded that a reduction in this factor is not warranted at this time. Contrary to the Formaldehyde Council's statement that "the nature of the health effect does not suggest that there are particularly susceptible subpopulations which would warrant application of the 10x intraspecies UF," the 1999 ATSDR Toxicological Review of formaldehyde (ATSDR, 1999) noted two studies "...providing suggestive evidence that children may be more sensitive to the irritant effects of formaldehyde." These studies were not intentional exposure studies. It is also noted in the ATSDR review that "additional research is necessary to confirm or discard the hypothesis that children may be more susceptible than adults to the irritant effects of formaldehyde..."

The ADTC concluded that, based on the available data, it is appropriate to remain with the NOAEL value selected from the 1988 Horvath et al. publication and with the 10-fold uncertainty factor for risk assessments to the general population. The ADTC is also aware, however, of ongoing efforts by ORD/NCEA to develop an inhalation reference concentration, or RfC for formaldehyde. OPP will continue to coordinate its efforts with ORD and other program offices to refine the non-cancer inhalation assessment as necessary.

b. Formaldehyde Cancer Assessment

The Agency is currently reevaluating the carcinogenic potential of formaldehyde. The historical and ongoing development of an inhalation unit risk value to assess the carcinogenic potential of formaldehyde is briefly summarized below. Contributors to this summary included scientists from several EPA program offices (Office of Pesticide Programs [OPP], Office of Pollution, Prevention, and Toxics [OPPT], Office of Research and Development,/National Center for Environmental Assessment [ORD/NCEA], Office of Research and Development/National Health Effects Exposure Research Laboratory [ORD/NHEERL], and Office of Air and Radiation [OAR]).

- In 1991 IRIS published a weight-of-evidence characterization for carcinogenicity of formaldehyde, classifying formaldehyde as a B1 probable human carcinogen with a potency factor of 1.3 E-5 per ($\mu g/m^3$)) on the basis of squamous cell nasal tumors observed in a two-year study in rats (Kerns et al., 1983).

- In 1999 the Chemical Industry Institute of Toxicology (CIIT) developed a health risk assessment for formaldehyde based upon the animal toxicology data (CIIT, 1999). This document presented the dose-response modeling of these data in two distinct parts: 1) based upon a biologically-based dose response (BBDR) model, and 2) benchmark dose models that were based upon point of departures at various response

levels of the tumor and precursor data. Both these approaches made extensive use of the available time-to-tumor and mechanistic information. The 1999 assessment was subsequently published in various articles in peer-reviewed journals (2001, 2002, 2003, 2004).

- In 1999, the U.S. EPA's Office of Air and Radiation and Office of Research and Development, in conjunction with Health Canada, conducted an external peer review workshop for the CIIT BDDR model as well as an external written peer review and public comment period for their assessments. While the review was largely positive on the overall approach in the assessment, reviewers also pointed to the potential for significant uncertainty due to model mis-specification and uncertainties in key parameters involved in the BBDR model.

- Based on the peer review of the CIIT model, OAR determined in 2004 that the CIIT model was the most appropriate tool for risk assessment for formaldehyde. OAR has subsequently used the formaldehyde cancer potency derived using the CIIT model for a number of risk assessments involving formaldehyde emissions to the atmosphere such as the Plywood and Composite Wood Products National Emission Standard for Hazardous Air Pollutants (final rule 2004, reconsidered final rule 2006, remanded to EPA by court 2007); Control of Hazardous Air Pollutants from Mobile Sources (Final Rule 2007); and Proposed Rule for National Emission Standard for Combustion Turbines (2004). Health Canada, Australia, the World Health Organization, and the German Maximale Arbeitsplatzkonzentrationen (MAK) Commission have also used the CIIT model. Model strengths include consideration of the mode of action data for formaldehyde and a conservative approach to account for potential direct DNA interaction and mutation induction. Model uncertainties include variability for some of the parameters of the model (e.g., cell proliferation) which can affect predictions of risk (Subramanian et. al., 2007; 2008 [in press]).

- In 2004, NCEA convened a panel of experts, including scientists from CIIT, to provide advice on these and other critical biological and statistical uncertainties. The strength of the CIIT model is its consideration of mode of action and extensive mechanistic information.

- Although current OAR assessments still use the CIIT model, these assessments now acknowledge previously unknown uncertainties with the CIIT model when characterizing the risk results.

- In 2004, the International Agency for Research on Cancer (IARC) characterized formaldehyde as a human carcinogen based on their review of the current literature (IARC, 2004), including data in humans on nasopharyngeal cancer, cancer of the nasal cavity and paranasal sinuses, and leukemia. It should be noted that some epidemiology studies did not find a reported association between formaldehyde exposure and carcinogenicity. For example, Coggon et. al., 2003 studied over 14,000 workers exposed to formaldehyde in industrial workplaces and reported no excesses of either leukemia or nasal and nasopharyngeal cancer.

- In 2005, the Scientific Review Panel (SRP) of the California Office of Environmental Health Hazard Assessment responded to the CA Air Resources Board request to reevaluate the carcinogenic potential of formaldehyde. The Panel noted in this 2005 review that California's Office of Environmental Health (OEHHA)'s November 2002 evaluation of a petition had included the 1999 report on the CIIT model and other information, and that OEHHA had concluded that "*the evidence…(1) did not change the determination that formaldehyde is a carcinogen; (2) presented information that considered the possibility of non-linear dose response relationships, but presented no clear grounds to review the original "no threshold" determination; and (3) did not provide any new epidemiology or bioassays supporting a change in potency. In addition, there was insufficient information to fully evaluate the CIIT model, issues such as model uncertainty were not adequately addressed.…*" The Scientific Review Panel's overall conclusion in 2005 was, *"The Panel concluded that there was not sufficient new data to support the petition to review the [OEHHA's earlier 1992] formaldehyde risk assessment. In addition, the newly published studies represented relevant new information, but they did not allow determination of a causal relationship between formaldehyde exposure and leukemia. These studies deserve further evaluation over time given their potential importance."* (Froines, 2005).

- EPA is currently completing a new IRIS assessment and unit risk value for formaldehyde; the reassessment is scheduled to start internal peer review in May 2008 and begin independent external peer review in January 2009 (http://cfpub.epa.gov/ncea/iristrac/index.cfm?fuseaction=viewChemical.showChemical&sw_id=1031). EPA anticipates that the peer review of the formaldehyde assessment will be a longer process then that of EPA's reregistration process scheduled to conclude in September 2008.

Based of the on going development of the science to predict carcinogenic potential of formaldehyde, OPP has decided to present the formaldehyde cancer risks for the pesticidal uses using both the existing 1991 IRIS cancer unit risk of 1.3 E-5 per ($\mu g/m^3$) and the CIIT BBDR model until any new cancer estimates are fully peer reviewed. OPP also acknowledges the wide range in cancer risks using these approaches and will coordinate with other offices in EPA on the outcome of the upcoming peer review process on the carcinogenicity of formaldehyde. Because formaldehyde air concentrations approach those associated with ocular and respiratory tract irritation, the risk mitigation measures to be implemented in the meantime for the pesticidal uses will be based on mitigating the non-cancer effects at a limit of 0.01 ppm. It is believed that this level will reduce exposures sufficiently such that the cancer risks would not be of concern. The EPA process of regulating pesticides allows for reevaluation at any time if new information from the peer review process of the carcinogenic potential of formaldehyde warrants.

2. Toxicity Profile

The toxicological databases for HHT and formaldehyde are adequate to support a reregistration eligibility decision. As discussed above, HHT and formaldehyde are considered toxicologically unique and were evaluated separately.

a. Acute Toxicity Profile

HHT has moderate to low acute toxicity via the oral, dermal, and inhalation routes (Category III and IV). It is an eye irritant (Category I), a moderate dermal irritant (Category III), and not a skin sensitizer. Table 2 presents the acute toxicity profile for HHT. The acute toxicity profile for formaldehyde is presented in the June 2008 Formaldehyde RED available at http://www.regulations.gov in docket number EPA-HQ-OPP-2008-0121.

Table 2. Acute Toxicity Profile for HHT

Guideline Number	Study Type/Test substance (% a.i.)	MRID Number	Results	Toxicity Category
870.1100 (§81-1)	Acute Oral – Rat Purity 79.4%	41675206	LD_{50} =1250 mg/kg (males) LD_{50} =763 mg/kg (females)	III
870.1100 (§81-1)	Acute Oral – Mouse (Supplemental) Purity 78.5%	00155959	LD_{50} = 1.30 mL/kg	III
870.1200 (§81-2)	Acute Dermal – Rabbit Purity 79.96%	00155984	LD_{50} > 2000 mg/kg	III
870.1300 (§81-3)	Acute Inhalation – Rat	N/A	N/A	N/A
870.2400 (§81-4)	Primary Eye Irritation – Rabbit Purity 79.96%	00155985	Corrosive	I
870.2500 (§81-5)	Primary Dermal Irritation – Rabbit Purity 79.96%	00155986	Mild irritant	IV
870.2500 (§81-5)	Primary Dermal Irritation – Guinea pigs Purity 79.96%	00155987	Mild irritant	IV
870.2600 (§81-6)	Dermal Sensitization – Guinea pigs	00155987	Not a Sensitizer	N/A

Guideline Number	Study Type/Test substance (% a.i.)	MRID Number	Results	Toxicity Category
	Purity 79.96%			

b. Toxic Effects and Carcinogenicity

The target organ following oral and inhalation exposure to HHT is believed to be the gastrointestinal tract. The target organs following inhalation exposure to formaldehyde is believed to be the eye, nose, and throat.

HHT is not classified as a carcinogen (no data available); therefore, quantification of cancer risk is not required for HHT and a cancer analysis was not performed. Formaldehyde is classified as a B1 substance (probable human carcinogen - based on limited evidence of carcinogenicity in humans); therefore, quantification of cancer risk is needed and a cancer analysis was performed for formaldehyde.

c. Toxicological Endpoints

i. HHT Toxicological Endpoints

The toxicological endpoints used in the human health risk assessment for HHT are presented in Table 3. The uncertainty and safety factors used to account for interspecies extrapolation, intraspecies variability, and for completeness of the database are also presented.

Table 3. Summary of HHT Toxicological Endpoints

Exposure Scenario	Dose Used in Risk Assessment, UF	Special FQPA SF and Level of Concern (LOC) for Risk Assessment	Study and Toxicological Effects
Dietary Risk Assessment			
Acute Dietary (All populations)	Oral NOAEL = 500 mg/kg/day UF = 1,000 (10x – Inter; 10x – Intra; and 10x – database UF)	N/A	Rat Developmental Toxicity (MRID 41161801), based on ulcerations and scarring of the stomach mucosa
Chronic Dietary (All populations)	Oral NOAEL = 50 mg/kg/day UF = 100 (10x – Intra; 10x – Inter)	N/A	Rat 90-day Oral Study (MRID 41483001), based on lymphocytic infiltration in females and erosion of gastric mucosa and prominence of the limiting ridge of the stomach in males

Exposure Scenario	Dose Used in Risk Assessment, UF	Special FQPA SF and Level of Concern (LOC) for Risk Assessment	Study and Toxicological Effects
Non-Dietary Risk Assessments			
Short-Term Incidental Oral (1-30 days)	Oral NOAEL = 500 mg/kg/day UF = 1,000 (10x – Inter; 10x – Intra; and 10x – database UF)	N/A	Rat Developmental Toxicity (MRID 41161801), based on ulcerations and scarring of the stomach mucosa
Intermediate-Term Incidental Oral (30 days- 6 months)	Oral NOAEL = 50 mg/kg/day UF = 100 (10x – Intra; 10x – Inter)	N/A	Rat 90-day Oral Study (MRID 41483001), based on lymphocytic infiltration in females and erosion of gastric mucosa and prominence of the limiting ridge of the stomach in males
Dermal Absorption Factor	Not required as a dermal toxicity study has been used for the dermal endpoint.		
Dermal Short-Term (1-30 days)	No risk assessment necessary. No adverse systemic effects observed in a 21-day dermal toxicity study up to 1,000 mg/kg/day.		
Dermal Intermediate- and long-term (30 days- 6 months and >6 months)	Oral NOAEL = 250 mg/kg/day UF = 1,000 (10x – Intra; 10x – Inter; and 10x – database UF)	N/A	Rat 90-day dermal Study (MRID 41483002), based on systemic NOAEL was found to be greater than 250 mg/kg/day (the HDT)
Inhalation (all durations)	Oral NOAEL = 50 mg/kg/day UF = 100 (10x – Inter; 10x – Intra); extra 10x – database UF to require inhalation toxicity study)	N/A	Rat 90-day Oral Study (MRID 41483001), based on lymphocytic infiltration in females and erosion of gastric mucosa and prominence of the limiting ridge of the stomach in males
Cancer (oral, dermal, inhalation)	No cancer data are available.		

ii. Formaldehyde Toxicological Endpoints

Although HHT is known to release formaldehyde, the exact rate of release and transformation cannot be meaningfully estimated based on currently available data. For example, because actual air monitoring data for laundry detergents and cleaners were not available, EPA made the conservative assumption that 100% formaldehyde formation

occurred from HHT. Confirmatory data are needed to refine estimates based on the actual amount of formaldehyde formation to better estimate exposure and risk.

The toxicological endpoints used in the human health risk assessment for formaldehyde are presented in Table 4. The uncertainty and safety factors used to account for interspecies extrapolation, intraspecies variability, and for completeness of the database are also presented. Formaldehyde is classified as a B1 substance (probable human carcinogen - based on limited evidence of carcinogenicity in humans); therefore, quantification of cancer risk is required and a cancer analysis was performed. EPA estimates lifetime cancer risk using the estimated exposure and the carcinogenic potential of the compound (Q_1* or "cancer slope factor"). The risk is expressed as a probability of developing cancer (e.g., one-in-a-million or 1 x 10^{-6}).

Table 4. Summary of Formaldehyde Toxicological Endpoints

Exposure Scenario	Dose Used in Risk Assessment (mg/kg/day)	Target MOE, UF, Special FQPA SF* for Risk Assessment	Study and Toxicological Effects
Dietary Risk Assessments			
Acute Dietary (general population including infants and children)	An acute dietary assessment is not needed for the registered antimicrobial uses of formaldehyde; however, an indirect food use assessment was conducted.		
Chronic Dietary (all populations)	A chronic dietary assessment is not needed for the registered antimicrobial uses of formaldehyde; however, an indirect food use assessment was conducted.		
Non-Dietary Risk Assessments			
Incidental Oral	An incidental oral risk assessment is not required for the registered antimicrobial uses of formaldehyde.		
Dermal (all durations)	A dermal risk assessment is not required for the registered antimicrobial uses of formaldehyde.		
Inhalation (all durations)	**NOAEL** (human) = 0.1 ppm	**UF = 1 (occupational)** **UF = 10 (residential)**	ACGIH 2001 publication on formaldehyde Horvath, E.P. et al. (1986): JAMA 259(5): 701-707. Based on complaints of eye, nose, and throat irritation in particle board workers at concentrations of formaldehyde from 0.4 – 1.0 ppm. Redden, J. (2005): Section 18 Emergency Exemption for the use of Paraformaldehyde: U.S. Army Medical Research Institute of Infectious Diseases.

Exposure Scenario	Dose Used in Risk Assessment (mg/kg/day)	Target MOE, UF, Special FQPA SF* for Risk Assessment	Study and Toxicological Effects
Cancer	**Lifetime extra cancer unit risk estimate of 1.3×10^{-5} per $\mu g/m^3$** (US EPA IRIS http://www.epa.gov/ncea/iris/subst/0419.htm) And **CIIT modeling**: Tables 8A (for residential) and B (for professional). Hockey stick-shaped CRCP (nonsmoking) (Conolly, 2004)		

3. Dietary Exposure and Risk from Food and Drinking Water

No direct food use is associated with HHT. However, because HHT products may be used in ways that could result in indirect food contact (e.g., use of cleaners on countertops or cutting boards), EPA estimated acute and chronic non-cancer dietary risk from exposure to HHT. The Agency did not identify a dietary endpoint for formaldehyde and therefore did not estimate dietary risk from exposure to formaldehyde.

HHT is largely used indoors as a materials preservative; therefore, effluents containing this chemical are not expected to contact fresh water environments. In addition HHT biodegrades with a short half-life in activated sludge (one week) and water that contains salts. Formaldehyde is the only metabolite identified for HHT. Formaldehyde has been determined not to be stable in soils or water. Therefore, based on the use patterns, and the short half-life, the potential for HHT to impact drinking water sources is negligible and, therefore, a quantitative drinking water assessment was not conducted. For additional information please see the Drinking Water Risk Assessment for HHT (Grotan), dated January 30, 2008.

Non-cancer dietary risk is expressed as a percentage of a level of concern. The level of concern is the dose at or below which no unreasonable adverse health effects to any human population subgroup are expected to occur. This dietary level of concern is termed the population adjusted dose (PAD), which reflects the reference dose (RfD), either acute or chronic, adjusted for (divided by) the FQPA safety factor. Estimated risks that are less than 100% of the PAD are below EPA's level of concern. The acute PAD (aPAD) is the highest predicted dose to which a person could be exposed on a single day with no expected adverse health effect. The chronic PAD (cPAD) is the highest predicted dose to which a person could be exposed over the course of a lifetime with no expected adverse health effect.

Using conservative assumptions, EPA estimated dietary exposure to HHT to be <1% of the aPAD and cPAD for adhesives and approximately 80% of the aPAD and cPAD for countertop and cutting boards. Therefore, because the aPAD and cPAD are well below 100%, dietary exposure does not exceed the Agency's level of concern. For additional information please see the Dietary Risk Assessment for HHT (Grotan), dated February 12, 2008.

4. Residential Exposure and Risk

Because HHT is currently registered for use in residential settings, residential users (handlers) have the potential to be exposed to HHT and formaldehyde by using products containing HHT. Therefore, EPA estimated risk to residential handlers as a result of exposure to HHT and formaldehyde from products containing HHT.

Residential non-cancer risk estimates are typically expressed as a margin of exposure (MOE) which is a ratio of the dose from a toxicological study selected for risk assessment, typically a NOAEL, to the predicted exposure (MOE = dose ÷ exposure). Estimated MOEs are then compared to the "target MOE" which represents the dose selected for risk assessment and uncertainty factors (UF) applied to that dose (target MOE = dose × uncertainty factors). The standard UF is 100x, which includes 10x for interspecies extrapolation (to account for differences between laboratory animals and humans) and 10x for intraspecies variation (to account for differences within the same species). Additional uncertainty or safety factors may also be applied.

Residential cancer risk estimates are typically expressed as a probability of developing cancer (e.g., one-in-a-million or 1 x 10^{-6}) which is calculated based on exposure estimates and the carcinogenic potential of the compound (Q_1* or "cancer slope factor").

There is the potential for individuals in residential settings to be exposed to HHT and formaldehyde during and following application of products containing HHT. Table 5 presents the representative scenarios used to estimate residential risk from products containing HHT.

Table 5. Representative HHT and Formaldehyde Residential Exposure Scenarios

Chemical	Representative Use	Exposure Scenario	Application Method
HHT	Using treated paints	Handler: ST inhalation (aerosol)	• brush/ roller • airless sprayer
	Using treated household cleaners	Handler: ST inhalation (aerosol) Post-app child: ST and IT incidental ingestion and IT dermal	• mop • wipe • trigger pump/ aerosol
	Using treated laundry detergents	Post-app child: ST and IT incidental ingestion and IT dermal	NA

Chemical	Representative Use	Exposure Scenario	Application Method
Formaldehyde	Using treated paints	Handler: ST inhalation (vapor) and cancer	NA
	Using treated household cleaners	Handler: ST inhalation (vapor) and cancer	NA
	Using treated laundry detergents	Handler: ST inhalation (vapor) and cancer	NA

The duration of exposure for most homeowner applications of cleaning and paint products is believed to be best represented by the short-term duration (1 to 30 days). Only short-term (ST) exposure durations were estimated for the painter based on the assumption that a homeowner or do-it-yourself painter would typically paint on an intermittent basis (i.e., a few times per year). Furthermore, household cleaning exposure scenarios are assumed to be episodic, not daily. In addition, homeowners are also assumed to use different cleaning products with varying active ingredients, not exclusively HHT treated products. For additional information, please see the Occupational and Residential Exposure and Risk Assessment, dated June 30, 2008.

a. HHT Residential Risk

Even using conservative assumptions, estimated risk from exposure to HHT in residential settings does not exceed the Agency's level of concern during application (lowest MOE = 12,000; target MOE = 100) or post-application (lowest MOE = 3,500; target MOE = 1,000). For additional information, please see the Occupational and Residential Exposure and Risk Assessment, dated June 30, 2008.

b. Formaldehyde Residential Risk

Because HHT is a formaldehyde releaser (i.e., formaldehyde is released from products containing HHT), EPA estimated residential risk from formaldehyde. Formaldehyde has a high vapor pressure (1mm Hg); therefore, vapor inhalation is the primary route of residential exposure.

Several scenarios exceeded the Agency's cancer and non-cancer levels of concern both during application and after application (post-application). Table 6 and Table 7 present the cancer and non-cancer risks of concern identified for residential handlers exposed to formaldehyde as a result of HHT use during application. Specific information related to

formaldehyde toxicity and calculation of risk estimates is presented in the Occupational and Residential Exposure and Risk Assessment, dated June 30, 2008. See Section IV of this document for EPA's HHT risk management strategy.

Table 6. HHT Residential Handler Cancer Risks of Concern: Inhalation of Formaldehyde

Representative Use	Percent Conversion	Cancer Risk Estimate		Cancer Risk Target
		IRIS	CIIT Modeling	
Paint	30%	6.8×10^{-6}	$<2.94 \times 10^{-9}$	1.0×10^{-6}
	100%	2.2×10^{-5}	$<2.94 \times 10^{-9}$	
Household cleaners	100%	2.5×10^{-5}	$<2.94 \times 10^{-9}$	
Laundry detergent	100%	1.5×10^{-5}	$<2.94 \times 10^{-9}$	

Table 7. HHT Residential Handler Non-Cancer Risks of Concern: Inhalation of Formaldehyde

Representative Use	Non-Cancer Risk Estimate (MOE)	Non-Cancer Target MOE
Paint	0.22	10
Household cleaners	0.41	10
Laundry detergent	0.22	10

The post-application residential scenarios assessed (dermal/incidental oral exposure for children contacting treated floors, exposure to laundered clothing) did not exceed the Agency's level of concern. The Agency did not estimate risks associated with post-application residential exposure to formaldehyde from paint because exposure during application exceeded EPA's level of concern by such a large degree; therefore, although post-application exposure to paint likely exceeds EPA's level of concern, the risks are likely lower than the residential handler scenario the Agency used to make its risk management decisions. See Section IV of this document for EPA's HHT risk management strategy.

5. Aggregate Exposure and Risk

The Food Quality Protection Act amendments to the Federal Food, Drug, and Cosmetic Act (FFDCA, Section 408(b)(2)(A)(ii)) require "that there is reasonable certainty that no harm will result from aggregate exposure to pesticide chemical residue, including all anticipated dietary exposures and other exposures for which there are reliable information." Aggregate exposure is the total exposure to a single chemical (or its residues) that may occur from dietary (i.e., food and drinking water), residential, and other non-occupational sources.

Table 8 summarizes the scenarios included in the short- and intermediate-term aggregate assessments. The Agency notes that based on the use patterns and probability of co-occurrence, an aggregate assessment was not necessary to conduct for FORMALDEHYDE residues resulting from the use of HHT treated products.

Table 8. Representative HHT Aggregate Exposure Scenarios

	Short-term Aggregate	Intermediate-Term Aggregate
Adults	Inhalation: • Mopping applicator • Wiping applicator • Trigger pump applicator	Dermal or Oral or Inhalation: • No applicable exposures
Children	Oral: • Post-app exposure to floor cleaner residues • Post-app exposure to laundry detergent residues	Oral: • Post-app exposure to floor cleaner residues • Post-app exposure to laundry detergent residues
		Dermal: • Post-app exposure to floor cleaner residues • Post-app exposure to laundry detergent residues

Aggregate exposure did not exceed EPA's level of concern for adult residential handlers of HHT products (lowest MOE = 23,000; target = 100) or children exposed to residues of HHT products (lowest MOE = 2,100; target = 1,000).

6. Occupational Exposure and Risk

Because HHT is currently registered for use in occupational settings, occupational handlers have the potential to be exposed to HHT and formaldehyde through mixing, loading, applying a pesticide or re-entering treated sites. Therefore, EPA estimated risk to occupational handlers as a result of exposure to HHT and formaldehyde from products containing HHT. Occupational non-cancer risks are presented as margins of exposure (MOE) and occupational cancer risks are presented as a probability of developing cancer (e.g., one-in-a-million or 1 x 10^{-6}).

There is the potential for individuals in occupational settings to be exposed to HHT and formaldehyde during and following application of products containing HHT. Table 9 presents the representative occupational uses assessed for HHT.

Table 9. Representative HHT and Formaldehyde Occupational Exposure Scenarios

Chemical	Representative Use	Exposure Scenario	Application Method
HHT	Paints[1]	Handler: ST inhalation (aerosol); IT dermal and inhalation (aerosol) Painter: ST inhalation (aerosol)	<u>Preservation of paint</u> • Liquid pour • Liquid pump <u>Professional painter</u> • Brush/Roller • Airless sprayer

Chemical	Representative Use	Exposure Scenario	Application Method
	Commercial/ household cleaners	Handler: ST inhalation (aerosol); IT dermal and inhalation (aerosol)	• mop • wipe • trigger pump/ aerosol
	Metal working fluids	Handler: ST inhalation (aerosol); IT dermal and inhalation (aerosol) Machinist: IT/LT dermal and ST/IT/LT inhalation (aerosol)	<u>Preservation of fluid</u> • Liquid pour • Liquid pump <u>Professional machinist</u>
	Oil field	Handler: ST inhalation (aerosol); IT dermal and inhalation (aerosol)	• Liquid pour • Liquid pump
Formaldehyde	Using treated paints	Handler and Bystander[1] : ST inhalation (vapor) and cancer	NA
	Using treated metal working fluids	Handler: ST inhalation (vapor) and cancer	NA

[1] The bystander scenario in a paint manufacturing facility also represents all occupational bystander scenarios in a general industrial facility.

To assess handler risk, the Agency used surrogate unit exposure data primarily from the proprietary Chemical Manufacturers Association (CMA) Antimicrobial Exposure Study (USEPA 1999) and the Pesticide Handlers Exposure Database (PHED) (USEPA 1998). For the occupational scenarios in which CMA data were insufficient, other data and methods were applied. For additional information, please see the Occupational and Residential Exposure and Risk Assessment, dated June 30, 2008.

a. HHT Occupational Risk

Even using conservative assumptions, most estimated risks from exposure to HHT in occupational settings did not exceed the Agency's level of concern during application or post-application. However, Table 10 presents the application occupational risks for HHT that exceeded EPA's level of concern.

Table 10. HHT Occupational Handler Non-Cancer Risks of Concern: Dermal Exposure to HHT

Representative Use	Non-Cancer Risk Estimate (MOE)	Non-Cancer Target MOE
Paint	N/A[1]	
Professional cleaners	400	1000
Oil field secondary recovery	690	1000

[1] Although assessed, intermediate-term dermal handler exposure to paint in occupational settings did not exceed EPA's level of concern

See Section IV of this document for EPA's HHT risk management strategy.

b. Formaldehyde Occupational Risk

Even using conservative assumptions, most estimated risks from exposure to formaldehyde in occupational settings did not exceed the Agency's level of concern during application or post-application. However, Table 11 and Table 12 present the cancer and non-cancer occupational handler risks for formaldehyde that exceeded EPA's level of concern.

Table 11. HHT Occupational Handler Cancer Risks of Concern: Inhalation of Formaldehyde

Representative Use	Percent Conversion	Cancer Risk Estimate		Cancer Risk Target
		IRIS	CIIT Modeling	
Metal working fluid	N/A[1]	2.2×10^{-4} to 3.7×10^{-4}	1.46×10^{-8} to 1.86×10^{-8}	1.0×10^{-4} to 1.0×10^{-6}
Paint	30%	8.7×10^{-4}	3.13×10^{-8}	
	100%	2.9×10^{-3}	1.11×10^{-7}	

[1] Not applicable; risk estimates for this scenario were based on exposure information from a study in metal working facilities that use HHT-preserved fluids

Table 12. HHT Occupational Handler Non-Cancer Risks of Concern: Inhalation of Formaldehyde

Representative Use	Non-Cancer Risk Estimate (MOE)	Non-Cancer Target MOE
Paint	0.22	1
Metal working fluid	0.21	1

See Section IV of this document for EPA's HHT risk management strategy.

7. Incident Reports

Only limited incident reports are associated with exposure to end-use products containing HHT. Dermal irritation and dermal sensitization are the primary concerns associated with HHT exposure; conjunctivitis and bronchial asthma have also been reported.

B. Environmental Fate and Ecological Hazard Assessment

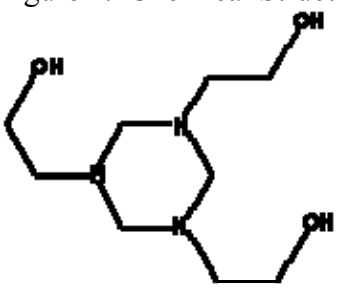
EPA has conducted an environmental fate assessment and an ecological hazard assessment for HHT to support the reregistration eligibility decision. Based on the currently registered use patterns, release and exposure levels are expected to be minimal when products are applied according to label directions and use precautions. EPA evaluated the submitted environmental fate and ecological studies as well as available open literature and determined that the data are adequate to support a reregistration eligibility decision. A summary of the ecological hazard and environmental fate findings and conclusions is provided below; the full risk assessments are available at http://www.regulations.gov in docket number EPA-HQ-OPP-2008-0193.

1. Environmental Fate

a. Hydrolysis

HHT is a symmetric triazine compound with three ethanol side chains attached to the meta nitrogens (see Figure 1). Triazine ethanol was hydrolyzed with an estimated half-life of 3.1 days at pH 5. The hydrolysis half-lives of HHT were 50 and 302 days for pH 7 and 9, respectively.

Figure 1. Chemical Structure of HHT



The only radiolabeled triazine hydrolytic degradate observed in the study was identified as formaldehyde. At pH 5, formaldehyde formation reached 50 % by 2 days, 85 % by 7 days, and 97-100 % by 14-30 days. At pH 7, formaldehyde reached 19 % by 1 day, 25 % by 14 days, and 31 % by 30 days. At pH 9, formaldehyde reached 17-21 % by 1-30 days.

HHT hydrolyzed more quickly at pH 8 than pHs 9.5 and 10.9. At 22 ^{o}C, the half-lives were 3.4 hours, 16 minutes, and 32 seconds at pH 10.9, 9.5, and 8.0, respectively. At 60 ^{o}C, the half-lives were 3.1 minutes and 6.3 seconds for pH 10.9 and 9.5, respectively. The degradation product was not identified, although it was likely to be formaldehyde from breakdown of the triazine ring.

b. Biodegradability

Based on Voets et al. (1975), HHT at 70 mg/L was tested in activated sewage sludge at 1/10th of its intended use concentration. Flasks were incubated at 28 ^{o}C for 24 hours on a

rotary shaker. Under both aerobic and anaerobic conditions, 100 % of HHT was degraded by direct metabolism. Formaldehyde was identified as the metabolism product of HHT.

2. Ecological Hazard

The potential for HHT to be released into the environment at exposure levels of concern to terrestrial and aquatic organisms is low for the registered indoor use patterns. Therefore, EECs have not been modeled and risk has not been assessed for any current HHT uses. The hazard assessment will be used to meet current labeling needs and to determine hazard endpoints for ecological organisms potentially exposed in the event of a spill or other potential environmental releases.

The toxicity endpoints used in the ecological hazard assessment were obtained from guideline toxicity studies conducted for wildlife, aquatic organisms, and plants (40 CFR §158.2060).

One available acute oral study on the bobwhite quail indicates that HHT is only slightly toxic to birds (LD_{50} of 1520 mg/kg). Although not required for the current uses of HHT, the three available dietary studies on the northern bobwhite quail and the mallard duck categorize HHT as being practically nontoxic when ingested (LC_{50} of >5000 ppm). An avian precautionary statement is not required on product labels.

Refer to the human toxicology chapter for details on the available acute mammalian toxicity studies submitted for human health assessment. Based on acute studies in mice and rats, HHT is slightly to moderately toxic via oral dosing (LD_{50} from 750-1300 mg/kg) and dermally in rabbit (>2000 mg/kg).

Honeybee toxicity data are not needed based on the current uses of HHT.

One acute toxicity study is required to establish the toxicity of HHT to freshwater fish. The preferred test species is either the rainbow trout (*Oncorhynchus mykiss*), a coldwater fish, or the bluegill (*Lepomis macrochirus*), a sunfish. For HHT, acute studies are available for both the rainbow trout and the bluegill and for the channel catfish (*Ictalurus punctatus*). The acute toxicity values from these studies categorize HHT as being slightly toxic to freshwater fish (96-hr LC_{50} of 36-77 mg/L). A precautionary label statement is not required.

One study is required to establish the acute toxicity (EC_{50}) of HHT to freshwater invertebrates. The preferred test species is *Daphnia magna*, a water flea. Based solely on mortality (LC_{50}), two studies categorize HHT as being moderately toxic to freshwater invertebrates (48-hr LC_{50} of 5.4-26 mg/L). However, an EC_{50} (based on immobility of exposed daphnids) was not determined in either study. The guideline requirement (OPPTS 850.1010) is satisfied for current uses. However, a study establishing an EC_{50} (based on mortality and immobility) would be needed to support any new uses in which HHT is expected to reach the aquatic environment at exposure levels of concern for aquatic organisms.

Acute toxicity testing with estuarine and marine organisms is required when an end-use product is intended for direct application to the marine/estuarine environment or the active ingredient is toxic to aquatic organisms and is expected to reach this environment via other transport pathways. Studies are required for HHT to support drilling uses in the estuarine/marine environment. The preferred test species are the sheepshead minnow (*Cyprinodon variegatus*), mysid shrimp (*Mysidopsis bahia*), and Eastern oyster (*Crassostrea virginica*). The available data are presented in Table 13. Test results indicate that HHT is practically nontoxic to moderately toxic to estuarine/marine organisms.

Table 13. Acute Toxicity of HHT to Estuarine/Marine Invertebrates

Test Species	% ai tested	96-h LC50 or EC50 (mg ai/L)	Toxicity Category	Study Status	MRID No.
Sheepshead minnow	83.8	>118	practically nontoxic	supplemental	43143102
Eastern oyster	83.8	2.3 (shell deposition)	moderately toxic	core	43175402
Mysid shrimp	83.8	12	slightly toxic	supplemental	43143103

3. Risk to Listed Species

Section 7 of the Endangered Species Act, 16 U.S.C. Section 1536(a)(2), requires all federal agencies to consult with the National Marine Fisheries Service (NMFS) for marine and anadromous listed species, or the United States Fish and Wildlife Services (FWS) for listed wildlife and freshwater organisms, if they are proposing an "action" that may affect listed species or their designated habitat. Each federal agency is required under the Act to insure that any action they authorize, fund, or carry out is not likely to jeopardize the continued existence of a listed species or result in the destruction or adverse modification of designated critical habitat. To jeopardize the continued existence of a listed species means "to engage in an action that reasonably would be expected, directly or indirectly, to reduce appreciably the likelihood of both the survival and recovery of a listed species in the wild by reducing the reproduction, numbers, or distribution of the species" (50 CFR §402.02).

To facilitate compliance with the requirements of the Endangered Species Act subsection (a)(2) the Environmental Protection Agency, Office of Pesticide Programs has established procedures to evaluate whether a proposed registration action may directly or indirectly reduce appreciably the likelihood of both the survival and recovery of a listed species in the wild by reducing the reproduction, numbers, or distribution of any listed species (U.S. EPA 2004). After the Agency's screening-level risk assessment is performed, if any of the Agency's Listed Species LOC Criteria are exceeded for either direct or indirect effects, a determination is made to identify if any listed or candidate species may co-occur in the area of the proposed pesticide use. If determined that listed or candidate species may be

present in the proposed use areas, further biological assessment is undertaken. The extent to which listed species may be at risk then determines the need for the development of a more comprehensive consultation package as required by the Endangered Species Act.

For certain use categories, the Agency assumes there will be minimal environmental exposure, and only a minimal toxicity data set is required (Overview of the Ecological Risk Assessment Process in the Office of Pesticide Programs U.S. Environmental Protection Agency - Endangered and Threatened Species Effects Determinations, 1/23/04, Appendix A, Section IIB, pg.81). Chemicals in these categories therefore do not undergo a full screening-level risk assessment, and are considered to fall under a no effect determination. The material preservative uses for HHT fall into this category.

IV. Reregistration and Risk Management Decisions

A. Determination of Reregistration Eligibility

1. Reregistration Eligibility Decision

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

The Agency has completed its assessment of the residential, occupational and ecological risks associated with the use of pesticide products containing the active ingredient HHT. The Agency has determined that all HHT containing products are eligible for reregistration provided that: 1) all risk mitigation measures are implemented; 2) current data gaps and confirmatory data needs are addressed; and 3) label amendments are made as described in Section V. Appendix A summarizes the uses of HHT that are eligible for reregistration. Appendix B identifies the generic data requirements that the Agency reviewed as part of its determination of reregistration eligibility of HHT and lists the submitted studies that the Agency found acceptable. Data gaps are identified as generic data requirements that have not been satisfied with acceptable data.

EPA considered the available information and has determined that the uses of HHT summarized in Table 14 will not pose unreasonable risks to humans or the environment if the requirements for reregistration outlined in this document are implemented; see Appendix A for a detailed list. Unless labeled and used as specified in this document, HHT would present risks inconsistent with FIFRA. Accordingly, should a registrant fail to implement any of the requirements for reregistration identified in this document, the Agency may take regulatory action to address the potential risk concerns from the use of HHT.

Table 14. Summary of HHT Uses Eligible for Reregistration

Use Site[1]	Mitigation Required
Metal working fluids	Yes[2]
Adhesives	No
Aqueous mineral slurries	No
Construction compounds (caulks, joint cements, spackling, grout, tapes, mortar	No
Aqueous analytical and diagnostic reagents	No
Synthetic fiber lubricants (spin finishes)	No
Fuel systems (diesel oil, fuel oil, gasoline or kerosene systems)	No
Oil field applications (drilling muds, workover/completion fluids, oil recovery injection systems)	Yes[2]

[1] Detailed information is presented in Appendix A

[2] This use is eligible for reregistration provided the mitigation measures and accompanying label changes identified in Table 15 and Table 17 are implemented.

a. Endocrine Disruptor Effects

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

b. Cumulative Risks

Risks summarized in this document are those that result only from the use of HHT. The Food Quality Protection Act (FQPA) requires that, when considering whether to establish, modify, or revoke a tolerance, the Agency consider "available information" concerning the cumulative effects of a particular pesticide's residues and "other substances that have a common mechanism of toxicity." Unlike other pesticides for which EPA has followed a cumulative risk approach based on a common mechanism of toxicity, EPA has not made a common mechanism of toxicity finding as to HHT. EPA has not assumed that the HHT share a common mechanism of toxicity with other compounds.

c. Public Comments and Response

Through EPA's public participation process, EPA worked with stakeholders and the public to reach the regulatory decisions for HHT. During the public comment period on the risk assessments, which closed on June 23, 2008, the Agency received one comment from the Troy Corporation including the submission of an additional inhalation exposure study for

paint. The results of this study, along with other information provided, are reflected in the final risk assessments and this document. All comments and EPA's official responses are available at http://www.regulations.gov in docket number EPA-HQ-OPP-2008-0193.

2. Regulatory Rationale

The Agency has determined that HHT is eligible for reregistration provided that the registrants implement the mitigation measures in this RED through amended labeling. With amended labeling, EPA believes that HHT will not present risks inconsistent with FIFRA and that the benefits of HHT to society – including antimicrobial use in metal working fluids and industrial materials – outweigh the remaining risks. A summary of EPA's rationale for reregistering and managing risks associated with HHT is presented below.

a. Performing Residential Activities

There is the potential for homeowners to be exposed to HHT and formaldehyde either during or after the application of HHT products. To estimate the potential risks associated with these exposures, the Agency assessed representative application and/or post-application exposure scenarios including treated paints, cleaning products, and laundry detergents.

Because the estimated risks associated with treated paints, cleaning products, and laundry detergents exceeded EPA's level of concern by such a large degree – in some cases by more than several orders of magnitude – the Agency believes that these and similar uses do not meet the "no unreasonable adverse effects" criteria of FIFRA. Therefore, HHT products for use in paints, stains, coatings, and institutional and household cleaning products in residential settings are not eligible for reregistration.

However, the Agency believes that certain other residential uses of HHT (see Appendix A) result in significantly lower exposure and risk and present a benefit to society. Therefore, residential uses other than paints, stains, coatings, and institutional and household cleaning products meet the "no unreasonable adverse effects" criteria of FIFRA and are eligible for reregistration.

b. Performing Occupational Activities

There is the potential for workers to be exposed to HHT and formaldehyde either during or after the application of HHT products in an occupational setting. To estimate the potential risks associated with these exposures, the Agency assessed representative application and/or post-application exposure scenarios including treated paints, metal working fluids, and oil fields.

Because the estimated risks associated with treated paints exceeded EPA's level of concern by such a large degree, the Agency believes that this use and similar uses (e.g., stains and coatings) do not meet the "no unreasonable adverse effects" criteria of FIFRA. Therefore, HHT products for use in paints, stains, and coatings in occupational settings are not eligible for reregistration.

However, the Agency believes that certain other occupational uses of HHT (see Appendix A) result in significantly lower exposure and risk and present a benefit to society. Therefore, occupational uses other than paints, stains, and coatings meet the "no unreasonable adverse effects" criteria of FIFRA and are eligible for reregistration provided the mitigation measures and associated label changes presented in Table 15 and Table 17 are implemented.

EPA notes that its level of concern for formaldehyde is below the Occupational Safety and Health Administration (OSHA) permissible exposure limit (PEL). EPA's mitigation measures to reduce exposure for non-cancer effects (e.g., irritation) also account for protecting exposures in the lower range of the cancer assessment.

B. Risk Management Decision

HHT uses presented in Appendix A are eligible for reregistration provided that registrants comply with the requirements outlined in this document including implementing risk mitigation measures, amending product labels, and submitting required confirmatory data.

1. Risk Mitigation Measures

Products containing HHT are eligible for reregistration provided that the registrants implement the risk mitigation measures presented in Table 15. Specific labeling requirements to implement these measures are presented in Table 17. In the future, registrants may request that EPA remove or reduce certain restrictions or mitigation measures upon submission of acceptable toxicity and exposure studies that demonstrate risk exposure to HHT is below OPP's level of concern.

Table 15. Risk Mitigation Measures for HHT

Use Site	Risk(s) of Concern	Mitigation Measures[1]
Paints, Stains, and Coatings	Residential handler inhalation exposure to HHT in paint Occupational handler inhalation exposure to formaldehyde in paint	• Delete use
Metal Working Fluids	Occupational handler inhalation exposure to formaldehyde in metal working fluids	• Reduce maximum application rate from 1600 ppb to 500 ppb
Institutional and Household Cleaning Products	Residential handler inhalation exposure to formaldehyde in cleaners Residential handler inhalation exposure to HHT in laundry detergent	• Delete use
Oil Field Secondary Recovery	Occupational handler dermal exposure to HHT in oil field secondary recovery uses	• Reduce maximum application rate from 0.16% active ingredient (ai) to 0.12% ai

[1] In the future, registrants may request that EPA remove or reduce certain restrictions or mitigation measures upon submission of acceptable toxicity and exposure studies that demonstrate risk to HHT is below OPP's level of concern.

2. Product Label Amendments

Manufacturing-Use Products and End-Use Products must be amended to reflect the mitigation measures presented in Table 15 and the label amendments presented in Table 17 (see Section V).

V. What Registrants Need to Do

The Agency has determined that HHT is eligible for reregistration provided that the requirements for reregistration identified in this RED are implemented (see Section IV). The registrant will also need to amend product labeling for each product.

The database supporting the reregistration of HHT has been reviewed and determined to be adequate to support a reregistration eligibility decision. However, additional confirmatory data are required to support continued registration.

A. Manufacturing Use Products

1. Generic Data Requirements

The generic database supporting the reregistration of HHT for currently registered uses has been reviewed and determined to be adequate to support a reregistration eligibility decision. However, the confirmatory data presented in Table 16 are required. Generally, registrants will have 90 days from receipt of a generic data call-in (GDCI) to complete and submit response forms or request time extensions and/or waivers with a full written justification. Timeframes for submitting generic data will be presented in the GDCI.

Table 16. Generic Data Required to Support HHT Registrations

EPA Guideline Number	Requirement Name
870.1300	Acute Inhalation Study
870.3150	90-day Oral Toxicity in (Non- Rodents)
870.3465	90-Day Inhalation Toxicity in Rats
870.3700	Developmental Toxicity (Non-Rodents)
870.3800	2-Generation Reproductive Toxicity Study
870.4100	Chronic Toxicity
870.4200	Carcinogenicity (Rat and Mouse)
875.1100	Dermal Outdoor Exposure
875.1200	Dermal Indoor Exposure
875.1300	Inhalation Outdoor Exposure
875.1400	Inhalation Indoor Exposure
875.1600	Applicator Exposure Monitoring Data Reporting
875.1700	Product Use Information
875.2700	Product Use Information
875.2800	Description of Human Activity
875.2900	Data Reporting and Calculations

The Agency determined that there are data gaps in the hazard database for HHT based on the current use patterns. Due to the potential inhalation exposure in occupational and residential settings, and based on the lack of inhalation toxicity data, an acute inhalation toxicity study (870.1300) and 90-day inhalation toxicity study (870.3465) must be performed for HHT. In addition, a 90-day oral toxicity in non-rodents (870.3150) is required to assess species sensitivities to the toxicity of HHT.

There are no chronic toxicity and carcinogenicity data for HHT. Risks from the metalworking fluid use of HHT cannot be adequately characterized without these data. Because there are potential endocrine disruption concerns, some positive mutagenicity study findings, and because HHT is a known formaldehyde producer, a chronic toxicity study (870.4100) and carcinogenicity studies (870.4200) in two species are needed. In addition, metalworking fluid use is considered a long-term exposure antimicrobial use pattern and triggers the requirement for carcinogenicity studies and chronic toxicity studies as described on the 1987 Antimicrobial Data Call-In Notice.

There are no data for the reproductive toxicity of HHT. The data for characterizing the developmental and reproductive toxicity of HHT are limited to only developmental toxicity study in rats. Specifically, a non-rodent species should be tested to assess species sensitivity to the toxicity of HHT. A reproductive toxicity study is also necessary to assess any effects on fertility and reproduction, and is required to support the current uses of HHT.

Surrogate dermal and inhalation unit exposure values were taken from the proprietary CMA antimicrobial exposure study (USE EPA 1999: DP Barcode D247642). Most of the CMA data are of poor quality and, therefore, the Agency requests that confirmatory monitoring data be generated to support the values used in the occupational and residential risk assessments and to further refine these assessments. The following confirmatory monitoring data are needed: dermal exposure-indoor & outdoor data (875.1200 and 875.1100, respectively), and inhalation exposure-indoor & outdoor data (875.1400 and 875.1300, respectively). Product use information (875.1700 and 875.2700), description of human activity data (875.2800), and data reporting and calculations (875.2900) are also needed to further define the exposure scenarios being supported and to further refine the assessments.

For HHT technical grade active ingredient products, the registrant needs to submit the following items:

Within 90 days from receipt of the generic data call-in (DCI):

1. Completed response forms to the generic DCI (i.e., DCI response form and requirements status and registrant's response form); and

2. Submit any time extension and/or waiver requests with a full written justification.

Within the time limit specified in the generic DCI:

1. Cite any existing generic data which address data requirements or submit new generic data responding to the DCI.

Please contact Lance Wormell at (703) 603-0523 with questions regarding generic reregistration.

By US mail:
Document Processing Desk
Lance Wormell
Office of Pesticide Programs (7510P)
U.S. Environmental Protection Agency
1200 Pennsylvania Ave., NW
Washington, DC 20460-0001

By express or courier service:
Document Processing Desk
Lance Wormell
Office of Pesticide Programs (7510P)
U.S. Environmental Protection Agency
One Potomac Yard, Room S-4900
2777 South Crystal Drive
Arlington, VA 22202

B. End-Use Products

1. Product Specific Data Requirements

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

Generally, registrants will have 90 days from receipt of a PDCI to complete and submit response forms or request time extensions and/or waivers with a full written justification. Registrants will have eight months to submit product-specific data.

For end-use products containing the active ingredient HHT, the registrant needs to submit the following items for each product.

Within 90 days from the receipt of the product-specific data call-in (PDCI):

1. Completed response forms to the PDCI (i.e., PDCI response form and requirements status and registrant's response form); and

2. Submit any time extension or waiver requests with a full written justification.

Within eight months from the receipt of the PDCI:

1. Two copies of the confidential statement of formula (EPA Form 8570-4);

2. A completed original application for reregistration (EPA Form 8570-1). Indicate on the form that it is an "application for reregistration";

3. Five copies of the draft label incorporating all label amendments outlined in Table 17 of this document;

4. A completed form certifying compliance with data compensation requirements (EPA Form 8570-34);

5. If applicable, a completed form certifying compliance with cost share offer requirements (EPA Form 8570-32); and

6. The product-specific data responding to the PDCI.

Please contact Marshal Swindell at (703) 308-6341 with questions regarding product reregistration and/or the PDCI. All materials submitted in response to the PDCI should be addressed as follows:

By US mail:
Document Processing Desk
Marshal Swindell
Office of Pesticide Programs (7510P)
U.S. Environmental Protection Agency
1200 Pennsylvania Ave., NW
Washington, DC 20460-0001

By express or courier service:
Document Processing Desk
Marshal Swindell
Office of Pesticide Programs (7510P)
U.S. Environmental Protection Agency
Room S-4900, One Potomac Yard
2777 South Crystal Drive
Arlington, VA 22202

2. Labeling for End-Use Products

To be eligible for reregistration, labeling changes are necessary to implement measures outlined in Section IV. Specific language to incorporate these changes is presented in Table 17. Generally, conditions for the distribution and sale of products bearing old labels/labeling will be established when the label changes are approved. However, specific existing stocks time frames will be established case-by-case, depending on the number of products involved, the number of label changes, and other factors.

Registrants may generally distribute and sell products bearing old labels/labeling for 26 months from the date of the issuance of this Reregistration Eligibility Decision document. Persons other than the registrant may generally distribute or sell such products for 52 months from the approval of labels reflecting the mitigation described in this RED. However, existing stocks time frames will be established case-by-case, depending on the number of products involved, the number of label changes, and other factors. Refer to "Existing Stocks of Pesticide Products; Statement of Policy," *Federal Register*, Volume 56, No. 123, June 26, 1991.

Table 17. Required Label Changes for Manufacturing and End-Use Products Containing HHT

Description	HHT: Required Labeling Language	Placement on Label
	Manufacturing-Use Products	
For all Manufacturing Use Products	"Only for formulation as a preservative for the following use(s) [fill blank only with those uses that are being supported by MP registrant]." "Only for formulation into end-use products with directions for use that prohibit use in paints, stains, coatings, and institutional and household cleaning products."	Directions for Use
One of these statements may be added to a label to allow reformulation of the product for a specific use or all additional uses supported by a formulator or user group.	"This product may be used to formulate products for specific use(s) not listed on the MP label if the formulator, user group, or grower has complied with U.S. EPA submission requirements regarding support of such use(s)." "This product may be used to formulate products for any additional use(s) not listed on the MP label if the formulator, user group, or grower has complied with U.S. EPA submission requirements regarding support of such use(s)."	Directions for Use
Environmental Hazards Statements Required by the RED and Agency Label Policies	"Do not discharge effluent containing this product into lakes, streams, ponds, estuaries, oceans, or other waters unless in accordance with the requirements of a National Pollution Discharge Elimination System (NPDES) permit and the permitting authority has been notified in writing prior to discharge. Do not discharge effluent containing this product to sewer systems without previously notifying the local sewage treatment plant authority. For guidance contact your State Water Board or Regional Office of the EPA."	Precautionary Statements
	End-Use Products	
PPE Requirements Established by the RED	"Personal Protective Equipment (PPE)" All mixers and other handlers must wear the following PPE: - long-sleeved shirt and long pants, - shoes plus socks, - chemical-resistant gloves, and - goggles, face shield, or safety glasses."	Immediately following/below Precautionary Statements: Hazards to Humans and Domestic Animals

User Safety Requirement	"Follow manufacturer's instructions for cleaning/maintaining PPE. If no such instructions for washables exist, use detergent and hot water. Keep and wash PPE separately from other laundry." "Discard clothing and other absorbent material that have been drenched or heavily contaminated with the product's concentrate. Do not reuse them."	Precautionary Statements: Hazards to Humans and Domestic Animals Immediately following the PPE requirements
User Safety Recommendations	"USER SAFETY RECOMMENDATIONS" "Users should wash hands before eating, drinking, chewing gum, using tobacco, or using the toilet." "Users should remove clothing/PPE immediately if pesticide gets inside. Then wash thoroughly and put on clean clothing." "Users should remove PPE immediately after handling this product. Wash the outside of gloves before removing. As soon as possible, wash thoroughly and change into clean clothing."	Precautionary Statements: Hazards to Humans and Domestic Animals immediately following Engineering Controls (Must be placed in a box.)
Other Application Restrictions (Risk Mitigation)	For products intended for use in metal working fluids, include the following: "For metal working fluids, the maximum use concentration is 500 parts per billion (ppb) of active ingredient." For products intended for use in oil field secondary recovery, include the following: "For oil field secondary recovery use, the maximum use concentration is 0.12% active ingredient."	Directions for Use Associated with the Specific Use Pattern
Other Application Restrictions (Risk Mitigation)	"Use of this product in paints, stains, coatings, and institutional and household cleaning products is prohibited."	Directions for Use under Other Use Precautions