United States
Environmental Protection
Agency

Prevention, Pesticides
and Toxic Substances
(7510P)

EPA 739-R-07-006
September 2007

Reregistration Eligibility Decision for Glutaraldehyde

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

OFFICE OF
PREVENTION, PESTICIDES
AND TOXIC SUBSTANCES

CERTIFIED MAIL

Dear Registrant:

This is to inform you that the Environmental Protection Agency (hereafter referred to as EPA or the Agency) has completed its review of the available data and public comments received related to the preliminary risk assessments for the antimicrobial glutaraldehyde. The Reregistration Eligibility Decision (RED) for glutaraldehyde was approved on September 28, 2007. Public comments and additional data received were considered in this decision.

Based on its review, EPA is now publishing its Reregistration Eligibility Decision (RED) and risk management decision for glutaraldlehyde and its associated human health and environmental risks. A Notice of Availability will be published in the *Federal Register* announcing the publication of the RED.

The RED and supporting risk assessments for glutaraldehyde are available to the public in EPA's Pesticide Docket EPA-HQ-OPP-2007-0364 at: www.regulations.gov.

The glutaraldehyde RED was developed through EPA's public participation process, published in the Federal Register on September 10, 2004, which provides opportunities for public involvement in the Agency's pesticide tolerance reassessment and reregistration programs. The public participation process encourages robust public involvement starting early and continuing throughout the pesticide risk assessment and risk mitigation decision making process. The public participation process encompasses full, modified, and streamlined versions that enable the Agency to tailor the level of review to the level of refinement of the risk assessments, as well as to the amount of use, risk, public concern, and complexity associated with each pesticide. Using the public participation process, EPA is attaining its strong commitment to both involve the public and meet statutory deadlines.

Please note that the glutaraldehyde risk assessment and the attached RED document concern only this particular pesticide. This RED presents the Agency's conclusions on the dietary, occupational, residential and ecological risks posed by exposure to glutaraldehyde alone. This document also contains both generic and product-specific data that the Agency intends to require in Data Call-Ins (DCIs). Note that DCIs, with all pertinent instructions, will be sent to registrants at a later date. Additionally, for product-specific DCIs, the first set of required responses will be due 90 days from the receipt of the DCI letter. The second set of required responses will be due eight months from the receipt of the DCI letter.

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

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

If you have questions on this document or the label changes relevant to this reregistration decision, please contact the Chemical Review Manager, Michelle Centra, at (703) 308-2476. For questions about product reregistration and/or the Product DCI that will follow this document, please contact Marshall Swindell at (703)-308-6341.

Sincerely,

Betty Shackleford for

Frank T. Sanders
Director, Antimicrobials Division

REREGISTRATION ELIGIBILITY
DECISION
for
Glutaraldehyde
List B
CASE 2315

Approved By:

Frank T. Sanders
Director, Antimicrobials Division
September 28, 2007

Attachment

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GLOSSARY OF TERMS AND ABBREVIATIONS

a.i.	Active Ingredient
aPAD	Acute Population Adjusted Dose
APHIS	Animal and Plant Health Inspection Service
ARTF	Agricultural Re-entry Task Force
BCF	Bioconcentration Factor
CDC	Centers for Disease Control
CDPR	California Department of Pesticide Regulation
CFR	Code of Federal Regulations
ChEI	Cholinesterase Inhibition
CMBS	Carbamate Market Basket Survey
cPAD	Chronic Population Adjusted Dose
CSFII	USDA Continuing Surveys for Food Intake by Individuals
CWS	Community Water System
DCI	Data Call-In
DEEM	Dietary Exposure Evaluation Model
DL	Double layer clothing {i.e., coveralls over SL}
DWLOC	Drinking Water Level of Comparison
EC	Emulsifiable Concentrate Formulation
EDSP	Endocrine Disruptor Screening Program
EDSTAC	Endocrine Disruptor Screening and Testing Advisory Committee
EEC	Estimated Environmental Concentration. The estimated pesticide concentration in an environment, such as a terrestrial ecosystem.
EP	End-Use Product
EPA	U.S. Environmental Protection Agency
EXAMS	Tier II Surface Water Computer Model
FDA	Food and Drug Administration
FFDCA	Federal Food, Drug, and Cosmetic Act
FIFRA	Federal Insecticide, Fungicide, and Rodenticide Act
FOB	Functional Observation Battery
FQPA	Food Quality Protection Act
FR	Federal Register
GL	With gloves
GPS	Global Positioning System
HIARC	Hazard Identification Assessment Review Committee
IDFS	Incident Data System
IGR	Insect Growth Regulator
IPM	Integrated Pest Management
RED	Reregistration Eligibility Decision
LADD	Lifetime Average Daily Dose
LC_{50}	Median Lethal Concentration. Statistically derived concentration of a substance expected to cause death in 50% of test animals, usually expressed as the weight of substance per weight or volume of water, air or feed, e.g., mg/l, mg/kg or ppm.
LCO	Lawn Care Operator
LD_{50}	Median Lethal Dose. Statistically derived single dose causing death in 50% of the test animals when administered by the route indicated (oral, dermal, inhalation), expressed as a weight of substance per unit weight of animal, e.g., mg/kg.
LOAEC	Lowest Observed Adverse Effect Concentration
LOAEL	Lowest Observed Adverse Effect Level
LOC	Level of Concern
LOEC	Lowest Observed Effect Concentration
mg/kg/day	Milligram Per Kilogram Per Day
MOE	Margin of Exposure
MP	Manufacturing-Use Product
MRID	Master Record Identification (number). EPA's system of recording and tracking studies submitted.
MRL	Maximum Residue Level

N/A	Not Applicable
NASS	National Agricultural Statistical Service
NAWQA	USGS National Water Quality Assessment
NG	No Gloves
NMFS	National Marine Fisheries Service
NOAEC	No Observed Adverse Effect Concentration
NOAEL	No Observed Adverse Effect Level
NPIC	National Pesticide Information Center
NR	No respirator
OP	Organophosphorus
OPP	EPA Office of Pesticide Programs
ORETF	Outdoor Residential Exposure Task Force
PAD	Population Adjusted Dose
PCA	Percent Crop Area
PDCI	Product Specific Data Call-In
PDP	USDA Pesticide Data Program
PF10	Protection factor 10 respirator
PF5	Protection factor 5 respirator
PHED	Pesticide Handler's Exposure Data
PHI	Pre-harvest Interval
ppb	Parts Per Billion
PPE	Personal Protective Equipment
PRZM	Pesticide Root Zone Model
RBC	Red Blood Cell
RED	Reregistration Eligibility Decision
REI	Restricted Entry Interval
RfD	Reference Dose
RPA	Reasonable and Prudent Alternatives
RPM	Reasonable and Prudent Measures
RQ	Risk Quotient
RTU	(Ready-to-use)
RUP	Restricted Use Pesticide
SCI-GROW	Tier I Ground Water Computer Model
SF	Safety Factor
SL	Single layer clothing
SLN	Special Local Need (Registrations Under Section 24C of FIFRA)
STORET	Storage and Retrieval
TEP	Typical End-Use Product
TGAI	Technical Grade Active Ingredient
TRAC	Tolerance Reassessment Advisory Committee
TTRS	Transferable Turf Residues
UF	Uncertainty Factor
USDA	United States Department of Agriculture
USFWS	United States Fish and Wildlife Service
USGS	United States Geological Survey
WPS	Worker Protection Standard

ABSTRACT

The Environmental Protection Agency (EPA or the Agency) has completed the human health and environmental risk assessments for glutaraldehyde and is issuing its risk management decision. The risk assessments, which are summarized below, are based on the review of the required target database supporting the use patterns of currently registered products and additional information received through the public docket. After considering the risks identified in the revised risk assessments, comments received, and mitigation suggestions from interested parties, the Agency developed its risk management decision for uses of glutaraldehyde that pose risks of concern. As a result of this review, EPA has determined that glutaraldehyde -containing products are eligible for reregistration, provided that risk mitigation measures are adopted and labels are amended accordingly. That decision is discussed fully in this document.

I. Introduction

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

On August 3, 1996, the Food Quality Protection Act of 1996 (FQPA) was signed into law. This Act amends FIFRA to require tolerance reassessment. The Agency has decided that, for those chemicals that have tolerances and are undergoing reregistration, the tolerance reassessment will be initiated through this reregistration process. The Act also required that by 2006, EPA must review all tolerances in effect on the day before the date of the enactment of the FQPA. FQPA also amends the Federal Food, Drug, and Cosmetic Act (FFDCA) to require a safety finding in tolerance reassessment based on factors including consideration of cumulative effects of chemicals with a common mechanism of toxicity. This document presents the Agency's revised human health and ecological risk assessments; and the Reregistration Eligibility Decision (RED) for glutaraldehyde.

Glutaraldehyde is a disinfectant, sanitizer, biocide, fungicide, microbiocide, tuberculocide, and virucide antimicrobial chemical. As an antimicrobial agent, glutaraldehyde is applied to various sites, including food handling and food storage establishments such as commercial egg hatcheries, poultry/livestock equipment and processing premises, animal feeding and watering equipment; commercial/industrial buildings and trucks, construction materials, and laundry equipment; oil recovery drilling muds and secondary oil recovery injection water; metalworking fluids; commercial/industrial evaporative condensers and heat exchanger water systems; hospital, veterinary and laboratory premises/equipment; non-critical hospital plastic and rubber items; industrial coatings; and in the manufacture of a variety of materials as a preservative: cleaners, adhesives, paper and paperboard, water based coatings, latex paints, inks and dyes. Glutaraldehyde-containing products are also approved for use in aquatic areas such as ponds, flood water, and sewage water. It is not registered for any direct food uses.

The Agency has concluded that the special hazard-based FQPA Safety Factor should be removed (reduced to 1x) for glutaraldehyde based on the following: (1) the toxicology data base is complete with respect to assessing the increased susceptibility to infants and children as required by FQPA; (2) there is no concern for developmental neurotoxicity resulting from exposure to in the rat and rabbit prenatal developmental studies and 2-generation reproduction study; (3) there is no evidence of increased susceptibility to the fetus following *in utero* exposure in the prenatal developmental toxicity studies or to the offspring when adults are exposed in the two-generation reproduction study; and (4) the risk assessment does not underestimate the potential exposure for infants and children.

Risks summarized in this document are those that result from the use of the active ingredient glutaraldehyde. The Food Quality Protection Act (FQPA) requires that the Agency consider available information concerning the cumulative effects of a particular pesticide's residues and other substances that have a common mechanism of toxicity. The reason for consideration of other substances is due to the possibility that low-level exposures to multiple chemical substances that cause a common toxic effect by a common toxic mechanism could lead to the same adverse health effect that would occur at a higher level of exposure to any of the substances individually. 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 for glutaraldehyde and any other substances. Glutaraldehyde does not appear to produce a toxic metabolite produced by other substances. For the purposes of this action, therefore, EPA has not assumed that glutaraldehyde has a common mechanism of toxicity with other substances. For information regarding EPA's efforts to determine which chemicals have a common mechanism of toxicity and to evaluate the cumulative effects of such chemicals, see the policy statements released by EPA's Office of Pesticide Programs concerning common mechanism determinations and procedures for cumulating effects from substances found to have a common mechanism on EPA's website at http://www.epa.gov/pesticides/cumulative.

This document presents the Agency's decision regarding the reregistration eligibility of the registered uses of glutaraldehyde. In an effort to simplify the RED, the information presented herein is summarized from more detailed information which can be found in the technical supporting documents for glutaraldehyde referenced in this RED. The revised risk assessments and related addenda are not included in this document, but are available in the Public Docket at http://www.regulations.gov (Docket ID #EPA-HQ-OPP-2007-0364).

This document consists of six sections. Section I is the introduction. Section II provides a chemical overview, a profile of the use and usage of Glutaraldehyde, and its regulatory history. Section III, Summary of Glutaraldehyde Risk Assessments, gives an overview of the human health and environmental assessments based on the data available to the Agency. Section IV, Risk Management, Reregistration, and Tolerance Reassessment Decision, presents the reregistration eligibility and risk management decisions. Section V, What Registrants Need to Do, summarizes the necessary label changes based on the risk mitigation measures outlined in Section IV. Finally, the Appendices list all use patterns eligible for reregistration, bibliographic information, related documents and how to access them, and Data Call-In (DCI) information.

II. Chemical Overview

A. Regulatory History

The first product containing glutaraldehyde was registered on March 5, 1963. This reregistration case consists of a single pc code, 043901. There are currently 60 active products and two pending registrations for antimicrobial pesticide products containing glutaraldehyde as an active ingredient registered under Section 3 of the Federal Insecticide, Fungicide, and Rodenticide Act (FIFRA).

B. Chemical Identification

1. Chemical Identity of Glutaraldehyde:

Chemical Name: 1, 5 Pentanedial
Chemical Family: Aldehyde
Common/Trade Name: Glutaraldehyde, Ucarcide 250, Glutaral
CAS Number: 111-30-8
Molecular Formula: $C_5H_8O_2$
Chemical Structure:

$OHC\text{-}CH_2\text{-}CH_2\text{-}CH_2\text{-}CHO$

Table 1. Chemical Characteristics for Technical Grade Active Ingredient Glutaraldehyde

Chemical Characteristics	
Molecular Weight	100.11
Color	Colorless
Odor	Sharp and pungent
Physical State	Liquid/Pale Yellow Liquid
Specific Gravity	1.13 at 20 ^oC
Dissociation Constant	Not applicable
pH	3.1-4.5 / 3.5
Stability	Stable for extended period of time at proper conditions
Melting Point	Not applicable to a liquid. The freezing point is -18 ^oC to -21.2 ^oC.
Boiling Point	100.7 ^oC at 760 mm Hg / 95 ^oC
Water Solubility	51.3 g/L
Octanol-Water Partition constant (Log K_{OW})	-0.18
Vapor Pressure	17 mm Hg @ 20 ^oC 11.5 mm Hg 20 mm Hg
Henry's Law Constant	2.4 x 10^{-8} atm-m^3 / mol
Half Life (in air)	3.0 hours
Oxidation/Reduction	Not applicable. Technical grade active ingredient does not contain any oxidizing or reducing agents
Flammability	Not reported

Chemical Characteristics	
Explodability	Technical grade active ingredient is not explosive
Viscosity	20.15 cp @ 20 ^{o}C/2 cps @ 20 ^{o}C
Miscibility	Miscible
Corrosion Characteristic	Not applicable
Dielectric Breakdown Voltage	Not established for technical grade active ingredient

C. Use Profile

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

Type of Pesticide: Algaecide
Bacteriocide
Fungicide

Summary of Use:

Products containing glutaraldehyde as an active ingredient are intended for use in agricultural, food handling, commercial/institutional/ industrial, residential and public access, and medical settings (Use Site Categories I, II, III, IV and V, respectively), as well as a materials preservative for a variety of products (Use Site Category VII) and as an industrial processes and water systems treatment (Use Site Category X). Some examples of uses are listed below, for a detailed use description please refer to Appendix A.

Agricultural Premises and Equipment:
Glutaraldehyde is used for egg sanitation, in hatcheries, setters and chick processing facilities; in animal housing buildings; on farm equipment, trays, racks, carts, chick boxes, cages, trucks, vehicles, and other hard surfaces.

Commercial/Institutional/Industrial: Glutaraldehyde is used in janitorial, commercial, and industrial facilities; in laboratories, biomedical research facilities, nursing homes, veterinary hospitals and facilities, on cages, urinals, and hard surfaces; and in the treatment of medical waste, human waste and animal waste.

Residential and Public Access: Glutaraldehyde is used in applications to treat hard surfaces in public access premises.

Materials Preservatives:
Glutaraldehyde is used in industrial, institutional, and consumer in-can process and products; concrete admixtures; and reverse osmosis membranes.

Medical Premises and Equipment:
Glutaraldehyde is used to disinfect hospital, medical, and dental office equipment/ premises/surfaces; and solid and liquid medical waste.

Industrial Processes and Water Systems: Glutaraldehyde is used in oil-storage tanks; water floods; drilling muds, drilling, completion, and workover fluids; packer fluids; gas-production and transmission pipe systems; gas storage wells and systems; hydrotesting; pipeline pigging and scraping operations; paper mills and paper mill process water systems; pigments, filler slurries and water based coatings for paper and paperboard; metalworking fluids; water-based conveyor lubricants; air washer and industrial scrubbing; systems/recirculating cooling and process water systems; service water and auxiliary systems; heat transfer systems; industrial waste-water systems; and sugar beet mills and process water systems.

Target Pests: Deterioration/spoilage bacteria, fungi (coatings, leather, metal working coolants), mildew, mold, pseudomonas spp.

Formulation Types of Glutaraldehyde:

Soluble concentrates, ready-to-use solutions, impregnated materials, water soluble packages, and microencapsulated preparations (medical waste). Glutaraldehyde is not available as a neat, undiluted chemical. However, it is commercially available as 4%, 15%, 25%, 45%, and 50% (v/v) aqueous solutions.

Method and Rates of Application:

The methods and rates of application for Glutaraldehyde-containing products vary greatly depending on use site. Please refer to Appendix A for more detailed application rates for each use site and methods of application..

Use Classification: General use.

Manufactures (Technical Grade Active Ingredient):

The Dow Chemical Company
BASF Corporation

III. Summary of Glutaraldehyde Risk Assessments

The purpose of this summary is to assist the reader by identifying the key features and findings of these risk assessments and to help the reader better understand the conclusions reached in the assessments. 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 glutaraldehyde. While the risk assessments and related addenda are not included in this document, they are available from the OPP Public Docket EPA-HQ-OPP-2007-0364, and may also be accessed from www.regulations.gov. Hard copies of these documents may be found in the OPP public docket. The OPP public docket is located in Room S-4900, One Potomac Yard, 2777 South Crystal Drive, Arlington, VA 22202, and is open Monday through Friday, excluding Federal holidays, from 8:30 a.m. to 4:00 p.m.

The Agency's use of human studies in the glutaraldehyde 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

1. Toxicity of Glutaraldehyde

A brief overview of the toxicity studies used for determining endpoints in the risk assessment is outlined below in Table 1. Further details on the toxicity of glutaraldehyde can be found in the supporting toxicology documents listed in Appendix C. These documents are available on the Agency's website in the EPA Docket at: http://www.regulations.gov (Docket ID #EPA-HQ-OPP-2007-0364).

The Agency has reviewed all toxicity studies submitted for glutaraldehyde as well as open literature data and determined that the toxicological database is substantially complete for the purpose of reregistration. Most of these studies have been submitted to support the guideline requirements for toxicity testing.

Major features of the toxicology profile are presented below. Glutaraldehyde exhibits low acute dermal and inhalation toxicity (Toxicity Category III and IV, respectively). However, it is highly toxic via the acute oral route (Toxicity Category II) and highly irritating to the eyes and skin (Toxicity Category I). In a submitted local lymph node assay, glutaraldehyde produced a dose-related increase in proliferative activity, indicating that it is a positive dermal sensitizer.

Table 2. Summary of Acute Toxicity Data for Glutaraldehyde

Guideline Number	Study Type/ Test substance (% a.i.)	MRID #(s)	Results	Toxicity Category
870.1100	Acute Oral - Rat Glutaraldehyde (50% a.i.)	00011706 00164370	LD_{50} = 360 mg/kg (male) LD_{50} = 420 mg/kg (female) LD_{50} = 460 mg/kg (combined)	II
870.1200	Acute Dermal - Rabbit Glutaraldehyde (50.2%)	44691606	LD_{50} > 2000 mg/kg (combined)	III

Guideline Number	Study Type/ Test substance (% a.i.)	MRID #(s)	Results	Toxicity Category
870.1300	Acute Inhalation - Rat.	00060275	LC_{50} > 4.16 mg/L	IV
870.2400	Primary Eye Irritation - Rabbit Glutaraldehyde (0.5%)	00117066	Corrosive at high concentrations, such as 50% a.i.	I
870.2500	Primary Dermal Irritation - Rabbit Glutaraldehyde (50%)	00117061	Corrosive Primary Irritation Score (PIS) = 6.34	I
870.2600	Dermal Sensitization –LLNA Assay in Mice	43330201	SI > 3 ; positive sensitizer	N/A

Notes: LC = Lethal Concentration; LD = Lethal Dose; NA = Not Applicable

The doses and toxicological endpoints selected for the dietary exposure scenarios are summarized in Table 3 below:

Table 3. Dietary Toxicological Endpoints for Glutaraldehyde

Exposure Scenario	Dose Used in Risk Assessment, UF	Special FQPA SF* and Level of Concern for Risk Assessment	Study and Toxicological Effects
Acute Dietary (females 13-49)	No appropriate endpoints were identified that represent a single dose effect. Therefore, this risk assessment is not required.		
Chronic Dietary (all populations)	**NOAEL**= 16.1 mg/kg/day	**UF** = 100 (10x inter-species extrapolation and intra-species variation) **FQPA SF** = 1x **Chronic RfD = cPAD =** 0.16 mg/kg/day	Carcinogenicity Study (drinking water) in the Rat (MRID 46212701) **LOAEL** = 61 mg/kg/day based on increases in non-neoplastic lesions (squamous metaplasia, foreign body granuloma, pirulent inflammation) of the respiratory tract and erosion/ulceration in the mucosa of the glandular stomach.
Cancinogenicity	In accordance with the EPA Final Guidelines for Carcinogen Risk Assessment (March 29, 2005), the Health Effects Division's Carcinogenicity Assessment Review Committee concluded that glutaraldehyde was **"not likely to be carcinogenic to humans"** by any route of exposure.		

Notes: UF = uncertainty factor, FQPA SF = FQPA safety factor, NOAEL = no observed adverse effect level, LOAEL = lowest observed adverse effect level, PAD = population adjusted dose (a = acute, c = chronic) RfD = reference dose

General Toxicity Observations

Developmental and Reproductive/Fertility Effects

Developmental toxicity studies conducted in rats and rabbits were available for glutaraldehyde. In a developmental toxicity study conducted in rabbits, a NOAEL of 15 mg/kg/day and a NOAEL of 45 mg/kg/day was established for maternal and developmental toxicity, respectively. For maternal toxicity, the LOAEL was based on maternal death (4/15 treatment-related), sharply decreased food consumption, markedly decreased body weight/ body weight gain, and increased incidence of soft stool, diarrhea, or no defecation. For developmental toxicity, the LOAEL is based on almost complete early resorption (1 surviving litter) and

decreased body weight of 4 surviving fetuses. In two developmental (oral) toxicity studies conducted in the rat, NOAELs for maternal and developmental toxicity were greater than the highest doses tested (50 and 68 mg/kg/day, respectively) and therefore, LOAELs were not established.

Two-generation reproduction toxicity studies were submitted for glutaraldehyde. In the first study, a parental systemic toxicity and reproductive toxicity were not observed in rats at concentrations up to the highest dose tested, 1000 ppm. For pups in both generations, systemic/developmental toxicity was observed as decreased body weight gain on lactation days 14, 21, and 28; a NOAEL of 250 ppm and a LOAEL of 1000 ppm was established. In the second reproduction toxicity study, a parental systemic toxicity LOAEL of 76 mg/kg/day and 95.6 mg/kg/day and a NOAEL of 22.4 mg/kg/day and 28.7 mg/kg/day for males and females, respectively, based on decreased body weight, body weight gain, and food consumption, as well as macroscopic and microscopic changes in the glandular stomach. Adverse effects on reproductive performance and fertility effects were not observed at the highest doses tested, 76 mg/kg/day for males, 95.6 mg/kg /day for females. The offspring LOAEL is 76 mg/kg/day and 95.6 mg/kg /day and the NOAEL is 22.4 mg/kg/day and 28.7 mg/kg/day for males and females, respectively, based on decreased litter and pup weights.

Subchronic Toxicity

Several subchronic oral, dermal and inhalation toxicity studies were conducted with glutaraldehyde. In a range-finding (14-day) oral toxicity study in mice, no toxicities were observed and the NOAEL was established at the highest doses tested (257.4 and 327.6 mg/kg/day in males and females, respectively). In the 90-day subchronic oral toxicity study conducted in mice, glutaraldehyde was administered in drinking water and a NOAEL of 60.8 and 74.3 mg/kg/day for males and females, respectively was established based on a treatment-related increase in gastritis and possibly treatment-related decreases in urine volume and osmolality that occurred at a LOAEL of 199.8 and 238.1 mg/kg/day for males and females, respectively. In a combined 90-day oral (drinking water) subchronic and neurotoxicity study in rats, NOAELs of 52.9 and 71.5 mg/kg/day were established at the highest doses tested for males and females, respectively. A LOAEL was not established in this study and there were no observed neurotoxic effects. The 90-day oral (drinking water) toxicity study conducted in dogs established a NOAEL of 9.8 mg/kg/day based on increased incidence of vomiting in males and females that occurred at a LOAEL of 14.6 mg/kg/day.

Following a subchronic, 28-day dermal exposure, glutaraldehyde, caused dermal irritation (erythema and edema) and skin lesions (discoloration, acanthosis, hyperkeratosis, dermatitis, epidermitis and dermal fibrosis) in rats at the LOAEL of 100 mg/kg/day. The NOAEL was established at 50 mg/kg/day in this study.

In a 14-day subchronic inhalation toxicity study conducted in F344/N rats and $B_6C_3F_1$ mice, animals were exposed to glutaraldehyde by whole-body inhalation. Toxicities observed at the LOAEL of 0.5 ppm (2.0 mg/m^3) included histopathological changes in the nasal passages and turbinates (hyperplasia and squamous metaplasia), the larynx and trachea (inflammation, necrosis and squamous metaplasia), and the lung and bronchi (inflammation); the NOAEL was established at 0.16 ppm (0.7 mg/m^3). In a longer duration (90-day) subchronic inhalation

(whole-body) toxicity study conducted in same species, the NOAEL was established at 125 ppb (0.512 mg/m^3) based on histopathological changes in the nasal and respiratory tract (hyperplasia, squamous metaplasia and inflammation of the nasoturbinate/septal epithelium, degeneration of the olfactory epithelium and squamous exfoliation of the nasal vestibule/anterior nares) observed at the LOAEL of 250 ppb (1.02 mg/m^3). A second 90-day inhalation (whole-body) toxicity study conducted in F344 rats showed only decreased body weight gains throughout the study at 49.3 ppb and above.

Chronic Toxicity

Three chronic toxicity studies are available for glutaraldehyde, including three oral studies (two in the rat and one in the dog) and one chronic inhalation study in rats and mice. In the first oral (drinking water) toxicity study, the NOAEL was established at 500 ppm (15.4 and 23.2 mg/kg/day in males and females, respectively) based on decreased body weight in males, increased incidence of erosions and ulcers in the glandular stomach of both sexes and a slight increase in clear cell foci of the liver in males observed at the LOAEL of 2000 ppm (58.9 and 77.4 mg/kg/day in males and females, respectively). The second drinking water toxicity study toxicities that included slightly decreased body weight/body weight gain in males and decreased food consumption in males and females; the NOAEL was established at 50 ppm (17 and 25 mg/kg/day in males and females, respectively). In the dog drinking water toxicity study, no toxicities were observed and the NOAEL established in this study is the highest dose tested (500 ppm (15.6 mg/kg/day).

In the two-year chronic toxicity/carcinogenicity inhalation toxicity study conducted in F344/N rats and $B_6C_3F_1$ mice, whole-body exposure to glutaraldehyde resulted in microscopic lesions (inflammation, hyperplasia, squamous metaplasia and hyaline degeneration of the epithelium) of the nose and respiratory tract observed at the LOAEL of 250 ppb (1.02 mg/m3; lowest dose tested) in rats and at the LOAEL of 62.5 ppb (0.26 mg/m3; lowest dose tested) in mice; the NOAEL was not established in either species. At the concentrations tested in this study, there was no evidence for carcinogenicity of glutaraldehyde in either rats or mice.

Neurotoxicity

The available toxicity data do no indicate neurotoxicity in rats exposed to glutaraldehyde by the oral (drinking water) route of administration.

Dietary

An acute dietary endpoint was not identified in the glutaraldehyde toxicology database because no effect observed could be attributed to a single dose effect. Therefore, an acute RfD was not calculated for glutaraldehyde.

The chronic RfD for glutaraldehyde is 0.16 mg/kg/day for all populations. The chronic RfD was established by using a NOAEL of 16.1 mg/kg/day, which is based on increases in non-neoplastic lesions (squamous metaplasia, foreign body granuloma, pirulent inflammation) of the respiratory tract and erosion/ulceration in the mucosa of the glandular stomach.observed at the LOAEL of 61 mg/kg/day in a carcinogenicity study conducted in rats. An uncertainty factor of 100

(10x for inter-species extrapolation and 10x for intra-species variation) was applied to the selected endpoint.

Short-term Dermal

The short-term dermal NOAEL is 50 mg/kg/day (2.5% @ 40 µl/cm^2 ;1000 µg/cm^2) based on dermal irritation (erythema and edema) and skin lesions (discoloration, acanthosis, hyperkeratosis, dermatitis, epidermitis and dermal fibrosis) in rats observed at the LOAEL of 100 mg/kg/day in a 28-day dermal toxicity study. The "target" MOE, for the short-term dermal exposure is 10X (3x for inter-species extrapolation and 3x intra-species variation).

Short-term Inhalation

The short-term inhalation NOAEL is 0.7 mg/m^3 based on histopathological changes in the nasal passages and turbinates (hyperplasia and squamous metaplasia), the larynx and trachea (inflammation, necrosis and squamous metaplasia), and the lung and bronchi (inflammation) observed at the LOAEL of 2.0 mg/m^3 in a 14-day inhalation toxicity study conducted in mice and rats. The NOAEL value of 0.7 mg/m^3 was converted to a human equivalent concentration of 0.041 and 0.014 mg/m^3 for occupational and residential exposures, respectively. The "target" MOE, for the short-term inhalation exposure is 30 (3x for inter-species extrapolation and 10x for intra-species variation).

Intermediate-term Inhalation

The intermediate-term inhalation NOAEL is 0.512 mg/m^3 based on histopathological changes in the nasal and respiratory tract (hyperplasia, squamous metaplasia and inflammation of the nasoturbinate/septal epithelium, degeneration of the olfactory epithelium and squamous exfoliation of the nasal vestibule/anterior nares) observed at the LOAEL of 1.02 mg/m^3 in a 90-day (whole-body) inhalation toxicity study conducted in rats and mice. The NOAEL value of 0.512 mg/m^3 was converted to a human equivalent concentration of 0.03 and 0.01 mg/m^3 for occupational and residential exposures, respectively. The "target" MOE, for the intermediate-term inhalation exposure is 30 (3x for inter-species extrapolation and 10x for intra-species variation).

Long-term Inhalation

The long-term inhalation LOAEL is 0.26 mg/m^3 based on microscopic lesions (inflammation, hyperplasia, squamous metaplasia and hyaline degeneration of the epithelium) of the nose and respiratory tract observed in a two-year chronic inhalation (whole-body) toxicity study conducted in mice. A NOAEL value was not established. The LOAEL value of 0.26 mg/m^3 was converted to a human equivalent concentration of 0.019 and 0.004 mg/m^3 for occupational and residential exposures, respectively. The "target" MOE, for the long-term inhalation exposure is 300 (3x for inter-species extrapolation, 10x for intra-species variation and 10x for use of a LOAEL).

Carcinogenicity Classification

The carcinogenic potential of glutaraldehyde was tested in several two-year rat studies via the inhalation and oral (drinking water) route of administration. By the inhalation route, there was no evidence of carcinogenicity for glutaraldehyde in either Fischer 344 rats or $B_6C_3F_1$ mice. In a drinking water carcinogenicity study, Wistar rats showed no carcinogenic response to glutaraldehyde. However, a positive carcinogenic response was observed in a second oral (drinking water) carcinogenicity study conducted in Fischer 344 rats, a strain of rat known to be susceptible to development of large granular lymphocyte leukemia (LGLL). In female Fischer 344 rats, an increased incidence of LGLL was observed in this study. Although the highest dose tested showed a significant increase in LGLL tumor incidence, the lower doses gave no clear indication of a dose-response. In addition, comparison of the response at lower doses with historical control data showed that this tumor type in general has a wide variability of incidence even in untreated animals. Thus, the increased incidence of LGLL is not considered a treatment-related effect of glutaraldehyde. This conclusion is supported by the available experimental evidence that has not identified a clear etiology for LGLL in the rat. These data were reviewed by OPP's Carcinogenicity Assessment Review Committee (CARC) in February of 2006. The CARC classified glutaraldehyde as **"**Not Likely to be Carcinogenic to Humans" by any route of exposure.

Mutagenicity Potential

Based on the results of a battery of submitted mutagenicity studies as well as published literature, glutaraldehyde produced reverse gene mutations in *Salmonella typhimurium*, and showed positive responses for forward gene mutations in Chinese hamster (CHO) cell and mouse lymphoma cells . However, glutaraldehyde was not mutagenic at the HGPRT locus and was negative for chromosome aberration studies in CHO cells. Glutaraldehyde has produced inconsistent results in several *in vitro* tests. Consequently, these data results are considered equivocal. The negative results shown in sister chromatid (SCE) induction in CHO cells together with the no cell transformation occurring in an in vitro Syrian hamster embryo cells suggests that glutaraldehyde has limited mutagenic potential because of its high cytotoxicity. Therfore, glutaraldhyde is considered non mutagenic or genotoxic.

Endocrine Disruption Potential

EPA is required under the Federal Food Drug and Cosmetic Act (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 such endocrine effects as the Administrator may designate." Following recommendations of its Endocrine Disruptor 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 the Program include evaluations of potential effects in wildlife. For pesticide chemicals, EPA will use FIFRA and, to the extent that effects in wildlife may help determine whether a substance may have an effect in humans, FFDCA authority to require the wildlife evaluations. As the science develops and resources

allow, screening of additional hormone systems may be added to the Endocrine Disruptor Screening Program (EDSP). When the appropriate screening and/or testing protocols being considered under the Agency's Endocrine Disrupting Screening Program (EDSP) have been developed, glutaraldehyde may be subjected to additional screening and/or testing to better characterize effects related to endocrine disruption.

2. FQPA Safety Factor

The FQPA Safety Factor (as required by the Food Quality Protection Act of 1996) is intended to provide an additional 10-fold safety factor (10x), to protect for special sensitivity in infants and children to specific pesticide residues in food, drinking water, or residential exposures, or to compensate for an incomplete database. The Agency has concluded that the special hazard-based FQPA safety factor can be removed (i.e., reduced to 1x) for glutaraldehyde based on: (1) a complete toxicology data base with respect to assessing increased susceptibility to infants and children as required by FQPA; (2) a lack of evidence that glutaraldehyde will induce neurotoxic effects; (3) no evidence of increased susceptibility to the fetus following *in utero* exposure in the prenatal developmental toxicity studies; (4) no evidence of increased susceptibility to the offspring when adults are exposed in the two-generation reproduction study; and (5) the risk assessment does not underestimate the potential exposure for infants and children. Based on the analysis of submitted toxicity studies, the Agency determined that no special hazard-based FQPA Safety Factor was needed since there were no residual uncertainties for pre- and/or post-natal toxicity.

3. Population Adjusted Dose (PAD)

Dietary risk is characterized in terms of the Population Adjusted Dose (PAD), which reflects the reference dose (RfD), either acute or chronic, that has been adjusted to account for the FQPA Safety Factor (SF). This calculation is performed for each population subgroup. A risk estimate that is less than 100% of the acute or chronic PAD is not of concern. The Agency has conducted a dietary exposure and risk assessment for the use of glutaraldehyde as a hard surface cleaner, in animal premises and poultry premises(including hatcheries) and as a slimicide and materials preservative in pulp and paper manufacturing.

a. Acute PAD

An acute dietary assessment was not conducted for glutaraldehyde because no appropriate endpoints were identified in the toxicology database representative of a single dose effect.

b. Chronic PAD

Chronic dietary risk for glutaraldehyde is assessed by comparing chronic dietary exposure estimates (in mg/kg/day) to the chronic Population Adjusted Dose (cPAD). Chronic dietary risk is expressed as a percent of the cPAD. The cPAD is the chronic reference dose (0.16 mg/kg/day) modified by the FQPA safety factor. The cPAD was derived from a chronic oral (drinking water) toxicity study in rats in which the LOAEL (61 mg/kg/day) was determined. The glutaraldehyde cPAD is 0.16 mg/kg/day based on a reference dose of 0.16 mg/kg/day, which incorporates the FQPA safety factor (1x) for all populations.

4. Dietary Risk Assumptions

The use of glutaraldehyde on food or feed contact surfaces, agricultural commodities, and in animal premises and poultry premises (including hatcheries) may result in pesticide residues in human food and therefore, pose a risk to human health. The use sites which are quantitatively assessed in this document are listed in Table 4 along with the registration numbers and the maximum application associated with each dietary exposure scenario (Table 3). These scenarios represent worst-case estimates of indirect food contact dietary exposure and include application to hard surfaces in food processing plants, application to adhesives used in papermaking, application to pigments and fillers used in papermaking, and application to papermill process water systems as a slimicide.

Table 4: Use Site Categories and Application Rates

Scenario	Product Label[a] (EPA Registration No.)	Method of Application	Maximum Application Rate[b] (lb a.i./gal)	Label Notes Regarding Indirect of Direct Food Contact
Hard non-porous surfaces in food processing plants (including chicken processing facilities)	71355-1	Coarse spray, mop, sponge	536 ppm ai (1 gal product/ 200 gal water * 10^6 * 10.725 % ai)	"Before using this product, all food products and packaging materials must be removed from the room or carefully protected" "A potable water rinse is required for all surfaces that come into contact with food"
Paper mills and associated process water systems (including treatment at beaters, broke chest pump, save-all tank, or whitewater tank)	464-692, 464-700 464-702, 464-708 1448-354, 1448-421 1448-422, 1448-423 1448-429, 1448-430 1448-431, 1677-206 33753-26, 33753-27 33753-30, 33753-31 67869-36	Intermittent or continuous feed methods	750 ppm ai (0.075% ai) (50% ai * 3 lbs product / ton pulp or paper * 1 ton/ 2,000 lb * 10^6)	None

Scenario	Product Label[a] (EPA Registration No.)	Method of Application	Maximum Application Rate[b] (lb a.i./gal)	Label Notes Regarding Indirect of Direct Food Contact
Pigments and filler slurries for paper and paperboard	464-703, 464-708, 464-692, 1448-421, 1448-422, 1448-423, 1448-429, 1448-430, 1448-431, 1448-354 1677-206, 33753-26, 33753-27, 33753-30, 33753-31, 67869-36	Apply once during manufacturing	300 ppm ai (50% ai * 600 ppm as product [based on slurry solids] in mixed slurry) or 0.00030 lb ai/lb slurry or dry powder (50% ai * 6 lb product/10,000 lb dry powder)	"For Food and Non-Food Contact Paper and Paperboard"
Sugar beet mills and process water systems (including treatment at diffuser, transport water pump, weir box, or diffuser feed water pump)	464-692, 1677-206, 33753-26, 33753-27, 33753-30, 33753-31	Intermittent or continuous feed methods	0.45 lb ai/ton sliced beet (45% ai * 8.34 * 15.2 oz/ton sliced beet * 1 gal / 128 oz) or 252 ppm ai (45% ai * 560 ppm product)	None
Water based conveyor lubricants for use in brewery, juice, dairy, beverage, and food processing systems	464-692, 1677-206 33753-26, 33753-27 33753-31	Automatic feed system	300 ppm ai (600 ppm product *50% ai)	"Avoid contamination of food in application of this product"

Scenario	Product Label[a] (EPA Registration No.)	Method of Application	Maximum Application Rate[b] (lb a.i./gal)	Label Notes Regarding Indirect of Direct Food Contact
Farm equipment and animal housing buildings (including poultry grow-out and laying houses): hard non-porous surfaces such as floors, walls, forks, shovels And Hatcheries: trays, racks, carts, chick boxes, cages, hatchers, settlers, chick processing facilities, hatchery humidity control equipment, and other hard surfaces	464-689, 464-696, 464-689, 464-700, 464-702, 464-716**,** 464-715, 71355-1	Course sprayer, mop, sponge, immersion, fogging	0.0201 lb ai/gal (12.8% ai * 8.34 lb ai/gal * 2.41 oz/gal * 1 gal/128 oz) or 0.25% ai solution	"Sanitizing Non-food contact surfaces, farm, animal, and poultry housing facilities and equipment" "Thoroughly scrub treated feed racks, troughs, and other feeding and water appliances with soap or detergent and rinse with potable water before reuse"
Egg Sanitization: hatching eggs	464-689, 464-696, 464-689, 464-700, 464-702, 464-716, 464-715	Immersion (10 to 15 seconds) or fogging/ atomizing	Immersion 0.0091 lb ai/gal (14% ai * 8.34 lb ai/gal * 1 oz/gal * 1 gal/128 oz) Fogging/Atomizing 0.25% ai solution	"For treating hatching eggs only"

5. Dietary Risk Assessment

a. Food/Feed Contact Surfaces, Agricultural Commodities and Animal/Poultry Premises

Chronic dietary risk assessments were conducted for the use of glutaraldehyde on food or feed contact surfaces, agricultural commodities, and in animal and poultry premises including hatcheries. For all scenarios quantitatively evaluated, none of the calculated % cPAD values exceeded 100%. Therefore, the Agency has no risk concerns from the indirect food uses of glutaraldehdye, as indicated by the rates of application rates and the dietary exposure scenarios quantitatively assessed in this document.

In the absence of data for residues of glutaraldehyde on treated food and feed contact surfaces, the Agency has estimated residue levels that may occur in food using maximum

application rates from product labels and a variety of FDA models and assumptions. Using the residue estimates, Estimated Daily Intake (EDI) (mg/person/day) and Dietary Daily Dose (DDD) (mg/kg/day) values were calculated for each scenario. These daily estimates were conservatively used to assess chronic dietary risks by calculating the % cPAD (chronic population-adjusted dose). Risks exceed the Agency's level of concern when the % cPAD exceeds 100%.

For application to hard surfaces in food processing plants, the % cPAD values assuming a 10% transfer rate from the treated hard surface to food (from FDA Sanitizing Guidelines) were 0.96% for adult males, 1.12% for adult females, and 4.47% for children. Assuming a 100% transfer rate, the % cPADs were 9.57 for adult males, 11.17% for adult females, and 44.67% for children (Table 5).

Table 5. Calculated EDIs, DDDs and % cPADs for Hard Surfaces (Countertop) in Food Processing Plants

Exposure Group	Transfer Rate of 10%			Transfer Rate of 100%		
	EDI (mg/p/d)	DDD (mg/kg/d)	% cPAD[a]	EDI (mg/p/d)	DDD (mg/kg/d)	% cPAD[a]
Adult males	0.112	0.00160	1.00	1.12	0.0160	10.0
Adult females	0.112	0.00187	1.12	1.12	0.0187	11.7
Children	0.112	0.00747	4.67	1.12	0.0747	46.7

a. % cPAD = exposure (DDD) / (cPAD) x 100. cPAD = 0.16 mg/kg/day

Glutaraldehyde can be used as a general preservative in food-contact adhesives and mineral slurries used in papermaking. Glutaraldehyde is cleared for use by the Food & Drug Administration (FDA) as an adhesive component (21 CFR 175.105). For application to adhesives in papermaking, the % cPAD values were 0.00019% for adult males, 0.00022% for adult females, and 0.00044% for children (Table 6).

Table 6. Calculated EDIs, DDDs, and %cPADs for Adhesives Used in Papermaking

Exposure Group	EDI (mg/day)	DDD (mg/kg/day)	% cPAD[a]
Adult males	2.10E-05	3.00E-07	0.00019
Adult females	2.10E-05	3.50E-07	0.00022
Children	1.05E-05	7.00E-07	0.00044

a. % cPAD = exposure (DDD) / (cPAD) x 100

The Agency has used the FDA model to estimate the residue level of glutaraldehyde that will be present in treated paper from its use as a slimicide and which could then migrate into food exposed to the treated paper. The calculated EDIs, DDDs and %cPADs for glutarladehyde use as a slimicide are presented in Table 7. Glutaraldehyde is also cleared for use by the FDA as a slimicide (21 CFR 176.300) with no dosage limitations.

Table 7. Calculated EDIs, DDDs, and %cPADs for Slimicides Used in Papermaking

Exposure Group	EDI (mg/day)	DDD (mg/kg/day)	% cPAD[a]
Adult males	0.021	0.0003	0.185
Adult females	0.021	0.00035	0.219
Children	0.0105	0.0007	0.438

a. % AD = exposure (DDD) / (cPAD) x 100

Glutaraldehyde-containing products are used to inhibit the growth of spoilage microorganisms in pigments and filler slurries for food contact paper during their manufacture, storage, and distribution. The calculated EDIs, DDDs and %cPADs for glutarladehyde use in fillers for papermaking are presented in Table 8.

Table 8. Calculated EDIs, DDDs, and %cPADs for Filler Used in Papermaking

Exposure Group	EDI (mg/day)	DDD (mg/kg/day)	% cPAD [a]
Adult males	0.0015	0.000022	0.014
Adult females	0.0015	0.000026	0.016
Children	0.00075	0.000051	0.032

a. % AD = exposure (DDD) / (cPAD) x 100

Many glutaraldehyde product labels list directions for both application to food contact paper for the filler use and a non-food contact paper coating use. Presumably, both uses can be made to the same paper and therefore, addititve result exposures to glutaraldehyde from the use of the treated paper on food. The Agency considers all paper uses as having the potential for food contact. Thus, the EDIs, DDDs and %cPADs were calculated for coatings used in papermaking (Table 9).

Table 9. Calculated EDIs, DDDs, and %cPADs for Coatings Used in Papermaking

Exposure Group	EDI (mg/day)	DDD (mg/kg/day)	% cPAD [a]
Adult males	0.045	0.00064	0.4
Adult females	0.045	0.00075	0.47
Children	0.0225	0.0015	0.94

a. % AD = exposure (DDD) / (cPAD) x 100

Dietary exposures from general agricultural premise use (hard surfaces such as floors and walls in barns and animal houses, empty watering/feed troughs, animal halters, ropes and forks), poultry hatcheries (including egg sanitization) and poultry laying facilities (residues on egg shells) are expected to be much lower than the dietary exposures resulting from representative surface disinfectant and sanitizing uses that were quantitatively assessed. In the absence of any adverse data at this time, the Agency has no concerns for the agricultural uses listed.

b. Other Dietary Risks

Glutaraldehyde can also be used on conveyor belts in food processing plants. This use was determined to be a non food-contact use and, therefore, was not quantitatively assessed.

The use of glutaraldehyde-containing products in sugar beet mills and water systems for processing of sugarcane or sugar beet is considered a food use. However, glutaraldehyde may be safely used as a single additive for controlling microorganisms in sugar beet mills at a maximum level of 250 ppm in terms of the weight of the raw cane or raw beet (21 CFR 173.320). This level reflects the maximum application rate found on pesticide product labels and following processing of sugar cane or sugar beets, the residue levels of glutaraldehyde decrease to 1.72 ppm. Therefore, the Agency has no risk concerns from the food uses of glutaraldehdye, as indicated by the application rates and measured pesticide residue for this exposure scenario.

c. Dietary Risk from Drinking Water

There are no antimicrobial uses associated with glutarladehyde that are expected to significantly impact either surface or groundwater resources.

6. Residential Risk Assessment

Residential exposure to glutaraldehyde can occur from the antimicrobial uses of glutaraldehyde. The residential exposure assessment considers all potential pesticide exposure, other than exposure due to residues in food and drinking water. Exposure may occur during and after application methods including painting via brush/roller and airless sprayer. Each route of exposure (dermal, inhalation) is assessed, where appropriate, and risk is expressed as a Margin of Exposure (MOE), which is the ratio of estimated exposure to an appropriate No Observed Effect Level (NOAEL) dose. Based on the application methods, glutaraldehyde has been assessed for the residential mixing/loading/applicator (or “handler”) exposure.

a. Residential Toxicity

The toxicological endpoints and associated uncertainty factors used for assessing the non-dietary, residential and occupational risks for Glutaraldehyde are listed in Table 10. A MOE greater than or equal to 10 is considered adequately protective for the residential exposure assessment for the dermal route of exposure. The MOE of 100 includes 3x for inter-species extrapolation, 3x for intra-species variation. A MOE greater than or equal to 30 is considered adequately protective for the residential exposure assessment for the inhalation routes of exposure. The MOE of 100 includes 3x for inter-species extrapolation, 10x for intra-species variation. The Agency used the reference concentration (RFC) approach rather than the MOE approach for the inhalation risk assessment. Therefore, concentrations less that the RFC will be considered to be not of concern.

Table 10. Glutaraldehyde Toxicological Endpoints Used for Occupational and Residential Assessment

Exposure Scenario	Dose Used in Risk Assessment	UF	Study and Toxicological Effects
Dermal Exposures			
Short Term	Irritation NOAEL = 50 mg/kg/day (2.5% percent a.i.)	10	Rat 28 day dermal toxicity study (MRID 432591-01). LOAEL = 100 mg/kg/day (5.0% a.i.) based upon erythema, edema and skin lesions.
Intermediate Term	N/A	N/A	N/A
Long Term	N/A	N/A	N/A
Inhalation Exposures			
Short Term Occupational (8 hours/day)	NOAEL = 0.7 mg/m^3 HEC_{occ} = 0.041 mg/m^3 'RfC_{occ}' = 0.0013 mg/m^3 (0.32 ppb*)	30	Two-week inhalation toxicity study in rats and mice (NIH pub 93-3348). LOAEL = 2.0 mg/m^3 based upon histo-pathological alterations of the nasal passages, larynx, trachea and lung.
Short Term Residential (24 hours/day)	NOAEL = 0.7 mg/m^3 HEC_{res} = 0.014 mg/m^3 'RfC_{res}' = 0.0005 mg/m^3 (0.12 ppb*)	30	Same as above.
Intermediate Term Occupational (8 hours/day)	NOAEL = 0.51 mg/m^3 HEC_{occ} = 0.03 mg/m^3 'RfC_{occ}' = 0.001 mg/m^3 (0.24 ppb*)	30	Thirteen week inhalation toxicity study in rats and mice (NIH pub 93-3348). LOAEL = 1.02 mg/m^3 based upon histo-pathological changes of the nasal and respiratory tract epithelium.
Intermediate Term Residential (24 hours/day)	NOAEL = 0.51 mg/m^3 HEC_{res} = 0.01 mg/m^3 'RfC_{res}' = 0.0003 mg/m^3 (0.073 ppb*)	30	Same as above.
Long Term Occupational (8 hours/day)	LOAEL = 0.26 mg/m^3 HEC_{occ} = 0.019 mg/m^3 'RfC_{occ}' = 0.00006 mg/m^3 (0.015 ppb*)	300	Two -Year inhalation toxicity study in rats and mice (MRID 448422-02). LOAEL = 0.26 mg/m^3 based upon squamous epithelial hyperplasia/inflammation and turbinate necrosis.
Long Term Residential (24 hours/day)	LOAEL = 0.26 mg/m^3 HEC_{res} = 0.004 mg/m^3 'RfC_{res}' = 0.00002 mg/m^3 (0.005 ppb*)	300	Same as above
* Unit Conversion: ppb = (mg/m^3 x 24.45 x 1000 ug/mg) / mw. For glutaraldehyde: 1 ppb = 0.00409 mg/m^3			

b. Comparison to Other Endpoints

The American Conference of Governmental Hygienists (ACGIH) has evaluated the glutaraldehyde literature and recommended a threshold limit value (TLV) of 0.2 mg/m^3 (50 ppb) as a ceiling (C) value. A TLV-Ceiling is an exposure limit that should not be exceeded at any time during the workday and is normally assessed as a 15 minute exposure. Although the ACGIH did review the same animal toxicity studies that were used by EPA, the ACGIH chose a ceiling value because the literature indicated that short term exposures at or below 100 ppb resulted in symptoms of nose, throat, skin and eye irritation among medical workers using glutaraldehyde. The TLV-Ceiling for glutarladehyde was not based on the same methodology that EPA uses to establish RfCs.

c. Residential Handler Exposure

i. Summary of Registered Residential Uses

Most glutaraldehyde-containing products are intended for use only in industrial or medical areas. However, the residential population may be exposed to household items such as laundry detergents and paints that have been treated with glutaraldehyde as a materials preservative (e.g., a slimicide). Table 11 identifies the residential exposure scenarios assessed for glutaraldehyde and also lists the application rates and methods for each scenario.

Table 11. Glutaraldehyde Residential Exposure Scenarios

Use	Exposure Scenario	Exposure Duration	Exposure Pathway	Application Rate (ppm)
Material Preservation of Laundry Detergent	Handler Exposure While Using Treated Laundry Detergent	Short Term	Dermal and Inhalation	100 to 1000
Material Preservation of Latex Paint	Handler Exposure While Using Treated Paint	Short Term	Dermal and Inhalation	100 to 1000
	Post Application Exposure to Treated Paint	Short Term	Inhalation	

ii. Residential Exposure Assumptions

The residential handler exposures for the use of paint and laundry detergent treated with glutaraldehyde were assessed to determine dermal and inhalation exposures. Glutaraldehyde has a relatively high vapor pressure (0.3 mm Hg at 20^{o} C), therefore, the unit exposure data from PHED are not applicable because these data are generally based upon chemicals that have a much lower vapor pressure (less than 1.0×10^{-4} mm Hg). When the vapor pressure is less than 1.0×10^{-4}mm Hg, chemicals are airborne primarily as aerosols, while at higher vapor pressures, chemicals are airborne primarily as vapors. In addition, the toxicology endpoints were derived from inhalation studies where the test animals were exposed to glutaraldehyde vapor.

iii. Residential Handler Risk Assessment

Residential Handler Paint Inhalation Exposures

Residential handler inhalation exposure can occur when residents apply house paints that were treated with Glutaraldehyde as an in-can preservative at a rate of 100 ppm to 1000 ppm. The Agency used the EPA Wall Paint Exposure Model (WPEM) to estimate air concentrations resulting from these uses. When using the WPEM model with default assumptions, the 24 hour average air concentrations of 2.2 at the low rate or 22 ppb at the high rate exceed the short term RfC of 0.12 ppb and the inhalation exposures are of concern (Table 12).

In addressing public comments, limitations of the WPEM model were identified and an alternative method of assessing paint exposures using the box model approach (Landenburger,

2007b) was proposed. The results of the box model assessment indicate that the glutaraldehyde exposure of 1.0 ppb exceeds the RFC at the highest application rate of 1000 ppm and is of concern. The glutaraldehyde exposure of 0.10 ppb at the lowest application rate does not exceed the RfC and is not of concern (Table 12).

Table 12. Short-Term Inhalation Risk Summary for Residential Painters

Assessment Method Used	Application Rate	Time Spent Painting (hrs)	Painted Surface Area (ft^2)	Air Exchange Rate per hour	24-hour ADC[D]	Short Term RfC
WPEM Model	1000 ppm	3.42	452[A]	0.45	**22 ppb**	0.12 ppb
Box Model		1.5	353[B]	0.5[C]	**1.0 ppb**	
WPEM Model	100 ppm	3.42	452[A]	0.45	**2.2 ppb**	
Box Model		1.5	353[B]	0.5[C]	0.10 ppb	

A. Assuming the walls of one room are painted as specified in the RESDIY scenario of WPEM.
B. Assuming the walls of a 12'x12'x 8' room are painted minus the area of one door and one window.
C. 1.0 air change per hour times a factor of 0.5 to account for imperfect mixing.
D. The 24 hour average daily air concentration experienced by the residential painter on the day of painting.

Air concentrations in bold font indicate risks of concern because they exceed the RfC.

Result Comparison and Risk Characterization for Residential Handler Paint Inhalation Exposures

The Box Model assessment provided by the registrant indicates that exposures to glutaraldehyde are 22 times less than the exposures predicted by WPEM. Some of this difference can be explained by the different assumptions used such as time spent painting (WPEM = 3.4 hours, Dow = 1.5 hours) and the painted surface area (WPEM = 452 ft^2, Dow = 353 ft^2) which reduce the exposure. Other differences such as the assumption of living space volume (WPEM = 15583ft^3, Dow = 6890 ft^3) increase exposure. The remaining assumptions such as the air exchange rates and daily activity patterns are nearly identical. The most important input that creates a difference in the estimated exposures, however, is the glutaraldehyde emission rate. The WPEM model estimates this rate using two equations that are based upon chamber data collected for propylene glycol, ethylene glycol, butoxyethoxyethanol and texanol while the Dow assessment estimated this rate based upon chamber emission data for Bioban CS-1246. As shown in Table 13 below, Bioban has a higher vapor pressure (VP) and Henry's law constant (HLC) than the chemicals used in the WPEM model or glutaraldehyde which indicates that it would evaporate from the paint at a higher rate. This suggests that glutaraldehyde exposures predicted using Bioban emission data are overestimates of actual glutaraldehyde exposures.

Table 13. VP and HLC Comparison of WPEM Chemicals, Bioban and Glutaraldehyde

Chemical	CAS #	Molecular Weight	Vapor Pressure (mm Hg)	Henry's Law Constant ($Pa\text{-}m^3/mol$)
Propylene Glycol*	57-55-6	76.1	0.13	0.0013
Ethylene Glycol*	107-21-1	62.1	0.092	0.006
Butoxyethoxyethanol*	112-34-5	162.2	0.02	0.0013
Texanol*	25265-77-4	216	0.0019	
Bioban CS-1246	7747-35-5	143	4.4	0.084
Glutaraldehyde	111-30-8	100.1	0.3	0.006
*These chemicals are used in the WPEM Model.				

Residential Handler Laundry Detergent and Fabric Softener Inhalation Exposures

The Agency used the EPA's Consumer Exposure Module (CEM) to estimate air concentrations resulting from the use of laundry detergent preserved with glutaraldehyde. Detailed information and the executable model can be downloaded from http://www.epa.gov/opptintr/exposure. For this exposure assessment, the CEM default scenario for the laundry detergent was the model of choice. This scenario assumes that the homeowner is exposed to the chemical in laundry detergent when using the laundry detergent in the utility room of a house and subsequently throughout the house for a 24-hr TWA. The results of the CEM model runs with default and updated assumptions are included in Table 11 and the model run details are included in Appendix B. The 24 hour TWAs range from 0.17 ppb to 7.5 ppb for the laundry detergent scenario depending upon the application rate and assumptions used and all exceed the short term RfC. The 24 hour TWAs exceed the RFC for the fabric softener scenario only at the maximum rate of 1000 ppm and are not of concern at the minimum rate of 100 pp (Table 14).

In addressing public comments, the limitations of the CEM model were identified and alternative methods of assessing laundry detergent exposures using the CEM model with modified inputs to correct the limitations were proposed. The most important limitation is that the inhalation exposure routine of CEM does not account for the dilution of the product in the wash water. Another limitation is that the assumption of 400 grams per load is outdated because detergents are now more concentrated. Alternative input parameters for the grams loaded were suggested; a value of 137 grams for laundry detergent and a value of 44 grams for fabric softeners. These values were based upon measured weights of selected detergent and fabric softener products.

Residential handler exposures to laundry detergent was reassessed using the CEM model with updated inputs for the amount of detergent used per day and also added an assessment of fabric softener exposures. Although a value of 137 grams was used for laundry detergent in the proposed assessment, a value of 200 grams was used because at least one major brand of laundry detergent is sold in 100 ounce containers which are advertised to treat 32 medium sized loads or 16 large size loads. When using the CEM model with the modified weight fraction to account for the wash water dilution and updated inputs, the 24 hour TWA Exposure of 0.019 ppb for the laundry detergent scenario does not exceed the RfC (Table 14). This assessment is also protective for fabric softeners because the amount of fabric softener used per load is less than amount of laundry detergent used.

Table 14. Inhalation Risks for Laundry Detergent and Fabric Softener Handlers

EFAST Assessment Method	Weight Fraction (ppm)	Amount of Laundry Detergent Used Per Day/ Duration of Use	Air Exchange Rate per hour	24-hour TWA[F]	Short Term RfC
Laundry Detergent					
Default Assumptions	1000[A]	400 grams/0.667 hours[C]	0.45	**7.5 ppb**	0.12 ppb
Default Assumptions	100[A]	400 grams/0.667 hours[C]		**0.75 ppb**	
Updated Assumptions	1000[A]	200 grams/0.667 hours[D]		**3.7 ppb**	
Updated Assumptions	100[A]	200 grams/0.667 hours[D]		**0.37 ppb**	
Modified Weight Fraction	1.5[B]	137 grams/0.417 hours[E]		0.019 ppb	
Fabric Softener					
Updated Assumptions	1000[A]	50 grams/0.667 hours[G]	0.45	**0.93**	0.12 ppb
	100[A]			0.093	

A. Weight fraction = The amount of GA in the laundry detergent.
B. Weight fraction = (137 ml of detergent containing 1000 ppm GA/ 92 liters of wash water)
C. Default assumptions as listed in the CEM Model documentation.
D. Updated assumption based upon more concentrated detergent formulations.
E. Assumptions used in the registrant assessment (Finking and McCready, 2007a).
F. The 24 hour TWA air concentration experienced by the laundry detergent handler on the day of detergent use.

***Air concentrations in bold font indicate risks of concern because they exceed the RfC.**

Result Comparison and Risk Characterization for Residential Handler Laundry Detergent and Fabric Softener Inhalation Exposures

The Modified CEM assessment indicates that exposures to glutaraldehyde are 400 or 200 times less than the exposures predicted by the default or updated CEM assessments. Some of this difference can be explained by the different assumptions used such as the amount of product used (default = 400 grams, updated = 200 grams, modified = 137 grams) and the event duration (default = 0.667 hours, modified = 0.417 hours). The largest source of the difference is the weight fraction which is 1000 ppm for the default and updated assessments and 1.5 ppm for the modified assessment.

Residential Handler Dermal Exposures

The residential handler dermal exposures to glutaraldehyde were assessed by comparing the concentrations in the paints and the laundry detergents with the concentrations used in the dermal toxicity studies. This comparison is shown in Table 15 and indicates that the dermal exposures are not of concern at the maximum application rate of 1000 ppm (0.1 percent) because the Margin of Exposure (MOE) of 25 exceeds the target MOE of 10.

Table 15. Residential Handler Dermal Exposures

Application Rate (ppm)	Application Rate (Percent)	Glutaraldehyde NOAEL	NOAEL Concentration[A]	MOE[B] (Target MOE = 10)
1000	0.1	50 mg/kg/day	2.5%	25

A. The concentration of glutaraldehyde in the test solution applied at the NOAEL dose.
B. MOE = NOAEL Concentration (percent) / Application Rate (percent)

d. Residential Post-application Assessment

i. Residential Post-application Exposure Assessment

The Wall Paint Exposure Model (WPEM) was used to estimate air concentrations resulting from the use of paint preserved with GA. The default assumptions from the WPEM RESADULT scenario were used. This scenario assumes that the home occupants are exposed to the chemical in paint in adjacent rooms (Zone 2) during painting and in the painted room (Zone 1) after painting. This scenario includes 7 hours in Zone 2, 8 hours in Zone 1 and 6 hours outside of the house.

In addressing public comments, the limitations of the WPEM model were reiterated and additional concerns that some of default assumptions included in the WPEM residential post application scenario are also unrealistic. The most important point of these assumptions is that a coat of primer would be applied immediately prior to the finish coat. The registrants contend that primer coats are only applied during extensive remodeling and that the residents would not be expected to be in Zone 1 for eight hours immediately following the painting because the room would not be ready for occupancy. Given these factors, the registrants did not submit a box model assessment of post application exposures for comparison to the WPEM assessment.

Since painting only occurs on an episodic basis and because the glutaraldehyde evaporates fairly quickly from the paint, only short term exposures were assessed. As was done for the residential handler assessment discussed previously, the WPEM model was set to run at one minute intervals for one 24 hour day with an exposure event frequency of 27,375 exposure events per lifetime to yield a 24 hour average daily concentration (ADC) that includes only the day of painting for comparison to the short term RfC. The air concentrations are given in Table 16 and exceed the RfC.

Table 16. Post Application Risk Summary for Glutaraldehyde Treated Paint

Assessment Method	Application Rate	Area Painted	Air Exchange Rate	C24 in Zone 1 (ppb)	C24 in Zone 2 (ppb)	24 Hour TWA [A] (ppb)	Short Term RfC (ppb)
WPEM	1000 ppm	452 ft^2 (one room)	0.45 ACH	97	33	**37**	0.12
	100 ppm			9.7	3.3	**3.7**	

A. TWA air concentration experienced by the resident person for the first 24 hours during and after painting.

Air concentrations in bold font indicate risks of concern because they exceed the RfC.

ii. Residential Post-application Risk Characterization

The 24 Hour TWA of 37 ppb calculated by the WPEM model for the post application scenario where the resident is not in the room during painting is greater than the 24 Hour TWA of 22 ppb that was calculated by WPEM for the residential handler scenario where the resident is in the room during painting. The primary reason for this difference is that 3.4 gallons of paint is applied during the post application scenario while only 1.1 gallons of paints are applied during the handler scenario. If it is assumed that the residents are not in the painted areas of the residence immediately following application of the primer and top coat then the post application exposures predicted by WPEM can be considered to be irrelevant.

7. Aggregate Risk Assessment

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 a 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 typically includes exposures from food, drinking water, residential uses of a pesticide, and other non-occupational sources of exposure.

An aggregate risk assessment was not conducted for glutaraldehyde. The dietary, dermal and inhalation endpoints are all based upon different studies and toxicological effects. There are no incidental oral exposure scenarios identified for glutaraldehyde. On this basis, no aggregation of exposures was performed and risks are as expressed for each scenario identified in the risk assessment for glutaraldehyde.

8. Occupational Risk

a. Occupational Toxicity

The toxicological endpoints used in the occupational handler assessment of glutaraldehyde can be found in Table 10, "Residential and Occupational Toxicological Doses and Endpoints for glutaraldehyde", of this document.

b. Occupational Handler Exposure Assumptions

Occupational risk for all potentially exposed populations is measured by a Margin of Exposure (MOE), which determines how close the occupational exposure comes to a No Observed Adverse Effect Level (NOAEL) from toxicological studies. Occupational risk is assessed for exposure at the time of application (termed "handler" exposure). Application parameters are generally defined by the physical nature of the formulation (e.g., formula and packaging), by the equipment required to deliver the chemical to the use site and by the application rate required to achieve an efficacious dose. The Agency evaluated representative occupational scenarios using the application rates as recommended on glutaraldehyde product labels.

c. Occupational Handler Exposures

Occupational Handler Scenarios

The term "handler" applies to individuals who mix, load, and apply pesticide products. There are several occupational handler exposure scenarios that involve glutaraldehyde products. These scenarios include: open pouring of products into industrial processes, automatic addition of products into industrial processes, mopping animal and poultry housing, spraying or fogging animal and poultry housing, applying RTU spray to non-critical hard surfaces in medical areas, applying RTU wipes to non-critical hard surfaces in medical areas and connecting medical waste collection devices that contain glutaraldehyde.

Occupational Handler Exposure Assessment Rationale

Glutaraldehyde dermal irritation exposures and risks were not estimated for occupational handler exposures. Rather, dermal irritation exposures and risks will be mitigated using default personal protective equipment (PPE) requirements based on the toxicity of the end-use product. To minimize dermal exposures, the minimum PPE required for mixers, loaders, and others exposed to end-use products containing concentrations of glutaraldehyde will be long-sleeve shirt, long pants, shoes, socks, chemical-resistant gloves, and chemical-resistant apron. Note that chemical-resistant eyewear will be required if the end-use product is classified as category I or II for eye irritation potential.

Glutaraldehyde has a relatively high vapor pressure (0.3 mm Hg at 100% solution concentration), therefore, the unit exposure data from PHED and CMA are not applicable because these data are generally based upon chemicals that have a much lower vapor pressure (less than 1.0×10^{-4} mm Hg). When the vapor pressure is less than 1.0×10^{-4}mm Hg, chemicals are airborne primarily as aerosols, while at a higher vapor pressure, chemicals are airborne primarily as vapors. There are 5 glutaraldehyde replicates in the CMA dataset, however, and they are summarized in Table 17. The CMA data is of limited usefulness because the limit of detections were very high due to the short sampling times and limitations of the adsorbent tube method that was used. However, based on these data, the air concentrations for occupational handlers exceed the RfC and are of concern.

Table 17. Summary of Glutaraldehyde Air Concentration Data from the CMA Study

CMA Rep	Use	Operation Monitored	Amount Handled During Monitoring	Sample Duration (minutes)	GA Air Concentration (ppb)
54	Cooling Tower	Liquid Pour from 55 gallon drum	504 lbs of a 45% product	5	<660
53	Metal Working Fluid	Liquid Pour from a 55 gallon drum	133 lbs of a 45% product	22	<290
82	Metal Working Fluid	Liquid Pump from a 55 gallon drum	92 lbs of a 45% product	16	<71
91	Disinfect dental instruments	Liquid Pour from a 1 gallon container into disinfection tray	1.8 lbs of 2.0% product	6	<160
98	Disinfect dental instruments	Liquid Pour from a 1 gallon container into disinfection tray	4.4 lbs of 2% product	5	540
The measured air concentrations exceed or potentially exceed the TLV-C of 50 ppb and RfC of 0.32 ppb.					

Use of Other Exposure Data to Estimate Glutaraldehyde Risks

Other air sampling data were reviewed to determine if measured glutaraldehyde exposures typically exceed the RfCs. The following data sources were reviewed: open Literature studies cited in the ACGIH Documentation of the Glutaraldehyde TLV and open literature and proprietary studies cited by The Dow Chemical in MRID 46682201 "Summary of Worker Inhalation and Exposure Data to Glutaraldehyde-Containing Biocidal Products."

Most of the above data were collected to compare glutaraldehyde exposure to the TLV which is a ceiling value and it is not comparable to the short term RfC of 0.32 ppb which is based upon an eight hour average exposure. When assessing ceiling values, air samples of 15 minutes or less in duration are collected at peak exposure periods during the workday. Because only peak exposures are of interest when comparing exposures to ceiling exposure limits, the intervals between peak exposures are usually not evaluated. By contrast, sampling that is conducted to evaluate 8 hour exposure limits usually include all parts of the workday.

Summary of Exposure Data Cited in the ACGIH TLV Documentation

Most of the exposure data cited in the ACGIH TLV documentation is from medical uses where instruments, such as endoscopes, were disinfected with glutaraldehyde. Although these uses are not regulated by EPA and the use concentrations and the potential exposures are substantially higher than pesticidal applications, these exposure data are included as weight of evidence that significant exposures occur when handling glutaraldehyde in relatively small amounts. Glutaraldehyde air concentrations ranged from <0.5 ppb to 570 ppb depending on the type of process, the ventilation conditions and other site specific factors. The highest result of 570 ppb was a peak measurement taken during the use of a 0.15% solution of GA and the corresponding 8 hour TWA was 100 ppb. Glutaraldehyde air concentrations were greater during manual disinfection than during automated disinfection. A summary of these data is included in Table 18.

Table 18. Glutaraldehyde Air Concentrations During Endoscopy Disinfection

Study	Operation	Solution Strength	Sample Type	GA Air Concentration (ppb)	Comments
Binding and Witting, 1990	Disinfection in operating theatres	0.025%	Peak 8 hr TWA	30 10	
		0.15%	Peak 8 hr TWA	570 100	
Leinster, Baum and Baxter, 1993	Cold Sterilization in English Hospitals		STEL	<0.8 to 30 (n=39)	Note 1
Tkaczuk, Pisaniello and Crea, 1993	Manual Cold sterilization of endoscopes		STEL TWA (133 min)	77 to 105 (n=2) 43 (n=1)	
	Dental assistant, radiography, embalmer and egg collectors		STEL and TWA	<50	
Campbell and Beach, 1994	Cold sterilization of endoscopes	2%	STEL	160 and 230	Note 2
Burge, 1989 Norback, 1988	Manual Cold Sterilization		STEL	<2.5 to 35	
	Automatic Sterilization		STEL	2.5 to 7.5	Good ventilation
	Automatic Sterilization		STEL	2.5 to 7.5	Poor ventilation
Jachuck et al, 1989	Cold sterilization of endoscopes	2%	TWA (60 min)	50 to 120	
Pisaniello, Gun, Tkaczuk, et al., 1997	Cold sterilization		STEL	>200 (n=4) <200 (n=58) 100 to 200 (n=10)	
NIOSH HETA 90-296	Cold Sterilization	2%	Various	ND to 80	

Note 1 - Sample times ranged from 4 to 26 minutes
Note 2 - Samples taken with and without overhead exhaust fan.
Some of the measured air concentrations exceed the TLV-C of 50 ppb and all exceed the RfC of 0.32 ppb.

Summary of Exposure Data Cited by the Registrant

The registrant provided a summary of glutaraldehyde exposure data reported in MRID # 46682201. Samples have been collected during glutaraldehyde use in industrial processes such as paper manufacture, aluminum rolling and oil drilling. Samples have also been collected during the manufacture and drumming (i.e., packaging) of glutaraldehyde products. Most of the data are in the form of 15 minute samples that were taken to compare exposures with the TLV-Ceiling, however, some of the drumming samples prior to 1989 were taken over a full shift. A summary of these data are given in Table 19 and a discussion of the data is included in the "Occupational Handler Exposure and Risk Assessment" section of this document.

Table 19. Glutaraldehyde Air Concentrations Measured During Industrial Operations

Location	Operation	Solution Strength	Sample Type	Sampled Period (minutes)	GA Air Concentration (ppb)	Source
Latex Plant (CA)	Addition to truck sump	45%	PBZ	15	27	SIDS
Paper Mill (GA)	3 feet above wire at machine #3		Area		ND	SIDS
Paper Mill (Canada)	1 foot above machine chest opening at various addition rates		Area	15	ND - 220 (LOD=20)	UCC, 1998
Paper Mill (Kent UK)	Above blend and machine chests at various addition rates		Area	15	ND (n=5) (LOD=30)	UCC 1998
Paper Mill (Belgium)	Pumping biocides at various locations	50%	Area	60	4 - 130	SIDS
Paperboard Mill	Various Locations throughout process	50%	Area	30-60	ND - 1.8 (n=18)	SIDS
Drilling Field (BP Alaska)	Addition to drilling mud	Aldacide G			20 - 120 (n=9)	SIDS
Aluminum Mill	Hot Rolling - Air in metal working fluid sump	45%	Area	30	6 - 122	SIDS
Aluminum Rolling Plant	Mill floor during rolling	Uconex	Area	15	ND	SIDS
	Inside covered sump	345	Area	15	122 - 175 (n=2)	SIDS
Breakdown Mill	Adjacent to spray nozzles near operators		Area	15	6 - 8 (n=3)	SIDS
Aluminum Hot Rolling Mill (NE US)	Addition areas over tanks near rolling mill	Not Reported	Area	15	ND - 180[A] (n=23) (LOD = 46)	UCC, 1994
	Walking around in mill during operation		PBZ	15	<46 (n=2)	UCC, 1994
Paint Spray Booth, GM Truck Plant	Emissions at various locations around booth		Area	30	ND - 158 (LOD=1)	SIDS
Glute Mfg Plant/(WV)	Drumming (prior to 1989)	25-50	PBZ	Full Shift	10 - 170	Teta 1995
	Drumming (1989 to 1992)	25-50	PBZ	15	10 - 340 (n=88)	SIDS
Glute Formulation Plant (Australia)	Formulating and packaging at a well ventilated facility	25-50	PBZ	15	70 - 100	SIDS
UCC Glute Mfg Plant (WV)	Drumming (1990-1996)	25-50	PBZ	15	70 - 130	SIDS
	Filling totes (1994-1997)	25-50	PBZ	15	<10 - 120	SIDS
	Disconnecting hose from truck (1994-1997)	25-50	PBZ	15	<50	SIDS

Notes
PBZ - Personal breathing zone sample taken on the worker.
Area - Area sample
A. The highest result of 180 ppb was measured during addition over the tank with the door open.

d. Occupational Handler Exposure and Risk Assessment

Most of the available exposure data are from short term samples of approximately 15 minutes in duration and they were taken as a comparison to the ACGIH TLV-Ceiling of 50 ppb. Although many of the short term samples exceeded the RfC of 0.32 ppb, these samples are not comparable to the RfC because the un-sampled periods probably had lower exposures than the sampled period.

i. Professional Painter Inhalation Exposure Assessment

The Agency used the EPA Wall Paint Exposure Model (WPEM) to estimate air concentrations resulting from the use of paint preserved with glutaraldehyde. The professional painter inhalation exposure to GA vapors during painting with GA treated paint was assessed using the WPEM Model. The WPEM default scenario (RESPROF) for the professional painter was used and this scenario assumes that two professional painters are exposed to a chemical in paint while painting an entire apartment in a work day. The WPEM model was set to run at one minute intervals for the duration of the work day with an exposure event frequency of 27,375 exposure events per lifetime to yield an 8 hour time weighted average (TWA) that includes only the day of painting for comparison to the short term RFC. The results of modeling runs are included in Appendix B and the risks are summarized in Table 17. Because the 8 hour TWA air concentrations exceed the short term RfC of 0.32 ppb, the inhalation exposures are of concern at both the maximum and minimum application rates. The C15-min air concentrations also exceed the TLV-Ceiling of 50 ppb Table 20).

In addressing public comments, limitations of the WPEM model were identified and an alternative method of assessing paint exposures using the box model approach (Landenburger, 2007a) was provided. The box model assessment of the occupational painter scenario (Landenberger 2007a) is similar to the box model assessment of the residential handler scenario discussed previously. One major difference is that a fixed release rate was used instead of the variable release rate that was used for the more refined residential handler assessment. The other major difference is that only one zone was used for the occupational handler assessment while two zones were used for the residential hander assessment. The results of the Box model assessment are included in Table 20 and indicate that the glutaraldehyde exposures exceed the RFC at both the maximum and minimum application rates and are of concern.

Table 20. Inhalation Risk Summary for Occupational Painters

Method	Painted Surface Area	Air Exchange Rate	Hours per Day	C15-min[A] (ppb)	ACGIH TLV-C (ppb)	C-8hour[B] (ppb)	Short Term RfC (ppb)
Maximum Application Rate = 1000 ppm							
WPEM	2131 ft^2 (one apartment)	0.45 ACH	8	**690**	50	**530**	0.32
Box Model	2130 ft^2 (6 standard rooms)	0.5 ACH[C]				**7.6**	
Minimum Application Rate = 100 ppm							
WPEM	2131 ft^2	0.45 ACH	8	**69**	50	**53**	0.32
Box Model	2130 ft^2	0.5 ACH[C]				**0.76**	

A. Maximum 15 minute average air concentration.
B. Maximum 8 hour time weighted average air concentration on the day of painting assuming one hour for lunch.
C. 1.0 air change per hour times a factor of 0.5 to account for imperfect mixing.

Air concentrations in bold font are of concern because they exceed the TLV-C and the Short Term RfC.

Risk Characterization for Professional Painter Inhalation Exposure

The Box Model assessment provided by the Dow Chemical Company indicates that occupational handler exposures to glutaraldehyde are 70 times less than the exposures predicted by WPEM. Most of the input values such as the painted surface area, air exchange rate are similar. As is the case for the residential handler assessment, the most important input that created a difference in the estimated exposures is the glutaraldehyde emission rate which was based on chamber testing of Bioban CS-1246 which has a higher vapor pressure and Henry's law constant than glutaraldehyde.

ii. Hard Surface Disinfectant Inhalation Exposure Assessment

Three glutaraldehyde-containing products (15136-9, 55195-3 and 55194-5) are used to disinfect non-critical hard surfaces in medical clinics, dental clinics and veterinary offices. Two of these products are RTU sprays and one is an RTU wipe. The Agency used the EPA CEM Model estimate air concentrations resulting from the use of glutaraldehyde in hard surface disinfectants. In addressing public comments, limitations of the CEM model were reiterated and an alternative method of assessing exposures using the chamber emissions data was provided together with the ConsExpo Model (McCready and Finking, 2007). A general purpose cleaner scenario of the CEM model was utilized to estimate air concentrations resulting from the use of glutaraldehyde as a hard surface disinfectant. Because the CEM model calculates either peak concentrations for comparison to an acute endpoint or Lifetime Average Daily Concentrations for comparison to chronic or cancer endpoints, the inputs were adjusted to force the model to calculate a one day average concentration for comparison to the short term endpoint.

The results of the CEM model runs and the risks are summarized in Table 22. It should be noted that CEM calculates daily exposures as 24 hour TWAs. The 24 TWAs were converted to 8 hour TWAs by assuming that all of the exposure occurs during the workday. This

assumption is valid because the activity pattern was set so that the person was out of the building during off duty hours. The 8 hour time weighted average (TWA) air concentrations exceed the short term RfC of 0.32 ppb, therefore, the inhalation exposures are of concern at both the low and high air exchange rates. The peak exposure is also of concern at the low air exchange rate because it exceeds the ACGIH TLV-Ceiling of 50 ppb.

Assessment Using Experimental Data and the ConsExpo Model

The registrant collected experimental data (Rowley, 2007) by measuring the GA air concentrations in a test chamber containing a 1.2 meter square of glass plate. A solution containing GA was applied to 0.92 m^2 of this plate with a foam strip mounted on a spreading bar. Air samples were collected for 15 minute periods via fixed PTFE sampling lines positioned 1.5 meters above the glass plate. These lines lead to a control room where they were connected to Water Sep Pak 'XpoSure' cartridges containing 2, 4-dinitrophenylhydrazine (DNPH) coated silica. The results of these samples are summarized in Table 21 below.

Table 21. Measurement of Glutaraldehyde Emissions from a Cleaning Product

Time Period[A] (minute)	Air Exchange Rate	Chamber Volume	Area Treated	Amount of Solution Applied	0.1% GA (ppb)	02% GA (ppb)
0 to 15	0.5	18 m^3	0.92 m^2	3.8 grams	3.7	2.2
15 to 30					10	10
30 to 45					11	17
45 to 60					5.4	19
60 to 75					6.4	12
75 to 90					5.1	11
90 to 105					5.4	6.6
105 to 120					2.9	6.6
165 to 180					1.5	2.9
240 to 256					<0.7	<0.7
453 to 468					<0.7	<0.7
0 to 480					0.97	0.97
A. The 15 minute samples were collected from inlet hose placed 1.5 meter above the center of the glass plate and the eight hour samples were collected from an inlet hose placed near the chamber exhaust vent.						

The emission data listed above was used in conjunction with the ConsExpo Model to estimate glutaraldehyde inhalation exposures from disinfecting hard surfaces. The ConsExpo Model was developed by the National Institute for Public Health and the Environment (RIVM) of the Netherlands and is used in the European Union to assess exposures to consumer products including cleaning products.

Because the ConsExpo also calculates either peak concentrations for comparison to an acute endpoint or Lifetime Average Daily Concentrations for comparison to chronic or cancer endpoints, input parameters were used to force the model to calculate a one day average concentration for comparison to the short term endpoint. The results of the CEM model runs are summarized in Table 24. Because the 8 hour time weighted average (TWA) air concentrations exceed the short term RfC of 0.32 ppb, the inhalation exposures are of concern at all solution

strengths. The peak exposures also probably exceed the ACGIH TLV-Ceiling because peak exposures are typically at least three times eight hour average exposures.

Table 22. Inhalation Risk Summary for Medical Hard Surface Disinfection

Assessment Method	Solution Strength	Amount of Product Used	Duration of Use	Air Exchange Rate	Peak Concentration (ppb)	ACGIH TLV-C (ppb)	8 Hour TWA (ppb)	Short Term RfC (ppb)
EFAST	0.275%	123 grams	1.42 hours	0.45	**240**	50	**135**	0.32
				6	29		**12**	
ConsExpo	0.275%		10 minutes	6	Not Calculated		**43**	
	0.2%						**31**	
	0.1 %						**16**	

e. Occupational Post-application Risk Summary

i. Fogging Exposure Assessment

Glutaraldehyde is used for fogging poultry houses in preparation for a new flock of birds. Exposures to GA can occur after fogging when the workers re-enter the fogged area to finish cleanup. Only inhalation exposures were assessed, because dermal post application exposures are presumed to be negligible because the GA evaporates rapidly from the fog as predicted by the Aero-Evap model presented in MRID 466822-07 (McCready, 2004). The inhalation exposure assessment was conducted using the single chamber decay formula from the Multi-Chamber Concentration and Exposure Model (MCCEM v1.2). This assessment was based upon the application parameters listed in the Virocide Label (EPA Reg #71355-1) because this label has the most explicit instructions for fogging application. A summary of the results is presented in Table 23. The air concentrations decline to less than the TLV-Ceiling in 94 minutes and to less than the RfC in 170 minutes.

Table 23. Glutaraldehyde Air Concentrations After Fogging a Poultry House

Elapsed Time After Ventilation Activation (minutes)	Air Concentration (ppb)	Relevant Standard (ppb)
0	25,000	50 - ACGIH TLV-Ceiling
94	47	50 - ACGIH TLV-Ceiling of 50
170	0.030	0.032 - EPA Short Term RfC

Exposure data for spraying and fogging applications was also included in the registrant's Exposure Data Summary (MRID # 46682201) and are summarized in Table 24.

Table 24. Glutaraldehyde Air Concentrations Measured During Spraying and Fogging Applications

Location	Operation	Solution Strength	Sample Type	Sampled Period (minutes)	Results (ppb)	Source
Poultry Hatchery	Machine washing hatching trays and chick boxes	1000 ppm	Area	10-60	ND-68 (n=3)	UCC 2000
	Spraying egg carts		Area	10-60	14	UCC 2000
	Atomizing hatcher and chick room		Area	10–60	150 – 1760[A] (n=4)	UCC 2000
Turkey Hatchery	Turkey housing treated with UCARSAN 4256	1000 ppm	PBZ	15	26 initial ND at 15 min 31 at 35 min	UCC 2000
Chicken Hatchery	Fogging: 0 to 135 minutes after application	500 ppm	Area	10 – 20	530 initial 20 at 135 min	UCC 2000
Chicken House – Broiler Production	Spraying – manual	2%	PBZ Area	15	120 (n=1) 30 to 80 (n=3)	SIDS
	Spraying - Automatic	2%	Area	15	20 to 50 (n=3)	SIDS
Chicken House – Broiler Production	Fogging	600 ppm	Area	15	20 to 50	UCC 2000
Church in Taiwan	Hot Fogging for SARS Disinfection Trial	3%	Area	15	>5000[B] at 30 min >5000[B] at 60 min 3000 at 120 min 140 at 240 min	Trawick

A. Fog contacted sampling tube. Next highest result was 1060 ppb
B. Break-through occurred. The calculated initial air concentration was 48,000 ppb based upon the application rate.

ii. Metal Working Fluids (MWF) Exposure Assessment

Dermal Exposure

There is a potential for dermal exposure when a machinist handles metalworking fluids treated with glutaraldehyde. The dermal exposure was assessed by comparing the maximum concentration of 270 ppm used in treating MWF with the concentrations used in the dermal toxicity studies. This comparison is shown in Table 25 below and indicates that the dermal MOE is 92, which is greater than the target MOE of 10 and is not of concern.

Table 25. Dermal Risks from MWF Treated with Glutaraldehyde

Application Rate (ppm)	Application Rate (Percent)	Glutaraldehyde NOAEL	NOAEL Concentration[A]	MOE[B] (Target MOE = 10)
270	0.027	50 mg/kg/day	2.5%	92

A. The concentration of glutaraldehyde in the test solution applied at the NOAEL dose.
B. MOE = NOAEL Concentration (percent) / Application Rate (percent)

Inhalation Exposure

Inhalation exposure to glutaraldehyde as a MWF additive was assessed by assuming that the MWF aerosol exposure would not exceed the OSHA PEL of 15 mg/m^3 and that glutaraldehyde would also be present as an aerosol in proportion to the amount added. It is further assumed that the glutaraldehyde would evaporate from the aerosol before the aerosol settles out as suggested by the data presented in study MRID 46682207. The estimated glutaraldehyde air concentration is then the product of the weight fraction of glutaraldehyde chemical added to the MWF times the OSHA-PEL. Given that machining operations can occur on a year round basis, particularly in manufacturing facilities, exposures are assumed to be long term in duration.

The risks for MWF treated with glutaraldehyde are summarized in Table 26. The glutarladehyde air concentrations exceed the long term RfC of 0.015 ppb at both the low and high application rates. The air concentrations do not exceed the ACGIH TLV-Ceiling which is 3,300 times greater than the long term RfC.

Table 26. Inhalation Risks from MWF Treated with Glutaraldehyde

Application Rate (ppm)	MWF Air Concentration (mg/m^3)	GA Air Concentration[A] (mg/m^3)	GA Air Concentration[B] (ppb)	ACGIH TLV-C (ppb)	Long Term RfC (ppb)
270	15 (OSHA PEL)	0.00405	**0.99**	50	0.015
36		0.00054	**0.13**		
A. GA Air Concentration = MWF Air Concentration *(GA Application Rate (ppm)/1000000 ppm)					
B. GA Air Concentration (ppb) = (GA Air Concentration (mg/m^3) * 1000 ug/mg) / 4.09 ug/ppb					

Risk Characterization for Metal Working Fluid Exposure

The calculated exposures are probably an overestimate because the typical machine shop air concentrations are well below the OSHA-PEL. According to data cited in Recognition of Health Hazards in Industry (Burgess, 1995), the arithmetic mean air concentration dropped from 5.42 mg/m^3 prior to 1970 to 1.82 mg/m^3 by 1989. This drop is attributed to the implementation of control measures such as local exhaust ventilation, general exhaust ventilation, enclosure of cutting tools and increased use of water based machining fluids. More recent data consisting of 374 air samples collected at four machining plants indicated that the MWF exposure ranged from 0.04 to 3.84 mg/m^3 with the geometric mean exposures of 0.22 to 0.39 mg/m^3 (Verma et. al. 2006).

There are several data limitations and uncertainties associated with the occupational handler and post-application exposure assessments. These include:

- It is important to note that the ACGIH TLV-Ceiling for glutaraldehyde is 50 ppb. Based on the occupational inhalation toxicological endpoint selected for glutaraldehyde (i.e., Short-term occupational RfC of 0.32 ppb), levels at or near the TLV-Ceiling are of concern. Reconciliation of the EPA risk-based RfC and the current TLV-Ceiling will be made during

the regulatory decision phase of the Reregistration Eligibility Decision (RED) for glutaraldehyde.

- Most of the air sampling data was collected to compare glutaraldehyde exposure to the TLV of 50 ppb which is a ceiling value and it is not comparable to the RfC of 0.32 ppb which is based upon an eight hour time weighted average (TWA) exposure. When assessing ceiling values, short term samples of 15 minutes or less in duration are collected at peak exposure periods during the workday. Because only peak exposures are of interest when comparing exposures to ceiling exposure limits, the intervals between peak exposures are usually not evaluated. By contrast, sampling that is conducted to evaluate 8 hour TWA exposure limits usually includes all parts of the workday.
- Most of the samples were collected prior to 1996 and in 1997 the OSHA sampling method was updated to allow for longer sampling times with lower detection limits. The updated method allows for samples up to 4 hours in duration to be collected with a limit of detection of 0.027 ppb which is less than the short term RFC of 0.32 ppb. This method is affected by ozone interference; however, when the ozone concentration exceeds 10 ppb, reduced sampling times may be required.
- Some of the data submitted by the registrant includes samples taken during drumming at the production plant. At the time that most of these samples were taken, the drumming operation was conducted in a warehouse type structure that had only general dilution (Dow, 2007). The drumming booths were not enclosed and the workers used hand-held hydraulic controlled delivery systems similar to gas station pumps. After the TLV-Ceiling was lowered from 200 to 50 ppb in 1997, the glutaraldehyde delivery system was changed to dripless pump nozzles and local exhaust ventilation was installed.

9. Human Incident Data

The Agency consulted the following sources of information for human poisoning incidents related to glutaraldehyde use: (1) OPP Incident Data System (IDS) - The Office of Pesticide Programs (OPP) Incident Data System contains reports of incidents from various sources, including registrants, other federal and state health and environmental agencies and individual consumers, submitted to OPP since 1992; (2) California Department of Pesticide Regulation (1982-2004) – The California Department of Pesticide Regulation pesticide poisoning surveillance program consists of reports from physicians of illness suspected of being related to pesticide exposure since 1982; (3) National Pesticide Information Center (NPIC) - NPIC is a toll-free information service supported by OPP that provides a ranking of the top 200 active ingredients for which telephone calls were received during calendar years 1984-1991; (4) National Poison Control Centers (PCC) (1993 – 1996); and (5) Published Scientific Literature on Incidents.

Dermal exposure is considered a significant route of exposure for glutaraldehyde. The most common symptoms reported for cases of dermal exposure were skin irritation/burning, rash, itching, skin discoloration/redness. Allergic type reactions have also been reported. The published scientific literature indicates that health care workers are more than 8 times more likely to be allergic to gluteraldehyde than non-health care working peers. Eye pain, burning of eyes, conjunctivitis, blurring vision, and acute inflammation are the primary symptoms

associated with ocular exposure incidents. The most common symptoms reported for cases of inhalation exposure were respiratory irritation/burning, irritation to mouth/throat/nose, coughing/choking, shortness of breath, dizziness. There is even evidence that glutaraldehyde can cause occupational asthma.

Other systemic effects associated with glutaraldehyde include headache, dizziness, nausea, stomach ache, sore throats, numbness of limbs, and cardiac effects (heart palpitations and tachycardia).

B. Environmental Risk Assessment

A summary of the Agency's environmental risk assessment is presented below. Glutarladehyde has several registered use sites that could result in environmental exposures. Given the current use patterns of glutaraldehyde, indoor uses as well as industrial uses were not assessed. The following risk characterization is intended to describe the magnitude of the estimated environmental risks for glutaraldehyde use sites and any associated uncertainties.

For a detailed discussion of all aspects of the environmental risk assessment, refer to the Environmental Risk Assessment; "Glutarladehyde Risk Assessment for the Reregistration Eligibility Decision (RED) Document," dated September, 2007; the "Glutaraldehyde Ecological Hazard and Environmental Risk Assessment Chapter-Revised," dated September, 2007; and the "Environmental Fate Assessment of Glutaraldehyde for the Reregistration Eligibility Decision (RED) Document," dated September 18, 2007.

1. Environmental Fate and Transport

The environmental fate assessment for glutaraldehyde was based on guideline data required by the Agency for an environmental fate assessment. These studies were submitted by the technical registrants. However, not all of these studies fulfill guideline requirements. For additional information, please refer to the environmental fate assessment listed in Appendix C of this document.

An assessment of the various studies indicates that the hydrolysis of glutaraldehyde is pH and temperature dependent. Glutaraldehyde is hydrolytically stable under abiotic and acidic to neutral conditions, but degrades more rapidly in alkaline environments, forming a cyclic dimer. The stability of glutaraldehyde decreases as the temperature increases. At 25°C, glutaraldehyde degrades with half-lives of 628, 394, and 63.8 days at pH levels of 5, 7, and 9, respectively. Consistent with these findings, results of another study were 508 days, 102 days, and 46 days at pH levels 5, 7, and 9, respectively. At 70°C, hydrolysis of glutaraldehyde proceeds more rapidly with half-lives of 53, 6.5, and 0.23 days at pH levels of 5, 7, and 9, respectively. Photolytically, glutaraldehyde degrades slightly in natural sunlight at 25°C in a pH 5 buffered aqueous solution with a calculated half-life of 195 days. Based on its slow hydrolysis and photolysis degradation rates, glutaraldehyde may be of a short-term concern as a contaminant in surface water runoff.

However, upon contact with soil and sediment and further dilution in surface waters, glutaraldehyde may likely degrade via biodegradation and reaction with organic matter in soil.

When glutaraldehyde is introduced into the environment, it is most likely to remain in the aquatic compartment, given the small air/water partition and soil/water partition coefficients. Aquatic metabolism, under aerobic and anaerobic conditions, and aerobic soil metabolism are major routes of dissipation of glutaraldehyde. The calculated aerobic and anaerobic pseudo first-order half-lives of glutaraldehyde in flooded river sediment are 10.6 and 7.7 hours, respectively. Glutaraldehyde meets the (Organization for Economic Cooperation and Development) OECD criteria for classification as readily biodegradable in freshwater environments and as having the potential to be biodegradable in marine environments. In addition, the metabolism of glutaraldehyde is rapid and proceeds via the formation of glutaric acid as an intermediate to complete mineralization. Because of its biodegradation, glutaraldehyde is not likely to contaminate surface and ground waters.

Glutaraldehyde's tendency to bind with agricultural soils varies according to soil type. Glutaraldehyde is highly mobile in sandy sediment and moderately mobile in sandy loam, silt loam, silty clay loam, and loamy sand soils. The Freundlich adsorption coefficients ranged from 0.59 in sandy sediment to 4.96 in silty clay loam. Based on its adsorptions coefficients, and the tendency for glutaraldehyde to partition into the water phase, glutaraldehyde is not likely to contaminate soils. There may be a water/sediment partitioning issue and acute adverse impacts on benthic organisms. However, glutaraldehyde degrades fairly rapidly in freshwater and soils, and the impacts may be short-lived.

a. Bioaccumulation in Aquatic Organisms

The tendency of glutaraldehyde to bioaccumulate is low, based on its high water solubility and low n-octanol/water partition coefficient. Glutaraldehyde should not pose a concern for bioconcentration in aquatic organisms.

2. Ecological Risk

In addition to estimating risks to human health, the Agency also assesses risks to terrestrial animals, aquatic organisms, and plants. An ecological risk assessment compares toxicity endpoints from ecological toxicity studies to estimated environmental concentrations based on environmental fate characteristics and pesticide use data. A summary of data submitted to meet the Agency's data requirements for the uses of glutaraldehyde is provided below.

a. Environmental Toxicity

For the indoor and aquatic industrial uses patterns of glutaraldehyde, avian acute oral toxicity testing (850.2100) and avian subacute oral toxicity testing (850.2200), preferably using preferably using Mallard duck (a water fowl) or bobwhite quail, freshwater fish acute toxicity testing [(850.1075), preferably using rainbow trout (a coldwater fish) and bluegill sunfish (a warmwater fish)], freshwater invertebrate acute toxicity testing [(850.1010), preferably using *Daphnia magna*], estuarine and marine organisms [((850.1035, 850.1055, and 850.1075), the

preferred fish test species is sheepshead minnow and the preferred invertebrate test species are mysid shrimp and Eastern oyster] and terrestrial and aquatic plant testing are generally needed for the technical grade active ingredient (TGAI) to establish toxicity and to support the registered uses of this chemical.

Based on the results of mammalian studies conducted to meet human toxicity data requirements, glutaraldehyde exhibits low acute dermal and inhalation toxicity (Toxicity Category III and IV, respectively); however, it is highly irritating to the eyes and skin (Toxicity Category I). Glutaraldehyde is also considered to be highly toxic via the oral route of exposure (Toxicity Category II) and it is a dermal sensitizer.

Available ecological data indicate that glutaraldehyde is slightly toxicity to birds on an acute oral basis and practically non toxic on a subacute dietary basis. For freshwater fish, glutaraldehyde is slightly toxic to warmwater fish and moderately to slightly toxic to coldwater fish on an acute basis. Glutaraldehyde is highly to slightly toxic to freshwater invertebrates, slightly toxic to estuarine/marine fish, slightly to moderately toxic to shrimp on an acute basis and highly toxic to oysters. These studies fulfill the guideline requirements for acute and subacute toxicity testing.

A summary of results from submitted acute ecological toxicity data for glutaraldehyde along with avian sub-acute dietary toxicity data are provided in Tables 27 and 28, respectively.

Table 27. Acute Ecological Toxicity of Glutaraldehyde

Species	Chemical	% Active Ingredient (a.i.)	Endpoint	Toxicity Category	Satisfies Guideline/ Comments	MRID No./ Reference
Birds						
Mallard duck (*Anas platyrhynchos)*	Glutaraldehyde	50%	LD_{50} = 820 (product)	Slightly toxic	Yes* - core study - formulated product - 14-day test duration - formulation considered TGAI	117070 164373 47854
Mallard duck (*Anas platyrhynchos)*	Glutaraldehyde	14%	LD_{50} = 2109 (product)	Practically non-toxic	Yes - core study - formulated product - 28-day test duration	42110201
Mallard duck (*Anas platyrhynchos)*	Glutaraldehyde	50%	LD_{50} = 907 (product)	Slightly toxic	No - supplemental study - formulated product - 8-day test duration - deviations from guideline include test duration, age of birds, and acclimation period	00125518

Species	Chemical	% Active Ingredient (a.i.)	Endpoint	Toxicity Category	Satisfies Guideline/ Comments	MRID No./ Reference
Mallard duck (*Anas platyrhynchos)*	Glutaraldehyde	25%	LD_{50} = 1589 (product)	Slightly toxic	No - supplemental study - formulated product - 8-day test duration - deviations from guideline include test duration, age of birds, and acclimation period	00125509
Mammals						
Laboratory rat (*Rattus norvegicus*)	Glutaraldehyde	50%	LD_{50} = 460 mg/kg (males + females)	Highly toxic	Yes TGAI	00011706 00164370
Freshwater Fish						
Bluegill sunfish (*Lepomis macrochirus)*	Glutaraldehyde	50%	LC_{50} = 22.6 NOEC = 10 (product) Adjusted for 100% a.i.: LC_{50} = 11.3 NOEC = 5	Slightly toxic	Yes* - core study - formulated product - 96-hr test duration - static test system - formulation considered TGAI	125515
Bluegill sunfish (*Lepomis macrochirus)*	Glutaraldehyde,	50%	LC_{50} = 12.2 NOEC = 7.8 (a.i.)	Slightly toxic	Yes* - core study - formulated product - 96-hr test duration - static test system - formulation considered TGAI	117077
Rainbow trout (*Salmo gairdneri)*	Glutaraldehyde,	50%	LC_{50} = 9.5 NOEC<1.7 (a.i.)	Moderately toxic	Yes* - core study - formulated product - 96-hr test duration - static test system - formulation considered TGAI	117076
Rainbow trout (*Salmo gairdneri)*	Glutaraldehyde,	50%	LC_{50} = 23.9 NOEC = 18 (product)	Slightly toxic	Yes* - core study - formulated product - 96-hr test duration - static test system - formulation considered TGAI	42612102
Freshwater Invertebrates						

Species	Chemical	% Active Ingredient (a.i.)	Endpoint	Toxicity Category	Satisfies Guideline/ Comments	MRID No./ Reference
Waterflea (*Daphnia magna)*	Glutaraldehyde	50%	LC_{50} = 14.6 NOEC = 6.6 (a.i.)	Slightly toxic	Yes* - core study - formulated product - 48-hr test duration - static test system - formulation considered TGAI	117075
Waterflea (*Daphnia magna)*	Glutaraldehyde	50%	LC_{50} = 0.75 NOEC = 0.56 (product)	Highly toxic	Yes* - core study - formulated product - 48-hr test duration - static test system - formulation considered TGAI	125516
Waterflea (*Daphnia magna)*	Glutaraldehyde	14%	LC_{50} = 3.5 NOEC = 1.8 (product)	Moderately toxic	Yes - core study - formulated product - 48-hr test duration - static test system	42110101
Estuarine and Marine Organisms						
Sheepshead minnow (*Cyprinodon variegatus*)	Glutaraldehyde	51%	LC_{50} = 31.4 NOEC = 24 (a.i.)	Slightly toxic	Yes* - core study - formulated product - 96-hr test duration - flow-through test system - formulation considered TGAI	42753201
Sheepshead minnow (*Cyprinodon variegatus*)	Glutaraldehyde	50%	LC_{50} = 40 NOEC = 22 (a.i.)	Slightly toxic	Yes* - core study - formulated product - 96-hr test duration - static test system - formulation considered TGAI	117074
Mysid shrimp (*Mysidopsis bahia)*	Glutaraldehyde	51%	LC_{50} = 7.1 NOEC = 0.78 (a.i.)	Moderately toxic	Yes* - core study - formulated product - 96-hr test duration - flow-through test system - formulation considered TGAI - deviations from guideline include feeding during test	42952301

Species	Chemical	% Active Ingredient (a.i.)	Endpoint	Toxicity Category	Satisfies Guideline/ Comments	MRID No./ Reference
Mysid shrimp (*Mysidopsis bahia*)	Glutaraldehyde	50.2%	LC_{50} = 5.5 NOEC = 0.71 (a.i.)	Moderately toxic	No - supplemental study - formulated product - 96-hr test duration - flow-through test system - formulation considered TGAI - deviations from guideline include feeding during test	44880501
Mysid shrimp (*Mysidopsis bahia*)	Glutaraldehyde	50%	LC_{50} = 20.6 (a.i.)	Slightly toxic	No - supplemental study - formulated product - 96-hr test duration - static test system - formulation considered TGAI - deviations from guideline include use of adult shrimp instead of juvenile	117073
Eastern oyster (*Crassostrea virginica*)	Glutaraldehyde	51%	EC_{50} = 0.78 NOEC = 0.16 (a.i.)	Highly toxic	Yes* - core study - formulated product - 96-hr test duration - shell deposition - flow-through test system - formulation considered TGAI	42952101
Eastern oyster (*Crassostrea virginica*)	Glutaraldehyde	50.2%	EC_{50} = 0.75 NOEC < 0.089 (a.i.)	Highly toxic	Yes* - core study - formulated product - 96-hr test duration - shell deposition - flow-through test system - formulation considered TGAI	

* Acceptable for a formulated product or TGAI of 50% a.i.

Table 28. Avian Subacute Dietary Toxicity of Glutaraldehyde

Species	Chemical, % Active Ingredient (a.i.)	Endpoint (ppm)	Toxicity Category	Satisfies Guidelines/ Comments	Reference (MRID No.)
Mallard duck (*Anas platyrhynchos)*	Glutaraldehyde, 50%	LC_{50} > 5125 (product)	Practically non-toxic	Yes* - core study - formulated product - 8-day test duration - formulation considered TGAI	117071
Mallard duck (*Anas platyrhynchos)*	Glutaraldehyde, 50%	LC_{50}>10,000 (product)	Practically non-toxic	Yes* - core study - formulated product - 8-day test duration - formulation considered TGAI	125519
Mallard duck (*Anas platyrhynchos)*	Glutaraldehyde, 42.5%	LC_{50}>5620 (product)	Practically non-toxic	Yes - core study - formulated product - 8-day test duration	42110601
Mallard duck (*Anas platyrhynchos)*	Glutaraldehyde, 14%	LC_{50}>5620 (product)	Practically non-toxic	Yes - core study - formulated product - 8-day test duration	42110401
Bobwhite quail (*Colinus virginianus)*	Glutaraldehyde, 50%	LC_{50}>5100 (product)	Practically non-toxic	Yes* - core study - formulated product - 8-day test duration - formulation considered TGAI	117072

Species	Chemical, % Active Ingredient (a.i.)	Endpoint (ppm)	Toxicity Category	Satisfies Guidelines/ Comments	Reference (MRID No.)
Bobwhite quail (*Colinus virginianus)*	Glutaraldehyde, 50%	LC_{50}>10,000 (product)	Practically non-toxic	Yes* - core study - formulated product - 8-day test duration - formulation considered TGAI	125520
Bobwhite quail (*Colinus virginianus)*	Glutaraldehyde, 42.5%	LC_{50}>5620 (product)	Practically non-toxic	Yes - core study - formulated product - 8-day test duration	42110501
Bobwhite quail (*Colinus virginianus)*	Glutaraldehyde, 25%	LC_{50}>10,000 (product)	Practically non-toxic	Yes - core study - formulated product - 8-day test duration	125511
Bobwhite quail (*Colinus virginianus)*	Glutaraldehyde, 14%	LC_{50}>5620 (product)	Practically non-toxic	Yes - core study - formulated product - 8-day test duration	42110701

* Acceptable for a formulated product or TGAI of 50% a.i.

The acute toxicity of glutaraldehyde, complexed with sodium bisulfite, dibasic ammonium phosphate (DAP) and sodium hydroxide at varying concentrations was also investigated in freshwater fish, freshwater invertebrates and aquatic plants (Table 29). Results of the freshwater fish studies indicate that deactivation with sodium bisulfite reduces the acute toxicity of glutaraldehyde to warmwater fish when compared to untreated glutaraldehyde (MRID 43645701). Both freshwater fish studies fulfill guideline requirements for an acute toxicity test using the fathead minnow (850.1075), however, insufficient information was provided to assess the efficacy of DAP. In freshwater invertebrates (*Daphnia magna)*, acute toxicity of gluteraldehyde complexed with sodium bisulfite, sodium hydroxide, and DAP at varying concentrations was also reduced. Insufficient information was provided in the two supplemental studies concerning the detoxification process of sodium bisulfite (MRID 442108-01) and sodium hydroxide (MRID 442197-01/443358-01) to determine the adequacy of the test results. For aquatic plants, both sodium hydroxide and sodium bisulfide can serve to reduce algal toxicity when used in conjunction with glutaraldehyde. Sodium bisulfite was slightly less toxic than sodium hydroxide. This study does not fulfill guideline requirements.

Table 29. Acute Toxicity of Complexed Glutaraldehyde to Freshwater Fish/Invertebrates

Species	Chemical, % Active Ingredient (a.i.)	Endpoint (ppm)	Toxicity Category	Satisfies Guidelines/ Comments	Reference (MRID No.)
Freshwater Fish					
Fathead minnow *(Pimephales promelas)*	Glutaraldehyde, 50% (1 mole) plus 2 moles and 3 moles of Sodium Bisulfite (SBS)	Untreated: LC_{50} = 5.4 NOEC = 2.6 2 moles SBS: LC_{50} = 283 NOEC = 200 3 moles SBS: LC_{50} = 50 NOEC = 12.5 (a.i.)	Moderately toxic Practically non-toxic Slightly toxic	Yes* - core study - formulated product - 96-hr test duration - static test system - assess detoxification of a.i. - formulation considered TGAI	43982401
Fathead minnow *(Pimephales promelas)*	Glutaraldehyde, 50% (1 mole) plus 0.5 mole, 1.25 moles, and 2.5 moles of Dibasic Ammonium Phosphate (DAP)	0.5 mole DAP: LC_{50} = 3.78 NOEC = 1.9 1.25 moles DAP: LC_{50} = 1.38 NOEC = 0.62 2.5 moles DAP: LC_{50} = 0.76 NOEC = 0.31 (a.i.)	Moderately toxic Moderately toxic Highly toxic	Yes* - core study - formulated product - 96-hr test duration - static test system - assess detoxification of a.i. - formulation considered TGAI	43649001
Freshwater Invertebrates					
Waterflea *(Daphnia magna)*	Glutaraldehyde, 50% plus 0.5 mole, 1.25 moles, and 2.5 moles of Dibasic Ammonium Phosphate (DAP)	0.5 mole DAP: EC_{50} = 47 NOEC = 15 1.25 moles DAP: EC_{50} = 102 NOEC = 15.6 2.5 moles DAP: EC_{50} = 40.9 NOEC = 15 (a.i.)	Slightly toxic Practically non-toxic Slightly toxic	Yes* - core study - formulated product - 48-hr test duration - static test system - assess detoxification of a.i. - formulation considered TGAI	43645701
Waterflea *(Daphnia*	Glutaraldehyde, 50% plus 2 moles and 3	2 moles SBS:	Practically non-toxic	No - supplemental	44210801

Species	Chemical, % Active Ingredient (a.i.)	Endpoint (ppm)	Toxicity Category	Satisfies Guidelines/ Comments	Reference (MRID No.)
magna)	moles of Sodium Bisulfite (SBS)	EC_{50} = 109 NOEC = 16 3 moles SBS: EC_{50} = 41 NOEC = 16 (a.i.)	Sightly toxic	study - formulated product - 48-hr test duration - static test system - assess detoxification of a.i. - formulation considered TGAI - deviations from guideline include non-GLP and lack of raw data - adequacy of test results could not be assessed	
Waterflea *(Daphnia magna)*	Glutaraldehyde, 50% plus Sodium Hydroxide	EC_{50} = 4575 NOEC = 3000 (a.i.)	Practically non-toxic	No - supplemental study - formulated product - 48-hr test duration - static test system - assess detoxification of a.i. - formulation considered TGAI - deviations from guideline include non-GLP, lack of raw data, and description of study - adequacy of test results could not be assessed	44219701 44335801
Aquatic Plants					
Green alga (*Selenastrum*	Glutaraldehyde, 50% plus Sodium	Untreated:		No -supplemental	44443101

Species	Chemical, % Active Ingredient (a.i.)	Endpoint (ppm)	Toxicity Category	Satisfies Guidelines/ Comments	Reference (MRID No.)
capricornutum)	Hydroxide and Sodium Bisulfite	EC_{50} = 0.75 NOEC = 0.50 <u>Sodium Hydroxide</u>: EC_{50} = 2.1 NOEC = 1.3 <u>Sodium Bisulfite</u>: EC_{50} = 3.6 NOEC = 1.7 (a.i.)		study - formulated product - 5-day test duration - growth inhibition - static test system - assess detoxicification of a.i. - formulation considered TGAI	

* Acceptable for a formulated product or TGAI of 50% a.i.

Chronic toxicity testing (fish early life stage, 850.1400 and aquatic invertebrate life cycle, 850.1300) is required for pesticides when certain conditions of use and environmental fate apply. The preferred freshwater fish test species is fathead minnow (other species may be used) and the preferred freshwater invertebrate is *Daphnia magna*. Environmental fate data for glutaraldehyde indicates that it is likely to degrade quickly in water, however, the chronic *Daphnia magna* test is held in reserve pending further analysis of glutaraldehyde fate in the environment. Refer to the environmental fate chapter of this RED for further information. Available chronic toxicity data for glutaraldehyde (Table 30) indicate that continuous exposure results in measurable effects on coldwater fish at a concentration of 5.1 mg a.i./L. This study fulfills guideline requirements for a fish early life stage chronic test (850.1400). A second study on coldwater fish resulted in measurable effects at 2.5 mg a.i./L. However, this study (MRID 4666403) was classified as supplemental and does not fulfill guideline requirements. Measurable effects on freshwater invertebrates were noted at concentrations of 8.5 mg/L product and 4.9 mg a.i./L. However, both studies (MRID 42112501 and MRID 46660403) were classified as supplemental and do not fulfill guideline requirements for an aquatic invertebrate life cycle test.

Table 30. Chronic Toxicity of Glutaraldehyde to Freshwater Organisms

Species	Chemical, % Active Ingredient (a.i.)	Endpoint (mg/L)	Satisfies Guidelines/ Comments	Reference (MRID No.)
Rainbow Trout (*Oncorhynchus mykiss)*	Glutaraldehyde, 50%	LOEC = 5.1 NOEC = 1.6 (a.i.)	Yes* - core study - formulated product - 97-day test duration - early-life stage - flow-through test system	46373901

Species	Chemical, % Active Ingredient (a.i.)	Endpoint (mg/L)	Satisfies Guidelines/ Comments	Reference (MRID No.)
			- formulation considered TGAI	
Steelhead Trout *(Oncorhynchus mykiss)*	Glutaraldehyde, 50%	Survival (embryo): LC_{50} = NC LOEC = NC NOEC = 13.6 Hatch-out rate: IC_{50} = 1.82 LOEC = 2.5 NOEC = 1.3 Growth/Survival (larvae): IC_{50} = NC LOEC = NC NOEC = 1 (a.i.)	No - supplemental study - open literature - formulated product - 62-day test duration - early-life stage - static-renewal test system - deviations from guideline include lack of detailed information and missing raw data	4666403
Waterflea (*Daphnia magna)*	Glutaraldehyde, 50%	LOEC = 8.5 NOEC = 4.25 (product)	No - supplemental study - open literature - formulated product - 22-day test duration - life-cycle test - semi-static test system - formulation considered TGAI - deviations from guideline include MATC not established and missing raw data	42112501
Waterflea (*Ceriodaphnia dubia*)	Glutaraldehyde, 50%	Reproduction/ Survival: LC_{50}/IC50 = 4.7 LOEC = 4.9 NOEC = 2.4 Growth: IC_{50} = NC LOEC = NC NOEC = 4.9 (a.i.)	No - supplemental study - open literature - formulated product - 8-day test duration - three-brood reproduction test - static-renewal test system - deviations from guideline include short test duration period, MATC not established, and missing raw data	4666403

* Acceptable for formulated product or TGAI of 50% a.i. NC = Not calculable; no statistically significant response at tested concentrations

Nontarget plant phytotoxicity tests are required for pesticides when certain conditions of use and environmental fate apply. Testing is conducted with a rooted vascular plant rice (*Oryza* sativa), an aquatic floating vacular macrophyte (*Lemna gibba*), and four species of algae: (1) freshwater green alga, *Selenastrum capricornutum - Pseudokershneria subcapitatum,* (2) marine diatom, *Skeletonema costatum,* (3) freshwater diatom, *Navicula pelliculosa,* and (4) bluegreen alga, *Anabaena flos-aquae.* However, these tests while reserved, are not required for uses of glutaraldehyde classified as indoor. No further nontarget plant toxicity tests are required at this time. Results of available freshwater green algae toxicity studies are presented in Table 31. Study (MRID 45609401) indicates that a 50% reduction in growth in green alga occurred at a glutaraldehyde concentration of 0.31 mg a.i./L. However, this study was classified as supplemental and does not fulfill guideline requirements. The light intensity used in the study was too high, and the corresponding algal growth rate was too fast.

Table 31. Toxicity of Glutaraldehyde to Aquatic Plants

Species	Chemical, % Active Ingredient (a.i.)	Endpoint (mg/L)	Satisfies Guidelines/ Comments	Reference (MRID No.)
Green alga (*Selenastrum capricornutum)*	Glutaraldehyde, 50%	EC_{50} = 0.31 NOEC = 0.042 (a.i.)	No - supplemental study - formulated product - 96-hr test duration - growth inhibition - static test system - formulation considered TGAI - deviations from guideline include high light intensity	45609401
Green alga (Pseudokerch-neriella subcapitata*)*	Glutaraldehyde, 50%	Two studies: IC_{50} = 1.0 and 1.8 LOEC = 1.4 and 2.1 NOEC = 0.7 and 1.3 (a.i.)	No - supplemental study - open literature - formulated product - two bioassays - 96-hr test duration - growth inhibition - static test system - deviations from guideline include high light intensity, non-continuous photoperiod, lack of detailed information, and missing raw data	4666403

b. Ecological Exposure and Risk

Exposure and Risk to Nontarget Terrestrial Animals and Aquatic Organisms

Risk characterization integrates the results of the exposure and ecotoxicity data to evaluate the likelihood of adverse ecological effects. The means of this integration is called the quotient method. Risk quotients (RQs) are calculated by dividing exposure estimates by acute and chronic ecotoxicity values. RQ = EXPOSURE/TOXICITY

RQs are then compared to OPP's levels of concern (LOCs). These LOCs are used by OPP to analyze potential risk to nontarget organisms and the need to consider regulatory action. The criteria indicate that a pesticide used as directed has the potential to cause adverse effects on nontarget organisms. LOCs currently address the following risk presumption categories: (1) acute – potential for acute risk to non-target organisms which may warrant regulatory action in addition to restricted use classification, (2) acute restricted use – the potential for acute risk to non-target organisms, but may be mitigated through restricted use classification, (3) acute endangered species – endangered species may be adversely affected by use, (4) chronic risk - the potential for chronic risk may warrant regulatory action, endangered species may potentially be affected through chronic exposure, (5) non-endangered plant risk – potential for effects in non-

target plants, and (6) endangered plant risk – potential for effects in endangered plants. Currently, OPP does not perform assessments for chronic risk to plants, acute or chronic risks to nontarget insects, or chronic risk from granular/bait formulations to birds or mammals.

The ecotoxicity test values (measurement endpoints) used in the acute and chronic risk quotients are derived from required studies. Examples of ecotoxicity values derived from short-term laboratory studies that assess acute effects are: (1) LC_{50} (fish and birds), (2) LD_{50} (birds and mammals), (3) EC_{50} (aquatic plants and aquatic invertebrates) and (4) EC_{25} (terrestrial plants). Examples of toxicity test effect levels derived from the results of long-term laboratory studies that assess chronic effects are: (1) LOAEC (birds, fish, and aquatic invertebrates), and (2) NOAEC (birds, fish and aquatic invertebrates). For birds and mammals, the NOAEC generally is used as the ecotoxicity test value in assessing chronic effects, although other values may be used when justified. However, the NOAEC is used if the measurement endpoint is production of offspring or survival. Risk presumptions and the corresponding RQs and LOCs are presented in Table 32.

Table 32. Risk Presumption Categories

Risk Presumption for Terrestrial Animals	**LOC**
Acute: Potential for acute risk for all non-target organisms	>0.5
Acute Restricted Use: Potential for acute risk for all non-target organisms, but may be mitigated through restricted use classification	>0.2
Acute Endangered Species: endangered species may be adversely affected by use	>0.1
Chronic Risk: potential for chronic risk may warrant regulatory action	>1
Risk Presumption for Aquatic Organisms	**LOC**
Acute: Potential for acute risk for all non-target organisms	>0.5
Acute Restricted Use: Potential for acute risk for all non-target organisms, but may be mitigated through restricted use classification	>0.1
Acute Endangered Species: endangered species may be adversely affected by use	>0.05
Chronic Risk: potential for chronic risk may warrant regulatory action	>1
Risk Presumption for Terrestrial and Aquatic Plants	**LOC**
Potential for risk for all non-endangered and endangered plants	>1

Environmental Exposure and Risk

Freshwater and estuarine/marine aquatic animals and plants could potentially be exposed to glutaraldehyde discharged into the aquatic environment. Chronic ecotoxicity studies indicate the following: An analysis of glutaraldehyde use by the University of Michigan and the Great Lakes Research Laboratory, NOAA indicates that most current applications of glutaraldehyde result in relatively infrequent environmental releases over limited spatial areas. “There is strong

evidence that glutaraldehyde toxicity will be temperature dependent with lower environmental temperatures partially mitigating toxicity and higher temperatures augmenting it. This is further complicated by the fact that glutaraldehyde is degraded by microorganisms, which will demonstrate the opposite effect with higher temperatures resulting in more rapid degradation rates. The net effect will depend on the ambient temperatures where glutaraldehyde is released and the rates of degradation and dispersion." (MRID 466664-03).

Screening level modeling was conducted to estimate the exposure and environment risk resulting from industrial wastewater releases of glutaraldehyde into surface water using the "down-the-drain" model.

i. Down-the-Drain Model

The down-the-drain model was used to estimate exposure from industrial discharges into surface waters. To estimate the number of days of exceedance of a concentration of concern for aquatic organisms from disposal of consumer products containing glutaraldehyde, the Down-the-Drain model developed by EPA's Office of Pollution Prevention and Toxics (OPPT) was used employing the Probabilistic Dilution Model (PDM) option. The Down-the-Drain model is a screening-level model for estimating exposure to humans from ingestion of drinking water and fish based on concentrations of chemicals in surface water that may result from the disposal of consumer products into household wastewater. This model also includes a Probabilistic Dilution Model (PDM) option that attempts to account for the natural variability of stream flows and effluent flows when comparing an estimated environmental concentration to a concentration of concern (COC) for aquatic organisms. For a screening-level estimate of the number of days the COC for aquatic organisms is exceeded, results are based on a high-end scenario which represents the averaged probability of exceedance of the 10 percent of wastewater treatment plants that have the highest probability of exceedance of the COC following treatment based on the estimated typical daily per capita release of Glutaraldehyde. The COC values used as inputs to the model are derived from measurement endpoint values and Levels of Concern (LOCs) that correspond to risk presumption categories for aquatic animals and plants. Measurement endpoint values, COCs, and number of days of exceedance of the COC predicted by the Down-the-Drain model by type of aquatic organism are presented in the Table 33. Measurement endpoints are based on toxicity data for the most sensitive aquatic species tested.

Table 33. Screening Level Inputs and Results for High-End Scenario for Down-the-Drain Modeling for Glutaraldehyde Based on Assumptions of 1,000,000 kg/yr Wastewater Influent Volume and No Removal During Wastewater Treatment (EPA - Jennings, P. 2007)

Type of Organism	Measurement Endpoint (ppm)	Concentration of Concern (COC) (ppb)	Number of Days of Exceedance of COC
Freshwater Fish	Acute LC50: 9.5 Chronic NOAEC: 1.6	Acute:4750 Acute ES: 475 Chronic: 1600	Acute: 0 Acute ES: 0.11 Chronic: 0
Freshwater Invertebrate	Acute LC50: 0.75 Chronic NOAEC: 2.4	Acute:375 Acute ES: 37.5 Chronic: 2400	Acute: 0.2 Acute ES: 24.79 Chronic: 0
Aquatic Plant	Acute EC50: 0.31 Chronic NOAEC: 0.042	Acute: 310 Acute ES: 42	Acute: 0.32 Acute ES: 20.72

ES – Endangered Species
COC – Concentration of Concern
RQ – Risk Quotient; RQ = EEC/LC50 or EEC/NOAEC.
EEC – Estimated Environmental Concentration (usually ppb in water)
LOC – Level of Concern; the ratio of EEC/LC50 or EEC/NOAEC that triggers a potential for concern for a risk presumption category for aquatic plants and aquatic animals. Risk presumption categories include acute risk, acute restricted use risk, acute endangered species risk, and chronic risk. For aquatic animals, the LOC for acute risk is 0.5 and the LOC for endangered species acute risk is 0.05. For aquatic plants, the LOC is 1 for both acute risk and acute endangered species risk.
Sample calculation of COC: For freshwater fish, the LC50 for the most sensitive species for which test data were available was 9.5 ppm. The LOC for acute risk for freshwater fish is 0.5; consequently, 0.5 x RQ triggers the level of concern for acute risk for freshwater fish. The COC is the concentration in surface water at which the LOC would occur; consequently, based on RQ = EEC/LC50 and substituting LOC for the RQ and COC for EEC, 0.5 = COC/LC50. Rearranging this equation, COC = 0.5 x LC50 which corresponds to COC = 0.5 x 9.5 mg/L, which is 4.75 mg/L, or 4750 ug/L.

In interpreting the results of the Down-the-Drain model using the PDM option, OPPT uses the following criteria to trigger the potential for concern leading to more in-depth examination:

- for acute risk to freshwater fish, invertebrates, and plants exceedance of the COC by 4 days or more;
- for chronic risk to freshwater fish and invertebrates, exceedance of the COC by 20 days or more;

For other aquatic organisms, there are no established criteria and the potential for risk is determined on a case-by-case basis.

Conclusions

Results of the down-the-drain model indicate no acute or chronic risk to freshwater fish, freshwater invertebrates, or aquatic plants using an LOC of >0.5 for aquatic animals and >1.0 for aquatic plants. Using an LOC of >0.05 for aquatic animals and >1.0 for aquatic plants acute risk to endangered fish is not triggered. However, acute risk to endangered freshwater invertebrates and aquatic plants is triggered.

c. 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 andronomus 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 CFR402.02.

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, therefore, 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 majority of glutaraldehyde uses are spray applications to indoor surfaces such as hospital, veterinary, nursing home, and food processing plant equipment that are not expected to result in significant discharge into the environment. The down-the-drain model was used due to the relatively long half-life of glutaraldehyde in water. Tier I Down-the-drain modeling indicates that glutaraldehyde may pose an adverse risk to endangered freshwater invertebrates, however, further refinements and/or monitoring data are recommended as confirmatory. The Agency is not currently aware of any endangered or threatened green alga species, however, the non-target plant risk assessment is incomplete due to an incomplete toxicity data base for aquatic plants.

Factors that serve to reduce discharge impacts on aquatic species include the NPDES permitting process, rapid glutaraldehyde breakdown in the environment, and relatively short term impacts on aquatic ecosystems from currently registered uses. The down-the-drain model does

not account for degradation rates of glutaraldehyde in soil or water. An endangered species determination cannot be made at this time and will be deferred until confirmatory data are made available.

IV. Risk Management, Reregistration, and Tolerance Reassessment Decision

A. Determination of Reregistration Eligibility

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

The Agency has completed its assessment of the dietary, occupational, drinking water, and ecological risks associated with the use of pesticide products containing the active ingredient glutaraldehyde. Based on a review of these data and on public comments on the Agency's assessments for the active ingredient glutaraldehyde, the Agency has sufficient information on the human health and ecological effects of glutaraldehyde to make decisions as part of the tolerance reassessment process under FFDCA and reregistration process under FIFRA, as amended by FQPA. The Agency has determined that glutaraldehyde-containing products are eligible for reregistration provided that: (i) confirmatory data needs are addressed; (ii) the risk mitigation measures outlined in this document are adopted; and (iii) label amendments are made to reflect these measures. Label changes are described in Section V. Appendix A summarizes the uses of glutaraldehyde 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 glutaraldehyde 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.

Based on its evaluation of glutaraldehyde, the Agency has determined that glutaraldehyde products, unless labeled and used as specified in this document, would present risks inconsistent with FIFRA. Accordingly, should a registrant fail to implement the risk mitigation measures identified in this document, the Agency may take regulatory action to address the risk concerns from the use of glutaraldehyde. If all changes outlined in this document are incorporated into the product labels, then all current risks for glutaraldehyde will be substantially mitigated for the purposes of this determination. Once an Endangered Species assessment is completed, further changes to these registrations may be necessary as explained in Section III of this document.

B. Public Comments and Responses

Through the Agency's public participation process, the EPA worked with stakeholders and the public to reach the regulatory decision for glutaraldehyde. EPA released its preliminary risk assessment for glutaraldehyde for public comment on July 6, 2007. The Agency received several comments during the 60-day public comment period on the glutaraldehyde risk assessment and supporting science documents, which closed on September 4, 2007.

C. Regulatory Position

1. Food Quality Protection Act Findings

The Agency has determined that, if the mitigations described in this document are adopted and labels are amended, human health risks as a result of exposures to glutaraldehyde are within acceptable levels. In other words, EPA has concluded that glutaraldehyde meets FQPA safety standards. In reaching this determination, EPA has considered the available information on the special sensitivity of infants and children, as well as exposures to glutaraldehyde from all possible sources.

a. Determination of Safety to U.S. Population

As part of the FQPA tolerance reassessment process, EPA assessed the risks associated with glutaraldehyde. The Agency has determined that the amendments and changes for glutaraldehyde specified in this document meet the safety standards under the FQPA amendments to section 408(b)(2)(D) of the FFDCA, and that there is a reasonable certainty no harm will result to the general population or any subgroup from the use of glutaraldehyde. In reaching this conclusion, the Agency has considered all available information on the toxicity, use practices and exposure scenarios, and the environmental behavior of glutaraldehyde.

b. Determination of Safety to Infants and Children

EPA has determined that the currently registered uses of glutaraldehyde, with changes as specified in this document, meet the safety standards under the FQPA amendments to section 408(b)(2)(C) of the FFDCA, that there is a reasonable certainty of no harm for infants and children. The safety determination for infants and children considers factors of the toxicity, use practices, and environmental behavior noted above for the general population, but also takes into account the possibility of increased susceptibility to the toxic effects of glutaraldehyde residues in this population subgroup.

No special hazard-based FQPA Safety Factor is necessary to protect the safety of infants and children. In determining whether or not infants and children are particularly susceptible to toxic effects from glutaraldehyde residues, the Agency considered the completeness of the database for developmental and reproductive effects, the nature of the effects observed, and other information. The special hazard-based FQPA Safety Factor has been removed (i.e., reduced to 1x) for glutaraldehyde based on: (1) a complete toxicology database with respect to assessing the increased susceptibility to infants and children as required by FQPA; (2) no concern for developmental neurotoxicity resulting from exposure to glutaraldehyde in the rat and rabbit prenatal developmental studies and the 2-generation reproduction study; (3) no evidence of increased susceptibility to the fetus following *in utero* exposure in the prenatal developmental toxicity studies or to the offspring when adults are exposed in the two-generation reproduction study; and (4) the risk assessment does not underestimate the potential exposure for infants and children.

c. Endocrine Disruptor Effects

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

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

d. Cumulative Risks

Risks summarized in this document are those that result only from the use of glutaraldehyde. The Food Quality Protection Act (FQPA) requires that the Agency consider "available information" concerning the cumulative effects of a particular pesticide's residues and "other substances that have a common mechanism of toxicity." The reason for consideration of other substances is due to the possibility that low-level exposures to multiple chemical substances that cause a common toxic effect by a common toxic mechanism could lead to the same adverse health effect as would a higher level of exposure to any of the substances individually. 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 for glutaraldehyde. For information regarding EPA's efforts to determine which chemicals have a common mechanism of toxicity and to evaluate the cumulative effects of such chemicals, see the policy statements released by EPA's Office of Pesticide Programs concerning common mechanism determinations and procedures for cumulating effects from substances found to have a common mechanism on EPA's website at http://www.epa.gov/pesticides/cumulative/.

D. Regulatory Rationale

The Agency has determined that glutaraldehyde is eligible for reregistration provided that additional required data confirm this decision, the risk mitigation measures outlined in this document are adopted, and label amendments are made to reflect these measures.

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

1. Human Health Risk Management

a. Residential Risk Mitigation

i. Handler Risk Mitigation

Residential handler dermal and inhalation risks were assessed for the use of glutaraldehyde as a preservative in laundry detergents and fabric softeners and its use as a preservative in paints. Short-term (ST) dermal risks were not of concern for any residential use. The Agency used a number of models and refinements in developing risk estimates for inhalation exposures presenting a range of potential air concentrations.

For laundry detergents/fabric softeners, the Agency believes that the use of a modified weight fraction based upon the amount of wash water used is appropriate in this case. The estimated 24-hour time-weighted average (TWA) concentration using this assumption is 0.019 ppb which is below the short-term reference concentration of 0.12 ppb. Therefore, the Agency does not have risk concerns for the laundry detergent/fabric softener use pattern.

For paints, risks of concern were identified for residents when using the maximum application rate of 1000 ppm (concentrations ranging from 1.0 to 22 ppb). To mitigate this risk, the maximum application rate for paint preservation must be reduced to 100 ppm. At this rate, the expected air concentration falls below the reference concentration and the risk is not of concern.

The Agency believes that, given the chemical properties of this chemical, the level of glutaraldehyde present in finished paint products available to consumers is significantly lower than the rate applied during the manufacturing process. Therefore, the air concentrations predicted for the 1000 ppm rate are likely overestimated substantially. The registrants intend to generate data to characterize actual levels of glutaraldehyde in finished paint products to empirically demonstrate this expected reduction. Upon receipt and review of this information, the Agency will reevaluate the need for the mitigation described above.

ii. Post-Application Risk Mitigation

Residential post-application inhalation risks were assessed for the use of glutaraldehyde as a preservative paints. Modeled air concentrations ranged from 3.7 ppb to 37 ppb assuming that residents are in painted areas of a residence immediately following application of primer and paint exceeding the Agency's level of concern. The reduction of the maximum application rate described above will mitigate much of the potential exposure with a predicted air concentration of 3.7 ppb. Further, the Agency does not consider it likely that residents will immediately enter and spend significant time in a freshly primed or painted room and that, in the event they needed to enter these areas, steps would be taken to increase ventilation. Therefore, the air concentrations predicted by the model are considered to be conservative, worst-case estimates and actual exposure is likely to be significantly less. Based on this conservatism in the modeled results and the rate reduction, the Agency considers the post-application inhalation risks to be mitigated and not of concern.

b. Occupational Risk Mitigation

i. Handler Risk Mitigation

It should be noted that for the dermal route, only intermediate-term (IT) dermal exposure is assessed for occupational handler scenarios since the IT toxicity endpoint selected is based on systemic effects. Short-term (ST) dermal exposures were not evaluated because the ST toxicity endpoint is based on dermal irritation. Dermal irritation exposures and risks will be mitigated using label-specified personal protective equipment (PPE) or default PPE requirements based on the toxicity of the end-use product. To minimize dermal exposures, the minimum PPE required for mixers, loaders, and others exposed to end-use products that result in classification of category I, II, or III for skin irritation potential will be a long-sleeve shirt, long pants, shoes, socks, chemical-resistant gloves, and a chemical-resistant apron.

For occupational painters, inhalation risks of concern were identified with concentrations ranging from 0.76 to 530 ppb exceeding the Agency's short-term occupational reference concentration of 0.32 ppb. To mitigate this risk, the maximum application rate for paint preservation must be reduced to 100 ppm as described earlier. This reduction results is a predicted air concentration of 0.76 ppb. This reduction, together with consideration of the conservative assumptions used to estimate air concentrations, adequately address the Agency's risk concerns for this use scenario.

For occupational applicators of hard surface disinfectants in medical settings, inhalation risks of concern were identified with average concentrations ranging from 16 to 135 ppb exceeding the Agency's short-term occupational reference concentration of 0.32 ppb. In order to reduce exposures, the maximum use rates for these products must be reduced to 0.1% resulting in the concentration of 16 ppb. These products must also specify that they may only be used in areas where the air exchange rate is equal to or greater than 6 exchanges per hour which is believed to be the industry standard for non-critical medical premises. Additionally, these products are an important tool needed for control of public health microorganisms. If the rate reduction impacts the efficacy of the product, the registrant must consult further with the Agency to determine how to reduce exposure while maintaining efficacy.

For other industrial process applications the following mitigation is required to reduce the potential for inhalation exposures:

- The open pouring of glutaraldehyde solutions must be limited to low volume applications where the amount of concentrate handled is less than five gallons per day.
- Automatic addition systems that minimize operator exposure to the concentrated product must be used when handling larger amounts of glutaraldehyde. If this is not feasible then local exhaust ventilation must be used to reduce glutaraldehyde exposure.

ii. Post-Application Risk Mitigation

For the use as a fogger for animal premises, air concentrations within the structure remained above the short-term reference concentration for up to 3 hours following application. Based on this analysis, the Agency is requiring that fogger product labels include a 3-hour REI

so that workers will not enter the structure while levels of glutaraldehyde exceed the reference concentration without the appropriate personal protective equipment.

Occupational post-application inhalation risks (IT) of concern were identified for the machinist exposed to metal working fluids preserved with glutaraldehyde with an air concentration of 0.13 to 0.99 ppb. Based on the conservative assumptions used in the risk assessment, the Agency believes that the actual exposure will not result in a risk of concern especially considering the proximity of the risk estimates to acceptable reference concentrations.

2. Environmental Risk Management

No environmental risk mitigation measures are necessary for the antimicrobial use of glutaraldehyde at this time. The majority of glutaraldehyde uses are spray applications to indoor surfaces such as hospital, veterinary, nursing home, and food processing plant equipment that are not expected to result in significant discharge into the environment. However, the down-the-drain model was used to estimate environmental concentrations of glutaraldehyde in aquatic systems because of its relatively long half-life in water. Tier I Down-the-drain modeling indicates that glutaraldehyde may pose an adverse risk to endangered freshwater invertebrates. This model does not account for degradation rates of glutaraldehyde in soil or water, therefore, the following additional environmental fate data are required to confirm the decisions made in this document:

- Aerobic soil metabolism (162-1)

3. Other Labeling Requirements

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

4. Listed Species Considerations

a. The Endangered Species Act

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 andronomus 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 C.F.R. ' 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 Level of Concern 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, therefore, 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 majority of glutaraldehyde uses are spray applications to indoor surfaces such as hospital, veterinary, nursing home, and food processing plant equipment that are not expected to result in significant discharge into the environment. The down-the-drain model was used due to the relatively long half-life of glutaraldehyde in water. Tier I Down-the-drain modeling indicates that glutaraldehyde may pose an adverse risk to endangered freshwater invertebrates, however, further refinements and/or monitoring data are recommended as confirmatory. The Agency is not currently aware of any endangered or threatened green alga species, however, the non-target plant risk assessment is incomplete due to an incomplete toxicity data base for aquatic plants.

Factors that serve to reduce discharge impacts on aquatic species include the NPDES permitting process, rapid glutaraldehyde breakdown in the environment, and relatively short term impacts on aquatic ecosystems from currently registered uses. The down-the-drain model does not account for degradation rates of glutaraldehyde in soil or water. An endangered species determination cannot be made at this time and will be deferred until confirmatory data are made available..

b. General Risk Mitigation

Glutaraldehyde end-use products (EPs) may also contain other registered pesticides. Although the Agency is not proposing any mitigation measures for products containing glutaraldehyde specific to federally listed species, the Agency needs to address potential risks from other end-use products. Therefore, the Agency requires that users adopt all listed species risk mitigation measures for all active ingredients in the product. If a product contains multiple active ingredients with conflicting listed species risk mitigation measures, the more stringent measure(s) should be adopted.

V. What Registrants Need to Do

The Agency has determined that glutaraldehyde is eligible for reregistration provided that: (i) additional data that the Agency intends to require confirm this decision; (ii) the risk mitigation measures outlined in this document are adopted; and (iii) label amendments are made to reflect these measures To implement the risk mitigation measures, the registrants must amend their product labeling to incorporate the label statement set forth in the Label Changes Summary Table in Section B below (Table). The additional data requirements that the Agency intends to obtain will include, among other things, submission of the following:

For glutaraldehyde 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 Michelle Centra at (703) 308-2476 with questions regarding generic reregistration.

By US mail:

Document Processing Desk
Michelle Centra
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
Michelle Centra
Office of Pesticide Programs
(7510P)
U.S. Environmental Protection Agency
One Potomac Yard, Room S-4900
2777 South Crystal Drive
Arlington, VA 22202

For end-use products containing the active ingredient glutaraldehyde, 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 23 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 Marshall 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

A. Manufacturing Use Products

1. Additional Generic Data Requirements

The generic database supporting the reregistration of glutaraldehyde has been reviewed and determined to be substantially complete. However, the following additional data requirements have been identified by the Agency as confirmatory data requirements and will be included in the generic data call in (DCI) for this RED.

The requested storage stability study and environmental fate study listed in Table 36 are confirmatory data for the painting and aquatic industrial uses of glutaraldehyde.

Table 34. Confirmatory Data Requirements for Glutaraldehyde

Guideline Study Name	New OPPTS Guideline Number	Old Guideline Number
Confirmatory Data Requirements for Reregistration		
Storage stability (for glutaraldehyde as an in-can paint preservative)	830.6317	63-17
Aerobic soil metabolism	None	162-1

2. Labeling for Technical and Manufacturing Use Products

To ensure compliance with FIFRA, technical and manufacturing-use product (MP) labeling should be revised to comply with all current EPA regulations, PR Notices and applicable policies. The Technical and MP labeling should bear the labeling contained in Table 25, Label Changes Summary Table.

B. End-Use Products

1. Additional Product-Specific Data Requirements

Section 4(g)(2)(B) of FIFRA calls for the Agency to obtain any needed product-specific data regarding the pesticide after a determination of eligibility has been made. 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. A product-specific data call-in will be issued at a later date.

2. Labeling for End-Use Products

Labeling changes are necessary to implement measures outlined in Section IV above. Specific language to incorporate these changes is specified in Table 36, Label Changes Summary Table.

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.

a. Label Changes Summary Table

In order to be eligible for reregistration, all product labels must be amended to incorporate the risk mitigation measure outlined in Section IV of the glutaraldehyde RED. The following table describes how language on the labels should be amended.

Table 35. Labeling Changes Summary Table

Description	Amended Labeling Language	Placement on Label
Environmental Hazards Statements Required by the RED and Agency Label Policies	"This product is toxic to fish, aquatic invertebrates, oysters and shrimp. Do not discharge effluent containing this product into lakes, streams, ponds, estuaries, oceans, or other waters unless in accordance with the requirements of a National Pollution Discharge Elimination System (NPDES) permit and the permitting authority has been notified in writing prior to discharge. Do not discharge effluent containing this product to sewer systems without previously notifying the local sewage treatment plant authority. For guidance contact your State Water Board or Regional Office of the EPA."	Precautionary Statements
End Use Products Intended for Occupational Use		
PPE Requirements	"long-sleeve shirt, long pants, shoes, socks, chemical-resistant gloves, and chemical-resistant apron"	Immediately following/below Precautionary Statements: Hazards to Humans and Domestic Animals
Application of poulty house fogging end-use products	"Fogging of poultry houses should only be done in such a way that the operator is outside the poultry house when applying the fog"	This language is to be included in the Environmental Hazards section of the label.
Re-entry Interval for poultry house fogging end-use products	Add a re-entry interval (REI) of 3 hours to all end-use product labels listing poultry house fogging as a use.	This language is to be included in the Environmental Hazards section of the label.
Directions For Use		
Application restrictions	Use: paint preservative Maximum application rate of 100 ppm. This application reduction results is a predicted air concentration of 0.76 ppb.	Use Directions

Application restrictions	Use: medical premises disinfection Maximum application rate of 0.1% of the active ingredient by weight of material being treated. This application reduction results in an air concentration of 16 ppb.	Use Directions
Once-Through Cooling Tower	All glutaraldehyde once-through cooling tower uses are cancelled and must be deleted from current product labels.	
Macrofoulant Control	All glutaraldehyde macrofoulant control uses are cancelled and must be deleted from all product labels.	
Critical Medical Equipment/Instrument	All glutaraldehyde critical medical equipment/instrument uses are cancelled and must be deleted from all product labels. Critical medical equipment use is defined as use of a pesticide in or on any equipment that comes into contact with bodily fluids. Examples of critical medical equipment/instruments include, but are not limited to hemodyalysis tubing, dental instruments, etc.	