United States Environmental Protection Agency

Office of Prevention, Pesticides and Toxic Substances (7505P)

Pesticide Fact Sheet

Name of Chemical: **Alpha-Chlorohydrin**
Reason for Issuance: **New Chemical**

Date Issued: **December 2006**

Description of Chemical

Generic Name:	3-chloro-1,2-propanediol
Common Name:	alpha-chlorohydrin
End Use Product Trade Name:	Epibloc® Rodenticide
Chemical Type:	Organochlorine
EPA Chemical Code:	117101
Chemical Abstracts Service (CAS) Number:	96-24-2
Registration Status:	One End Use Product Registered
Pesticide Type:	Rodenticide
U.S. Registrant:	Gametrics Limited 426 Lonesome Country Road Alzada, Montana 59311

Use Pattern and Formulations

Alpha-chlorohydrin is formulated as a 1% rodenticide bait packaged in 5 gram "sachets" (also known as "place paks" for other rodenticide formulations). There is one end use product with the trade name "Epibloc® Rodenticide." Epibloc bait sachets must be placed in tamper-resistant bait stations and the use sites are limited to the indoors of industrial and commercial facilities only, and in sanitary sewers. Placement in sanitary sewers does not require use of tamper-resistant stations. No outdoor uses are permitted. The target pest is Norway rats. Epibloc is not registered for any other rodent species.

Epibloc® Rodenticide is a Restricted Use Pesticide product. The Restricted Use classification is based on the potential for toxicity and reproductive effects to non-target organisms.

As a rodenticide, alpha-chlorohydrin causes reversible infertility in male mammals at low doses and testicular lesions and/or mortality at high doses. The active ingredient exists as a racemic mixture of *R*- and *S*-alpha-chorohydrin. At relatively low doses in rats, alpha-chlorohydrin causes decreased sperm motility and sperm count. At higher doses, testicular pathology and/or death are induced. Information from the published literature suggests that *S*-alpha-chorohydrin is converted to *S* -3-chlorolactaldehyde, which then inhibits glyceraldehyde 3-phosphate dehydrogenase, an essential enzyme in sperm glycolysis (Jones 1998). This mechanism also operates in somatic cells; however, sperm are believed to contain a more susceptible isoform of this enzyme (Jelks and Miller 2001). Jones and Cooper (1999) have reported that the *R*-enantiomer is responsible for kidney toxicity at higher doses.

Science Findings

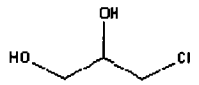
Table 1. Test Compound Nomenclature	
Chemical structure	
Common name	Alpha-chlorohydrin
Company experimental name	U-5897
CAS name	3-chloro-1,2-propanediol
CAS registry number	96-24-2
End-use product (EP)	Epibloc® Rodenticide (1% alpha-chlorohydrin)

Table 2. Physicochemical Properties of the Technical Grade Test Compound		
Parameter	**Value**	**Reference**
Melting point/range	-40°C	http://chemfinder.cambridgesoft.com
Density	1.322 g/cm^3	http://chemfinder.cambridgesoft.com
Water solubility	≥ 10g/100mL at 21°C	http://chemfinder.cambridgesoft.com
Vapor pressure	13 mbar at 115°C	MRIDs 00065658, 00097670, 00065657, 00071281
Dissociation half-life in water (abiotic)	500 days at pH 4	MRIDs 00065658, 00097670, 00065657, 00071281
Octanol/water partition coefficient, Log P_{OW}	-0.85	MRIDs 00065658, 00097670, 00065657, 00071281

TOXICOLOGY SUMMARY

Acute Toxicity

Alpha-chlorohydrin has a moderate order of acute toxicity (Table 3) via the oral route (Category II) and a low order of acute toxicity via the dermal route (Category III). No acute inhalation toxicity or dermal sensitization studies exist in the database for alpha-chlorohydrin. Alpha-chlorohydrin is not a dermal irritant (Category IV); however, it has been shown to be a severe eye irritant (Category I).

Table 3. ACUTE TOXICITY PROFILE FOR ALPHA-CHLOROHYDRIN			
Guideline No./Study Type	**Results**	**Toxicity Category**	**MRID/Reference No.**
870.1100/Acute oral toxicity (mouse)	LD_{50} = 159 mg/kg (M/F)	II	Glenn and Burr (1968)
870.1100/Acute oral toxicity (rat)	LD_{50} = 131 mg/kg (M/F)	II	Glenn and Burr (1968)
870.1200/Acute dermal toxicity (rabbit)	LD_{50} ≥ 2000 mg/kg (M/F); slight dermal irritation at 24 hrs. clearing by day 6	III	Meyer (1980)
870.2500/Primary dermal irritation (rabbit)	Not a dermal irritant	IV	Meyer (1980)
870.2400/Primary eye irritation (rabbit)	Corrosive; severe eye irritant	I	Glenn and Burr (1968)
870.2400/Primary eye irritation (rabbit)	Minimally irritating to washed/unwashed eyes at 48/24 hrs., resp., clearing by 72 hrs.	III	Meyer (1980)

Table 4. SUBCHRONIC AND CHRONIC TOXICITY AND GENOTOXICITY PROFILE FOR ALPHA-CHLOROHYDRIN			
Study Type	**Doses**	**Results**	**MRID/Reference No.**
7-day oral toxicity (dog; capsule)	0, 52, 83, or 131 mg/kg/day	NOAEL not observed. LOAEL = 52 mg/kg/day based on foci of demyelination, vacuolization, and	Glenn and Burr (1969)

		degenerative neurons and glial cells in thalamus and hippocampus and decreased body weight	
5-day inhalation toxicity (rat, rabbit, dog)	0 or 4 mg/L (4 hrs/day) (equivalent to 0 or 720/365/522 mg/kg/day for rat/rabbit/dog, respectively [1])	NOAEL not observed. LOAEL = 720/365/522 mg/kg/day based on pneumonitis, focal pulmonary hemorrhage, alveolar edema, slight bronchitis and hepatic congestion (dogs); pulmonary focal hemorrhage and congestion, cloudy swelling of the hepatocytes, testicular hypogenesis, and focal polioencephalomalacia (inflammation and softening of the grey matter of the brain) (rabbits); and testicular hypogenesis, renal tubular casts, renal cystic tubular dilatation, and pulmonary congestion (rats)	Glenn and Moe (1969)
≤60-day oral toxicity (monkey; dietary)	0, 10, 25, 30, 50, 150, or 200 mg/kg/day	NOAEL = 25 mg/kg/day LOAEL = 30 mg/kg/day based on death caused by severe bone marrow depression (neutropenia, thrombocytopenia, and anemia) and secondary hemorrhagic pneumonia, enteritis, pleuritis, and peritonitis	Ray and Ceru (1968); Kirton et al. (1970)
55-day oral toxicity (monkey; gavage)	0 or 25 mg/kg/day	NOAEL = 25 mg/kg/day LOAEL not observed	Ray et al. (1967)
30-day oral toxicity (dog; dietary)	0 or 35 mg/kg/day	NOAEL not observed LOAEL = 35	Glenn et al. (1969)

[1] Estimated in the absence of a physiologically based toxicokinetic (PBTK) model as follows: [(Concentration in mg/L) x 100% absorption x (45 L/hr/kg for a rat; 22.8 L/hr/kg for a rabbit; and 32.6 L/hr/kg for a dog) x 4hrs].

		mg/kg/day based on decreased prostate and testis weight and decreased body weight	
4-week oral toxicity (rat; gavage)	0, 30, or 60 mg/kg/day	NOAEL not observed LOAEL = 30 mg/kg/day based on increased relative kidney weight (F) on day 2; increased serum ALT (F), decreased Hb and MCV (M&F), and increased relative kidney and liver weights on day 25; and mild tubule dilatation of testes and decreased body weight gain at termination*	Marchesini and Stalder (1983)
90-day oral toxicity (rat; drinking water)	0, 9/11, 27/31, or 43/46 mg/kg/day (M/F)	NOAEL not observed LOAEL = 9/11 mg/kg/day (M/F) based on increased relative kidney weight, decreased serum creatinine, and increased number of exfoliated epididymal spermatozoids (M only)*	Marchesini and Stalder (1989)
Carcinogenicity (mouse; dermal)	0 or 2 mg/mouse (equivalent to 20 mg/kg/day; 3X/week) for 83 weeks	NOAEL = 20 mg/kg/day LOAEL not observed No skin papillomas or carcinomas observed	Van Duuren et al. (1974)
Chronic Oral Toxicity/Carcinogenicity (rat; gavage)	0, 30, or 60 mg/kg/day (2X/week); doses increased to 0, 35, or 70 mg/kg/day (after 10 weeks) up to week 72	NOAEL not observed LOAEL = 30 mg/kg/day based on severe testicular degeneration and atrophy Marginally positive trend (P=0.044) only for parathyroid adenomas in males	Weisburger et al. (1981)
Chronic Oral Toxicity/Carcinogenicity (rat; drinking water)	0, 20, 100, or 500 mg/L [equivalent to 0/0, 1.1/1.4, 5.2/7.0, or 28/35 mg/kg/day	NOAEL not observed LOAEL = 1.1/1.4 mg/kg/day (M/F)	Sunahara et al. (1993)

* As reported in Schlatter J, Baars AJ, DiNovi M, Lawrie S, and Lorentzen R. (2002). 3-chloro-1,2-propanediol. In: Proceedings of the Fifty-seventh Meeting of the Joint FAO/WHO Expert Committee on Food Additives (JECFA) of the Safety Evaluation of Certain Food Additives and Contaminants. WHO Food Additives Series No. 48, 401–432.

	(M/F)] for 104 weeks	based on decreased absolute kidney weight (in the absence of decreased body weight) and increased incidences of Leydig cell adenomas, mammary glandular hyperplasia, chronic progressive nephropathy, and kidney tubule hyperplasia in males; and increased incidences of kidney tubule hyperplasia in females*	
Non-guideline – Male reproductive function and performance (sheep; capsule)	0 or 25 mg/kg/day (25 days)	NOAEL not observed LOAEL = 25 mg/kg/day based on decreased sperm motility after 3 days (reversible), increased # abnormal sperm (irreversible), and decreased fertility (reversible)	Kreider and Dutt (1970)
Non-guideline – Male reproductive function and performance (boar; dietary)	1, 5, 25, or 50 mg/kg/day (25 days)	NOAEL not observed LOAEL = 1 mg/kg/day based on decreased sperm motility and concentration after 3 days (reversible) and infertility (reversible)	Johnson and Pursel (1972)
Non-guideline – Male reproductive function and performance (monkey; drinking water)	0 or 15 mg/kg/day (6 months)	NOAEL = 15 mg/kg/day LOAEL not observed	Ericsson et al. (1969)
Non-guideline – Male reproductive function (rat; gavage)	0, 30, 35, 45, 60, or 90 mg/kg/day (1 or 8 days)	NOAEL = 30 mg/kg/day LOAEL = 35 mg/kg/day (8 days) based on sterility from lesions in caput epididymis Epididymal lesions also observed at 35 mg/kg/day after single dose	Ericsson (1970)
Non-guideline – Male and female reproductive function and performance (rat;	0, 1, 1.5, 2, 3, 5, 10, 15, or 30 mg/rat (equivalent to 0, 2.9, 4.3, 5.7, 8.6, 14, 29, 43, or 86 mg/kg/day; 1, 2, or 8 days)	NOAEL = 2.9 mg/kg/day LOAEL = 4.3	Ericsson and Baker (1970)

gavage)		mg/kg/day based on infertility (8 days)	
Non-guideline – Male and female reproductive function and performance (rat; oral)	0, 0.2, 1, 1.25, 2.5, 5, 10, or 25 mg/rat (2 weeks-4 months)	NOAEL = 1 mg/kg/day LOAEL = 1.25 mg/kg/day based on decreased (30%) fertility and percentage of fertilized eggs	Vickery et al. (1974)
Non-guideline – Male reproductive function (rat; drinking water)	0, 50, 100, 150, 200, 250, or 300 mg/kg/day (10 days)	NOAEL not observed LOAEL = 50 mg/kg/day based on epididymal lesions	Kennelly et al. (1970)
Non-guideline – Male reproductive function (rat; gavage)	0 or 140 mg/kg *	NOAEL not observed LOAEL = 140 mg/kg/day based on sloughing of epididymal epithelium after 2 hrs. followed by obstruction of epididymal tract	Hoffer et al. (1973)
Non-guideline – Male and female reproductive performance (rat; gavage)	0, 0.1, 0.5, 1, 2, 3,4, 5, or 10 mg/kg *	NOAEL = 2 mg/kg/day LOAEL = 3 mg/kg/day based on increased incidence of pre-implantation loss	Parish (1989)
Non-guideline – Male and female reproductive performance (rat; gavage)	0, 5, 10, or 20 mg/kg (5 or 14 days)	NOAEL not observed LOAEL = 5 mg/kg/day based on decreased sperm motility, altered sperm motion, and decreased pregnancy rate (0%)	Woods and Garside (1996)
Non-guideline – Male and female reproductive performance (rat; gavage)	0, 5, or 20 mg/kg (3 or 18 days)	NOAEL not observed LOAEL = 5 mg/kg/day based on altered sperm motion and decreased pregnancy rate	Kawaguchi et al. (2004)
Non-guideline – Male and female reproductive performance and function and fetal effects (rat; gavage)	0, 0.01, 0.05, 0.25, 1, or 5 mg/kg (28 days)	NOAEL = 0.05 mg/kg LOAEL = 0.25 mg/kg/day based on decreased sperm count and motility	Kwack et al. (2004)
Non-guideline – Male reproductive function (rat; drinking water)	0, 5, 10, or 20 mg/kg (8 days)	NOAEL = 5 mg/kg/day LOAEL = 10	Toth et al. (1992)

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		mg/kg/day based on reduced percentage of motile sperm, curvilinear velocity, straight-line velocity, lateral head displacement, and linearity	
Non-guideline – Male reproductive function and performance (rat; gavage)	0, 1, 5, or 25 mg/kg (14 days)	NOAEL = 1 mg/kg/day LOAEL = 5 mg/kg/day based on reduced percentage of motile sperm and decreased fertility	Hoyt et al. (1994)
Non-guideline – Male and female reproductive function and performance (rat; gavage)	0, 1, 3, or 10 mg/kg (9 days)	NOAEL = 1 mg/kg/day LOAEL = 3 mg/kg/day based on decreased fertilization and pregnancy rates, # sperm reaching oviducts of females, sperm velocity, and lateral head displacement	Ban et al. (1999)
Non-guideline – Male and female reproductive function and performance (rat; gavage)	0, 2, or 8 mg/kg (14 days)	NOAEL not observed LOAEL = 2 mg/kg/day based on decreased sperm activity when incubated for 2 hrs.	Yamada et al. (1995)
Non-guideline – Immunotoxicity (rat; gavage)	0, 25, 50, or 100 mg/kg (14 days)	NOAEL = 50 mg/kg/day LOAEL = 100 mg/kg/day based on decreased absolute and relative thymus weight (in the absence of decreased body weight), # cells in spleen and thymus, and antibody forming response	Lee et al. (2004, 2005)
In vivo dominant lethal mutation (ICR/Ha Swiss mice)	125 mg/kg i.p. or 20 mg/kg/day (oral; 5 days)	Negative *	Epstein et al. (1972)
In vivo dominant lethal mutation (male mice)	0, 5, or 10 mg/kg/day (oral; 5 days)	Negative *	Jones et al. (1969)
In vivo dominant lethal	0, 5, 10, or 20 mg/kg/day (oral;	Negative *	Jones and Jackson

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mutation (male Wistar rats)	5 days)		(1976)
In vivo micronucleus test (bone marrow, OF_1 mice)	40-120 mg/kg	Negative *	Jaccaud and Aeschbacher (1989)
In vivo micronucleus test (bone marrow, male Han Wistar rats)	0, 15, 30, or 60 mg/kg/day (oral; 2 days)	Negative * Piloerection and bone marrow cytotoxicity observed after 2 days at 60 mg/kg/day	Marshall (2000)
In vivo unscheduled DNA synthesis (male Han Wistar rats)	0, 40, or 100 mg/kg (oral)	Negative *	Fellows (2000)
In vitro reverse mutation (S. typhimurium TA1535)	2-200 µmol/plate (0.2-22 mg/plate)	Positive with and without metabolic activation *	Silhankovà et al. (1982)
In vitro reverse mutation (S. typhimurium TA1537, TA1538, TA98)	2-200 µmol/plate (0.2-22 mg/plate)	Negative with and without metabolic activation *	Silhankovà et al. (1982)
In vitro reverse mutation (S. typhimurium TA100, TA1535)	10-1000 µmol/plate (1.1-110 mg/plate)	Positive with and without metabolic activation *	Stolzenberg and Hine (1979; 1980)
In vitro reverse mutation (S. typhimurium TA98)	100-1000 µmol/plate (11-110 mg/plate)	Negative with metabolic activation Equivocal without metabolic activation *	Stolzenberg and Hine (1979)
In vitro reverse mutation (S. typhimurium TA100, TA1535)	0.1-10 mg/plate	Positive with and without metabolic activation *	Zeiger et al. (1988)
In vitro reverse mutation (S. typhimurium TA97)	0.1-10 mg/plate	Negative with metabolic activation Not tested without metabolic activation *	Zeiger et al. (1988)
In vitro reverse mutation (S. typhimurium TA98)	0.1-10 mg/plate	Negative with metabolic activation Positive without metabolic activation *	Zeiger et al. (1988)
In vitro reverse mutation (S. typhimurium TA100)	Not reported	Negative with metabolic activation Not tested without metabolic activation*	Majeska and Matheson (1983)
In vitro reverse mutation (S. typhimurium TA100)	0.01-1.25 mg/plate	Positive with and without metabolic activation *	Ohkubo et al. (1995)

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In vitro reverse mutation (S. typhimurium TA677, TA98)	0.01-1.25 mg/plate	Negative with metabolic activation Positive without metabolic activation *	Ohkubo et al. (1995)
In vitro mutation (E. coli WP2, TM930, TM1080)	2-200 µmol/plate (0.2-22 mg/plate)	Negative with and without metabolic activation *	Silhankovà et al. (1982)
In vitro mutation (E. coli WP2, TM930, TM1080)	2-200 µmol/plate (0.2-22 mg/plate)	Negative with and without metabolic activation *	Ohkubo et al. (1995)
In vitro forward mutation (Schizosaccharomyces plombe)	100-300 mmol/L (11-33 mg/ml)	Negative with metabolic activation Positive without metabolic activation *	Rossi et al. (1983)
In vitro gene mutation (Mouse lymphoma cells, *Tk* locus)	2-9 mg/ml	Positive with metabolic activation Negative without metabolic activation *	Henderson et al. (1987)
In vitro mutation (HeLa cells)	Not reported	Negative with and without metabolic activation *	Painter and Howard (1982)
In vitro mutation (Mouse fibroblasts, M2 clone)	0.1-2 mg/ml	Positive *	Piasecki et al. (1990)
In vitro sister chromatid exchange (Chinese hamster V79 cells)	0.7-2.8 mg/ml	Positive with and without metabolic activation *	May (1991)
In vitro gene mutation (Chinese hamster V79 cells, *hprt* locus)	0.3-70 mmol/L (0.033-7.7 mg/ml)	Weak positive at toxic concentration of 50 mmol/L (5.5 mg/ml) *	Görlitz (1991)
Metabolism	0 or 100 mg/kg (i.p.) 0, 10 (rats, rabbits) or 17 (monkeys) mg/kg (oral)	After 24 hrs, 9% α-chlorohydrin excreted unchanged in urine; 30% exhaled as CO_2 (although much of dose unaccounted for); β-chlorolactate comprised ≥23% of urinary metabolites. Evidence for tissue-specific localization of is equivocal. Parent is detoxified by conjugation with glutathione and then by acetylation to form the corresponding mercapturic acid; compound also undergoes oxidation to β-chlorolactic acid and then oxalic acid	Jones et al. (1978)*; Miller and Krake (1968); Krake and Miller (1969)

Toxicological Endpoints

Table 5. Summary of Toxicological Doses and Endpoints for Alpha-chlorohydrin Used in Human Health Risk Assessments				
Exposure Scenario	**Point of Departure**	**Uncertainty/FQPA Safety Factors**	**RfD, PAD, Level of Concern for Risk Assessment**	**Study and Toxicological Effects**
Incidental Oral Short- and Intermediate-Term (1-30 days and 1-6 months)	NOAEL < 35 mg/kg/day	$UF_A = 10X$ $UF_H = 10X$ $UF_L = 10X$ $UF_{DB} = 3X$ [1,2]	Residential LOC for MOE = 3000	**30-day oral toxicity (dog)** LOAEL = 35 mg/kg/day based on decreased prostate and testis weights and decreased body weight (Glenn et al. 1969)
Dermal Short- and Intermediate-Term (1-30 days and 1-6 months)	NOAEL < 35 mg/kg/day 100% dermal absorption assumed	$UF_A = 10X$ $UF_H = 10X$ $UF_L = 10X$ $UF_{DB} = 3X$ [1,2]	Residential LOC for MOE = 3000	**30-day oral toxicity (dog)** LOAEL = 35 mg/kg/day based on decreased prostate and testis weights and decreased body weight (Glenn et al. 1969)
Dermal Long-Term (>6 months)	NOAEL < 1.1 mg/kg/day 100% dermal absorption assumed	$UF_A = 10X$ $UF_H = 10X$ $UF_L = 10X$ [1]	Residential LOC for MOE = 1000	**Chronic Oral Toxicity/Carcinogenicity (rat)** LOAEL = 1.1/1.4 mg/kg/day (M/F) based on decreased absolute kidney weight (in the absence of decreased body weight) and increased incidences of Leydig cell adenomas, mammary glandular hyperplasia, chronic progressive nephropathy, and kidney tubule hyperplasia in males; and increased incidences of kidney tubule hyperplasia in females (Sunahara et al. 1993, as reported in Schlatter et al. 2002)
Inhalation Short- and Intermediate-Term, (1-30 days and 1-6 months)	NOAEL < 35 mg/kg/day 100% inhalation assumed	$UF_A = 10X$ $UF_H = 10X$ $UF_L = 10X$ $UF_{DB} = 3X$ [1,2]	Residential LOC for MOE = 3000	**30-day oral toxicity (dog)** LOAEL = 35 mg/kg/day based on decreased prostate and testis weights and decreased body weight (Glenn et al. 1969)
Inhalation Long-Term (>6 months)	NOAEL < 1.1 mg/kg/day	$UF_A = 10X$ $UF_H = 10X$ $UF_L = 10X$ [1]	Residential LOC for MOE = 1000	**Chronic Oral Toxicity/Carcinogenicity (rat)** LOAEL = 1.1/1.4

	100% inhalation assumed			mg/kg/day (M/F) based on decreased absolute kidney weight (in the absence of decreased body weight) and increased incidences of Leydig cell adenomas, mammary glandular hyperplasia, chronic progressive nephropathy, and kidney tubule hyperplasia in males; and increased incidences of kidney tubule hyperplasia in females (Sunahara et al. 1993, as reported in Schlatter et al. 2002)
Cancer	Unclassified; increased incidence of Leydig cell adenomas (M) observed at 1.1 mg/kg/day; increased incidence of mammary gland fibroadenomas (M) and kidney tubule adenomas (M&F) observed at 28/35 (M/F) mg/kg/day (Sunahara et al. 1993, as reported in Schlatter et al. 2002)			

Abbreviations: UF = uncertainty factor, UF_A = extrapolation from animal to human (interspecies), UF_H = potential variation in sensitivity among members of the human population (intraspecies), UF_L = use of a LOAEL to extrapolate a NOAEL, UF_{DB} = to account for the absence of key data, NOAEL = no observed adverse effect level, LOAEL = lowest observed adverse effect level, RfD = reference dose (a = acute, c = chronic), PAD = population adjusted dose, MOE = margin of exposure, LOC = level of concern, N/A = Not Applicable

[1] An UF_L has been applied because a LOAEL was used to extrapolate a NOAEL
[2] An UF_{DB} has been applied for the lack of a developmental toxicity study in any species

Exposure Assessment

Dietary-Exposure Assessment: Dietary risk was not estimated since dietary exposure is not expected from the use of alpha-chlorohydrin as a rodenticide bait.

Residential (Non-Occupational) Exposure/Risk Pathway: As there are currently no registered or proposed residential uses for alpha-chlorohydrin, a residential exposure assessment was not conducted.

Occupational Exposure/Risk Pathway: Based on the current label, potential exposure of this Restricted Use pesticide is to Certified applicators and/or persons under their direct supervision. The end-use product, "Epibloc® Rodenticide" is packaged in poly-paper sachets, which are placed intact into tamper-resistant stations (closed loading system). Occupational risk is considered unlikely.

Environmental Fate and Effects Assessment

The label for alpha-chlorohydrin formulated as a rodenticide bait is restricted to application inside industrial and commercial buildings only. Placement is also permitted

inside sanitary sewers. No outdoor use of alpha-chlorohydrin is permitted on the Epibloc label, thus there is likely to be minimal nontarget exposure associated with placement of this bait.

- **Contact Person at USEPA**

Mailing address:

John Hebert
Product Manager (07)
Environmental Protection Agency
Office of Pesticide Programs
Registration Division (7505P)
Insecticide-Rodenticide Branch
1200 Pennsylvania Avenue NW
Washington, D.C. 20460

Office location and telephone number:

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DISCLAIMER: The information in this Pesticide Fact Sheet is for information only and is not to be used to satisfy data requirements for pesticide registration. The information is believed to be accurate as of the date on the document.

APPENDIX I

GLOSSARY OF TERMS AND ABBREVIATIONS

ADNT	Acute delayed neurotoxicity
a.i.	Active Ingredient
aPAD	Acute Population Adjusted Dose
ARI	Aggregate Risk Index
BCF	Bioconcentration Factor
CAS	Chemical Abstracts Service
ChE	Cholinesterase
ChEI	Cholinesterase inhibition
cPAD	Chronic Population Adjusted Dose
%CT	Percent crop treated
DAT	Days after treatment
DEEM-FCID	Dietary Exposure Evaluation Model - Food Consumption Intake Database
DNA	Deoxyribonucleic acid
DNT	Developmental neurotoxicity
DIT	Developmental immunotoxicity
DWLOC	Drinking Water Level of Comparison.
EC	Emulsifiable Concentrate Formulation
EEC	Estimated Environmental Concentration. The estimated pesticide concentration in an environment, such as a terrestrial ecosystem.
EPA	U.S. Environmental Protection Agency
FQPA	Food Quality Protection Act
GLC	Gas Liquid Chromatography
GLN	Guideline Number
LC_{50}	Median Lethal Concentration. A statistically derived concentration of a substance that can be expected to cause death in 50% of test animals. It is usually expressed as the weight of substance per weight or volume of water, air or feed, e.g., mg/l, mg/kg or ppm.
LD_{50}	Median Lethal Dose. A statistically derived single dose that can be expected to cause death in 50% of the test animals when administered by the route indicated (oral, dermal, inhalation). It is expressed as a weight of substance per unit weight of animal, e.g., mg/kg.
LOAEL	Lowest Observed Adverse Effect Level
LOAEC	Lowest Observed Adverse Effect Concentration
LOC	Level of Concern
LOD	Limit of Detection
LOQ	Limit of Quantitation
mg/kg/day	Milligram Per Kilogram Per Day
mg/L	Milligrams Per Liter
MOE	Margin of Exposure

MRID	Master Record Identification (number), EPA's system of recording and tracking studies submitted
MTD	Maximum tolerated dose
NA	Not Applicable
NOEC	No Observable Effect Concentration
NOEL	No Observed Effect Level
NOAEL	No Observed Adverse Effect Level
NOAEC	No Observed Adverse Effect Concentration
NPDES	National Pollutant Discharge Elimination System
OP	Organophosphate
OPP	EPA Office of Pesticide Programs
OPPTS	EPA Office of Prevention, Pesticides and Toxic Substances
PAD	Population Adjusted Dose
PAG	Pesticide Assessment Guideline
PAM	Pesticide Analytical Method
PHED	Pesticide Handler's Exposure Data
PHI	Preharvest Interval
ppb	Parts Per Billion
PPE	Personal Protective Equipment
ppm	Parts Per Million
PRZM/EXAMS	Tier II Surface Water Computer Model
RAC	Raw Agriculture Commodity
RBC	Red Blood Cell
RED	Reregistration Eligibility Decision
REI	Restricted Entry Interval
RfD	Reference Dose
SCI-GROW	Tier I Ground Water Computer Model
SF	Safety Factor
TGAI	Technical Grade Active Ingredient
UF	Uncertainty Factor
µg	micrograms
µg/L	Micrograms Per Liter
µL/g	Microliter per gram
USDA	United States Department of Agriculture
WPS	Worker Protection Standard

APPENDIX II

Citations Considered to be Part of the Data Base Supporting the Registration of Alpha-chlorohydrin.

MRID	Citation
42112	Kirton, K.T. (1979) Letter sent to Ron J. Ericsson dated Nov 19, 1979 (Purity determination of U-5897 (Chlorohydrin)). (Unpub- lished study received Jul 24, 1980 under 42882-EX-1; prepared by Upjohn Co., submitted by Gametrics, Ltd., Sausalito, Calif.; CDL:242993-B)
45524	Evans Chemetics (19??) Typical Analyses of alpha Monochlorohydrin by GLC. (Unpublished study received Jul 24, 1980 under 42882- EX-1; submitted by Gametrics, Ltd., Sausalito, Calif.; CDL: 242993-A)
45525	Ericsson, R.J. (1980) Method for Formulation of Epibloc Concen- trate. (Unpublished study received Jul 24, 1980 under 42882- EX-1; submitted by Gametrics, Ltd., Sausalito, Calif.; CDL: 242993-C)
45526	Curtis & Tompkins, Limited (1980) Report on Sample of Epibloc Con- centrate: Laboratory No. 80c324. (Unpublished study received Jul 24, 1980 under 42882-EX-1; submitted by Gametrics, Ltd., Sausalito, Calif.; CDL:242993-D)
45527	Dean, W.P.; Myer, J. (1980) Primary Dermal Irritation Test in Rabbits: IRDC No. 467-002. (Unpublished study received Jul 24, 1980 under 42882-EX-1; prepared by International Research and Development Corp., submitted by Gametrics, Ltd., Sausalito, Calif.; CDL:242993-E)
45528	Dean, W.P.; Myer, J. (1980) Eye Irritation Study in Rabbits: IRDC No. 467-001. (Unpublished study received Jul 24, 1980 under 42882-EX-1; prepared by International Research and Development Corp., submitted by Gametrics, Ltd., Sausalito, Calif.; CDL: 242993-F)
45529	Dean, W.P.; Myer, J.; Marroquin, F. (1980) Acute Dermal Toxicity (LDI50^) Study in Rabbits: IRDC No. 467-003. (Unpublished study received Jul 24, 1980 under 42882-EX-1; prepared by Inter- national Research and Development Corp., submitted by Gametrics, Ltd., Sausalito, Calif.; CDL:242993-G)
45530	Fink, R.; Beavers, J.B.; Brown, R.; et al. (1980) Final Report: Eight-Day Dietary LC50--Bobwhite Quail: Project No. 172-101. (Unpublished study received Jul 24, 1980 under 42882-EX-1; pre- pared by Wildlife International, Ltd., submitted by Gametrics, Ltd., Sausalito, Calif.; CDL:242993-H)
45531	Fink, R.; Beavers, J.B.; Brown, R.; et al. (1980) Eight-Day Dietary LC50-- Mallard Duck: 3-Chloro-1,2-propanediol. Final rept. (Un- published study received Jul 24, 1980 under 42882-EX-1; pre- pared by Wildlife International, Ltd., submitted by Gametrics, Ltd., Sausalito, Calif.; CDL:242993-I)
45532	Fink, R.; Beavers, J.B.; Brown, R.; et al. (1980) Acute Oral LD50-- Mallard Duck: 3-Chloro-1,2-propanediol. Final rept. (Unpub- lished study received

	Jul 24, 1980 under 42882-EX-1; prepared by Wildlife International, Ltd., submitted by Gametrics, Ltd., Sausalito, Calif.; CDL:242993-J)
65657	Nippon Oils & Fats Company Limited (19??) (Inert Ingredients). Tokyo, Japan. (Also in unpublished submission received Dec 28, 1979 under 42882-1; submitted by Gametrics Ltd., Sausalito, Calif.; CDL:243847-A)
65658	Evans Chemetics (1973?) Typical Analyses of alpha Monochlorophydrin by GLC. (Unpublished study received Dec 28, 1979 under 42882-1; submitted by Gametrics Ltd., Sausalito, Calif.; CDL:243847-B)
71280	W.R. Grace & Company (19??) Typical Analyses of Alpha Monochloro-hydrin by GLC. (Unpublished study received Jan 29, 1981 under 42882-1; submitted by Geometrics, Ltd., Sausalito, Calif.; CDL:244365-A)
71281	Gametrics, Limited (1980) Epibloc: (Physical Properties). (Un- published study received Jan 29, 1981 under 42882-1; CDL: 244365-B)
91193	Jones, A.R. (1978) The antifertility actions of ?alpha|-chlorohyd- rin in the male. Life Sciences 23(16):1625-1645. (Also~In~un- published submission received Jul 10, 1979 under 42882-1; sub- mitted by Gametrics, Ltd., Sausalito, Calif.; CDL:238814-A)
91194	Evans Chemetics, Incorporated (19??) Material Safety Data Sheet: ?alpha|-Monochlorohydrin. (Unpublished study received Jul 10, 1979 under 42882-1; submitted by Gametrics, Ltd., Sausalito, Calif.; CDL:238814-B)
91195	Marshall, J.P.; Walker, D. (1978) The Acute Oral Toxicity of Epi- bloc Rodenticide in Male Rats: Experiment Reference S78CJ02. (Unpublished study received Jul 10, 1979 under 42882-1; prepared by Wickham Research Laboratories, Ltd., England, submitted by Gametrics, Ltd., Sausalito, Calif.; CDL:238814-C)
91196	Glenn, M.W.; Burr, W.M. (1969) 3-Chloro-1,2-propanedial (U-5897): Acute Dermal LDI50^ in Rabbit. (Unpublished study received Jul 10, 1979 under 42882-1; prepared by Upjohn Co., submitted by Gametrics, Ltd., Sausalito, Calif.; CDL:238814-D)
91197	Glenn, M.W.; Burr, W.M. (1968) U-5897 (3-Chloro-1,2-propanediol): Primary Eye Irritation Study in the Rabbit. (Unpublished study received Jul 10, 1979 under 42882-1; prepared by Upjohn Co., submitted by Gametrics, Ltd., Sausalito, Calif.; CDL:238814-E)
91198	Glenn, M.W.; Moe, L.D. (1969) Five-day Inhalation Toxicity of U- 5897 in Rats, Rabbits, and Dogs. (Unpublished study received Jul 10, 1979 under 42882-1; prepared by Upjohn Co., submitted by Gametrics, Ltd., Sausalito, Calif.; CDL:238814-F)
91199	Ericsson, R.J. (1976?) Epibloc^(TM)l (a Rodenticide): Tests for Mutagenicity and Carcinogenicity. (Unpublished study received Jul 10, 1979 under 42882-1; submitted by Gametrics, Ltd., Sausa- lito, Calif.; CDL:238814-G)
91200	Brown, J.P.; Dietrich, P.S.; Bakner, C.M. (1977) Mutagenicity Eval- uation of Monochloropydrin, Lot No. 309-256, in Three Microbial Tests: Report No. BS-04-0250-77. (Unpublished study received Jul 10, 1979 under 42882-1; prepared by Dynapol, submitted by Gametrics, Ltd., Sausalito,

Calif.; CDL:238814-H)

91201 Stolzenberg, S.J.; Hine, C.H. (1979) Mutagenicity of Halogenated and Oxygenated 3-Carbon Compounds. (Unpublished study received Jul 10, 1979 under 42882-1; prepared by Univ. of California-- San Francisco, Dept. of Pharmacology, submitted by Gametrics, Ltd., Sausalito, Calif.; CDL:238814-I)

91202 Kirton, K.T.; Ericsson, R.J.; Ray, J.A.; et al. (1970) Male anti- fertility compounds: Efficacy of U-5897 in primates (~Macaca~ ?~mulatta~?). Journal of Reproduction and Fertility 21:275-278. (Also~In~unpublished submission received Jul 10, 1979 under 42882-1; submitted by Gametrics, Ltd., Sausalito, Calif.; CDL: 238814-J)

91302 Vilkas, A.G.; Seminara, J. (1980) The Acute Toxicity of Epibloc (3-chloro-1,2-propanediol) to the Rainbow Trout,~Salmo~ ?~gairdneri~Richardson: UCCES Project No. 11507-85-02. (Un- published study received Oct 6, 1981 under 42882-1; prepared by Union Carbide Corp., submitted by Gametrics, Ltd., Sausalito, Calif.; CDL:246029-A)

91303 Ericsson, R.J.; Daugherty, L. (1981) Epibloc: Field Trial to Test for Efficacy on~Rattus norvegicus~in the Sewer System of the City of Cincinnati, Ohio, USA. (Unpublished study received Oct 6, 1981 under 42882-1; prepared in cooperation with Cin- cinnati, Dept. of Health, Vector Control, submitted by Game- trics, Ltd., Sausalito, Calif.; CDL:246030-A)

97837 Vilkas, A.G.; Browne, A.M. (1980) The Acute Toxicity of Epibloc (3-chloro-1,2-propanediol) (99% Active Ingredient) to the Water Flea,~Daphnia magna~Straus: UCCES Project No. 11507-85-03. (Unpublished study received Oct 6, 1981 under 428821; prepared by Union Carbide Corp., Environmental Services, submitted by Gametrics, Ltd., CDL:246031-A)

97838 Vilkas, A.G.; Seminara, J. (1980) The Acute Toxicity of Epibloc (3-chloro-1,2-propanediol) to the Bluegill Sunfish,~Lepomis~ ?~macrochirus~Rafinesque: UCCES Project No. 11507-85-01. (Un-published study received Oct 6, 1981 under 42882-1; prepared by Union Carbide Corp., submitted by Gametrics, Ltd., Sausalito, Calif.; CDL:246032-A)

97870 Gametrics Limited (19??) Epibloc Sachets. (Unpublished study re- ceived Nov 5, 1981 under 42882-1; CDL:246528-A)

97871 Williams, S.B. (1981) Letter sent to R. Erickson dated Feb 11, 1981 ?Information on alpha monochlorohydrin|. (Unpublished study received Nov 5, 1981 under 42882-1; prepared by W.R. Grace & Co., submitted by Gametrics, Ltd., Sausalito, Calif.; CDL: 246528-B)

141215 Ericsson, R; Tong, C.; Shu-De, W. (1984) Epibloc: Field trial to Test for Efficacy on Rattus norvegicus at a Poultry Breeding In- stitute, Beijing, People's Republic of China: Code No: EPI/84/ RJE/01. Unpublished study prepared by Gametrics, Ltd., Fung Ping Fan, Ltd., and others. 11 p.

157074 Marsh, R.; Howard, W. (1970?) An Evaluation of alpha-Chlorohydrin (U-5897) as a Reproductive Inhibitor for Norway Rat Control in a Garbage Dump. Unpublished study prepared by Univ. of Califor- nia-Davis, Wildlife and Fisheries Biology. 13 p.

44833900	Gametrics, Ltd. (1999) Submission of Environmental Fate Data in Support of the Application for Registration of Epibloc. Transmittal of 1 Study.
44833901	SRP for the Hazardous Substances Data (1997) 3-Chloro-1 ,2-Dihydroxypropane (Environmental Fate Data). Unpublished study prepared in Cooperation with Gametrics, Ltd. 16 p.
45690900	Gametrics, Limited (2002) Submission of Product Chemistry, Toxicity and Environmental Fate Data in Support of the Application for Registration of Epibloc Rodenticide. Transmittal of 14 Studies.
45690901	Ericsson, R. (1999) Product Chemistry: (Epibloc Rodenticide). Unpublished study prepared by Gametrics, Limited. 30 p. {OPPTS 830.1550, 830.1600, 830.1620, 830.1650, 830.1670, 830.1750, 830.1800, 830.6302, 830.6303, 830.6313, 830.7000, 830.7200, 830.7300, 830.7550, 830.7840, 830.7950}
45690902	Glenn, M.; Burr, W. (1970) Acute Oral Toxicity: (Epibloc Rodenticide). Unpublished study prepared by The Upjohn Laboratory. 75 p. {OPPTS 870.1100}
45690903	Glenn, M.; Burr, W. (1980) Acute Dermal Toxicity; Technical and Formulated: (Epibloc Rodenticide): Lab Project Number: 467-003. Unpublished study prepared by The Upjohn Laboratory and International Research and Development Corporation. 39 p. {OPPTS 870.1200}
45690904	Glenn, M.; Moe, L. (1969) Acute Inhalation Toxicity: (Epibloc Rodenticide). Unpublished study prepared by The Upjohn Company. 12 p. {870.1300}
45690905	Glenn, M.; Burr, W. (1980) Acute Eye Irritation; Technical and Formulated: (Epibloc Rodenticide): Lab Project Number: 467-001. Unpublished study prepared by The Upjohn Company. 35 p. {OPPTS 870.2400}
45690906	Ericsson, R. (1980) Acute Dermal Irritation: (Epibloc Rodenticide): Lab Project Number: 467-002. Unpublished study prepared by International Research and Development Corporation. 19 p. {OPPTS 870.2500}
45690907	Glenn, M.; Burr, W. (1980) Skin Sensitization: (Epibloc Rodenticide): Lab Project Number: 467-002: 467-003. Unpublished study prepared by The Upjohn Company and International Research and Development Corporation. 50 p. {OPPTS 870.2600}
45690908	Brown, J.; Dietrich, P.; Bakner, C. (1997) Bacterial Reverse Mutation Test: (Epibloc Rodenticide): Lab Project Number: BS-04-0250-77. Unpublished study prepared by Dynapol. 42 p. {OPPTS 870.5100}
45690909	Beavers, J.; Fink, R.; Glenn, M.; et al. (1968) Avian Acute Oral: (Epibloc Rodenticide). Unpublished study prepared by Wildlife International, Ltd and The Upjohn Company. 31 p. {OPPTS 850.2100}
45690910	Beavers, J.; Fink, R. (1980) Avian Dietary Toxicity Test: (Epibloc Rodenticide): Lab Project Number: WI-447. Unpublished study prepared by Wildlife International, Ltd. 36 p. {OPPTS 850.2200}
45690911	Jones, P.; Kominkova, H.; Jackson, H.; et al. (1976) Avian Reproduction Test: (Epibloc Rodenticide). Unpublished study prepared by American Society for Testing Materials, Bowling Green State University and University of California. 27 p. {OPPTS 850.2300}

45690912	Seminara, J. (1980) Freshwater Fish LC-50-Bluegill & Rainbow: (Epibloc Rodenticide): Lab Project Number: 11507-85-01: 11507-85-02. Unpublished study prepared by Union Carbide Corporation Environmental Services. 22 p. {OPPTS 850.1075}
45690913	Browne, A. (1980) Aquatic Invertebrate Acute Toxicity, Daphnia: Lab Project Number: 11507-85-03. Unpublished study prepared by Union Carbide Environmental Services. 12 p. {OPPTS 850.1010}
45743200	Gametrics Limited (2002) Submission of Efficacy, Fate and Toxicology Data in Support of the Application for Registration of Epibloc Rodenticide. Transmittal of 3 Studies.
45743201	Ericsson, R.; Youngdale, G.; Baker, V. (1970) Prenatal Development Toxicity Study: (of alpha-Chlorohydrin). Unpublished study prepared by The Upjohn Company. 108 p. {OPPTS 870.3700}
45743202	Jones, A.; Milton, D.; Murcott, C. (1978) Metabolism (of alpha-Chlorohydrin by Various Lab Mammals). Unpublished study prepared by The Upjohn Company. 28 p. {OPPTS 870.7485}
45743203	Ericsson, R. (1999) Efficacy (of alpha-Chlorohydrin): Lab Project Numbers: 5301/68/7263/001: EPI/81/RJE/01. Unpublished study prepared by Gametrics Limited. 315 p.
	Ban Y, Asanabe U, Ingaki S, Sasaki M, Nakatsuka T, Matsumoto H. (1999). Effects of alpha-chlorohydrin on rat sperm motions in relation to male reproductive functions. *J. Toxicol. Sci.* 24, 407–413.
	Cavanagh JB, Nolan CC, Seville MP. (1993). The neurotoxicity of alpha-chlorohydrin in rats and mice: I. Evolution of the cellular changes. *Neuropathol. Appl. Neurobiol.* 19, 240–252.
	Connor, N.D. (1970). U-5897 (3-chloro-1, 2-propanediol). Acute oral toxicity (LD_{50}) in five strains of rats (Four wild). Agricultural Division – The Upjohn Co., Kalamazoo, MI. Report No 510-9670-005. February 26, 1970.
	Epstein, S.S., Arnold, E., Andrea, J., Bass, W. & Bishop, Y. (1972) Detection of chemical mutagens by the dominant lethal assay in the mouse. *Toxicol. Appl. Pharmacol.*, 23, 288–325.
	Erricsson, R.J., K.T. Kirton, A.D. Forbes, J.F. Norland, and K.K. Bergstrom. (1969) U-5897: Male antifertility in primates at a nontoxic dose. Pharmaceutical Research and Development Technical Report. No other citation provided.
	Ericsson, R.J. and V.F. Baker. (1970) Male antifertility compounds: biological properties of U-58 97 and U-15,646. Fertility Research, The Upjohn Co., Kalamazoo, MI. Published in J. Reprod. Fert. (1970). 21, 267-273.
	European Commission. (2001). Opinion of the Scientific Committee on Food on 2-monochloro-propane-1,2-diol (3-MCPD) updating the SCF opinion of 1994. SCF/CS/CNTM/OTH/17 Final. May 30, 2001.
	Fellows, M. (2000) 3-MCPD: Measurement of unscheduled DNA synthesis

in rat liver using an in vitro/in vivo procedure. Unpublished report No. 1863/1-D5140 from Covance Laboratories Ltd.

Glenn, M.W., and W.M. Burr (1968). U-5897 (3-chloro-1, 2-propanediol). Acute oral toxicity (LD_{50}) in the rat. The Upjohn Co., Kalamazoo, MI. Report No 510-9610-1.

Glenn, M.W., and W.M. Burr (1968). U-5897 (3-chloro-1, 2-propanediol). Acute oral toxicity (LD_{50}) in the mouse. The Upjohn Co., Kalamazoo, MI. Report No 510-9610-4. December 11, 1968.

Glenn, M.W., and W.M. Burr (1968). U-5897 (3-chloro-1, 2-propanediol). Acute oral toxicity (LD_{50}) in the cat. The Upjohn Co., Kalamazoo, MI. Report No 510-9610-6. January 21, 1969.

Glenn, M.W., and W.M. Burr (1968). U-5897 (3-chloro-1, 2-propanediol). Acute oral toxicity (LD_{50}) in gerbils. The Upjohn Co., Kalamazoo, MI. Report No 510-9610-7. December 26, 1968.

Glenn, M.W., and W.M. Burr (1968). U-5897 (3-chloro-1, 2-propanediol). Acute LD_{50} in the dog. The Upjohn Co., Kalamazoo, MI. Report No 510-9610-8. December 28, 1968.

Glenn, M.W., and W.M. Burr (1968). U-5897 acute oral toxicity (LD_{50}) in turkeys. The Upjohn Co., Kalamazoo, MI. Report No 510-9610-2. October 28, 1968.

Glenn, M.W., and W.M. Burr (1969). U-5897 (3-chloro-1, 2-propanediol). Acute lethal oral dose in yearling steers. The Upjohn Co., Kalamazoo, MI. Report No 510-9610-12. March 21, 1969.

Glenn, M.W., and W.M. Burr (1969). U-5897 (3-chloro-1, 2-propanediol). Acute oral toxicity (LD_{50}) in the rabbit. The Upjohn Co., Kalamazoo, MI. Report No 510-9610-9. January 21, 1969.

Glenn, M.W., and W.M. Burr (1969). U-5897 (3-chloro-1, 2-propanediol). Preliminary acute LD_{50} in sheep. The Upjohn Co., Kalamazoo, MI. Report No 510-9610-13. March 28, 1969.

Glenn, M.W., and W.M. Burr (1969). U-5897 (3-chloro-1, 2-propanediol). Oral tolerance in the dog. The Upjohn Co., Kalamazoo, MI. Report No 510-9610-14. April 15, 1969.

Glenn, J.L. and Sokolowski, J.H. (1969). The effects of U-5897 on the male beagle. I. Gross effects on the reproductive organs and related structures. Technical Report No. 618-9670-011. Agricultural Division, The Upjohn Co., Kalamazoo, MI. September 25, 1969.

Glenn, J.L. and Sokolowski, J.H. (1969). The effects of U-5897 on the male beagle. II. Fertility of male beagles after treatment with U-5897. Technical Report No. 604-9670-002. Agricultural Division, The Upjohn Co., Kalamazoo, MI. September 17, 1969.

Glenn, J.L., J. H. Sokolowski, and F. VanRavenswaay (1969). The effects of U-5897 (3-chloro-1, 2-propanediol) on the male beagle. I. Fertility of male beagles after treatment with U-5897. Agricultural Division, The Upjohn Co., Kalamazoo, MI. Report No 604-9670-011. September 23, 1969.

Görlitz, B.D. (1991) In vitro mammalian cell HPRT-test with 3-chloro-1,2-propanediol. Unpublished report No. G91/3 from Fraunhofer-Institute für Toxikologie und Aerosolforschung, Hanover, Germany.

Helal, T.Y. (1982) Chemosterilant and rodenticidal effects of 3-chloro-1,2-propanediol (Epibloc) against the albino laboratory rat and the Nile field rat. *Int. Pest. Control*, 24, 20–23.

Henderson, L.M., Bosworth, H.J., Ransome, S.J., Banks, S.J., Brabbs, C.E. & Tinner, A.J. (1987) An assessment of the mutagenic potential of 1,3-dichloro-2-propanol, 3-chloro-1,2-propanediol and a cocktail of chloropropanols using the mouse lymphoma TK locus assay. Unpublished report No. ULR 130 ABC/861423 from Huntingdon Research Centre Ltd, Huntingdon, Cambridgeshire, United Kingdom.

Hoffer, A.P., Hamilton, D.W. & Fawcett, D.W. (1973) The ultrastructural pathology of the rat epididymis and after administration of alpha-chlohydrin (U-5897). 1. Effects of a single high dose. *Anat. Rec.*, 175, 203–230.

Hoyt, J.A., Fisher, L.F., Hoffman, W.P., Swisher, D.K. & Seyler, D.E. (1994) Utilization of a short-term male reproductive toxicity study design to examine effects of alpha-chlorohydrin (3-chloro-1,2-propanediol). *Reprod. Toxicol.*, 8, 237–250.

Jaccaud, E. & Aeschbacher, H.U. (1989) Evaluation of 3-chloro-1,2-propanediol (3MCPD) in the bone marrow and colonic micronucleus mutagenicity tests in mice. Unpublished report No. 1265 from Nestec Ltd Research Centre, Nestlé, Switzerland.

Jelks KB, Miller MG. (2001). □-Chlorohydrin inhibits glyceraldehyde-3-phosphate dehydrogenase in multiple organs as well as in sperm. Toxicol Sci 62(1):115-23.

Johnson, L.A. and G. Pursel. (1972). Reversible infertility in male swine fed α-chlorohydrin. J. Animal Science 34(2):241-245.

Jones AR. (1983). Antifertility actions of alpha-chlorohydrin in the male. Aust J Biol Sci 36(4):333-50.

Jones AR. (1998). Chemical interference with sperm metabolic pathways. J Reprod Fertil Suppl 53:227-34.

Jones AR, Cooper TG. (1999). A re-appraisal of the post-testicular action and toxicity of chlorinated antifertility compounds. Int J Androl 22(3):130-8.

Jones, A.R., Milton, D.H. & Murcott, C. (1978) The oxidative metabolism of alpha-chlorohydrin in the male rat and the formation of spermatocele. *Xenobiotica* 8, 573–582.

Jones, P. & Jackson, H. (1976) Antifertility and dominant lethal mutation studies in male rats with dl-alpha-chlorohydrin and an amino-analogue. *Contraception* 13, 639–646.

Kawaguchi T, Kawachi M, Morikawa M, Kazuta H, Shibata K, Ishida M, Kitagawa N, Matsuo A, Kadota T. (2004). Key parameters of sperm motion in relation to male fertility in rats given alpha-chlorohydrin or nitrobenzene. J Toxicol Sci. 29(3):217-31.

Kennelly, J., M.V. Garrison, B.E. Johns. (1970). Laboratory studies of the effect of U-5897 on the reproduction of wild male rats. Journal references not provided.

Kirton, K.T., Erickson, R.J., Ray, J.A. & Porbes, A.D. (1970) Male antifertility compounds: Efficacy of N-5897 in primates (*Macaca mulatta*). *J. Reprod. Fertil.*, 21, 275–278.

Kreider, J.L. and R.H. Dutt. (1970). Induction of temporary infertility in rams with an orally administered chlorohydrin. University of Kentucky. Published in J. Animal Science, Vol 31, No. 1, July 1970.

Kwack SJ, Kim SS, Choi YW, Rhee GS, Da Lee R, Seok JH, Chae SY, Won YH, Lim KJ, Choi KS, Park KL, Lee BM. (2004). Mechanism of antifertility in male rats treated with 3-monochloro-1,2-propanediol (3-MCPD). J Toxicol Environ Health A 67(23-24):2001-11.

Krake JJ and Miller WL. (1969). Expired $^{14}CO_2$ following an oral dose of C^{14} U-5897 given male Rhesus monkeys. Pharmaceutical Research and Development Technical Report, Code No. 4101/69/7241/001. January 8, 1969.

Lee JK, Byun JA, Park SH, Kim HS, Park JH, Eom JH, and Oh YH. (2004). Evaluation of the potential immunotoxicity of 3-monochloro-1,2-propanediol in Balb/c mice. I. Effect on antibody forming cell, mitogen-stimulated lymphocyte proliferation, splenic subset, and natural killer cell activity, *Toxicology* 204, 1–11.

Lee JK, Byun JA, Park SH, Choi HJ, Kim HS, Oh HY. (2005). Evaluation of the potential immunotoxicity of 3-monochloro-1,2-propanediol in Balb/c mice II. Effect on thymic subset, delayed-type hypersensitivity, mixed-lymphocyte reaction, and peritoneal macrophage activity. Toxicology 211(3):187-96.

Majeska, J.B. & Matheson, D.W. (1983) Quantitative estimate of mutagenicity of tris-[1,3-dichloro-2-propyl]-phosphate (TCPP) and its possible metabolites in *Salmonella* (abstract). *Environ. Mutag.*, 5, 478.

Marchesini, M. & Stalder, R. (1983) Toxicity of 3-chloro-1,2-propanediol in a 4 weeks gavage study on rats. Part I. Unpublished report No. LA 70/1082 from the Société d'Assistance Technique Pour Produits Nestlé SA, Switzerland.

Marchesini, M., Stalder, R. & Perrin, I. (1989) Subchronic toxicity of 3-chloro-1,2-propanediol, 90 days administration in drinking water of Fischer F344 rats. Unpublished report No. 1264 from Nestec Ltd Research Centre, Nestlé, Switzerland.

Marshall, R.M. (2000) 3-MCPD: Induction of micronuclei in the bone-marrow of treated rats. Unpublished report No. 1863/2-D5140 from Covance Laboratories Ltd.

May, C. (1991) In vitro sister chromatid exchange assay in mammalian cells. Unpublished report No. 91/4 CM from Fraunhofer-Institute für Toxikologie und Aerosolforschung, Hanover, Germany.

Miller WL and Krake JJ. (1968). Expired $C^{14}O_2$ following oral doses of C^{14}-U-5897 given rats and rabbits. Biochemical Research Technical Report, Code No. 6/68/7241/002. June 26, 1968.

Ohkubo, T., Hayashi, T., Watanabe, E., Endo, H., Goto, S., Endo, O., Mizoguchi, T. & Mori, Y. (1995) Mutagenicity of chlorohydrins. *Nippon Suisan Gakkaishi,* 61, 596–601 (in Japanese).

Painter, R.B. & Howard, R (1982) The HeLa DNA synthesis inhibition test as a rapid screen for mutagenic carcinogens. *Mutat. Res.*, 92, 427–437.

Parish, W.E. (1989) Effect of 3-chloropropane-1,2-diol on rat fertility. Unpublished summary report No. D 89/005 from Unilever Research, Sharnbrook, Bedford, United Kingdom.

Piasecki, A., Ruge, A. & Marquardt, H. (1990) Malignant transformation of mouse M2-fibroblasts by glycerol chlorohydrines contained in protein hydrolysate and commercial food. *Arzneim.-Forsch./Drug Res.*, 40, 1054–1055.

Ray, J.A. and J.G. Ceru. (1968). Pathologic examination of certain monkeys from tolerance and efficacy studies. Performing Laboratory not provided. Report No 68PT005. August 2, 1968.

Ray, J.A., K.T. Kirton, A.D. Forbes, and J.G. Ceru. (1967). U-5897: Oral tolerance study in monkeys. Reporting Laboratory not provided.

Rey R. (1999). The prepubertal testis: a quiescent or a silently active organ? Histol Histopathol 14(3):991-1000.

Rossi, A.M., Migliore, L., Lascialfari, D., Sbrana, I., Lorieno, N., Tortoreto, M., Bidioli, F. & Pantarotto, C. (1983) Genotoxicity, metabolism and blood kinetics of epichlorohydrin in mice. *Mutat. Res.*, 118, 213–226.

Schlatter J, Baars AJ, DiNovi M, Lawrie S, Lorentzen R. (2002). 3-chloro-1,2-propanediol. In: Proceedings of the Fifty-seventh Meeting of the Joint FAO/WHO Expert Committee on Food Additives (JECFA) of the Safety Evaluation of Certain Food Additives and Contaminants. WHO Food Additives Series No. 48, 401–432.

Silhankovà, L., Smid, F., Cernà, M., Davidek, J. & Velisek, J. (1982) Mutagenicity of glycerol chlorohydrines and of their esters with higher fatty acids present in protein hydrolysate. *Mutat. Res.*, 103, 77–81.

Slott VL, Jeffay SC, Dyer CJ, Barbee RR, Perreault SD. (1997). Sperm motion predicts fertility in male hamsters treated with alpha-chlorohydrin. J Androl 18(6):708-16.

Stolzenberg, S.J. & Hine, C.H. (1979) Mutagenicity of halogenated and oxygenated three-carbon compounds. *J. Toxicol. Environ. Health*, 5, 1149–1158.

Stolzenberg, S.J. & Hine, C.H. (1980) Mutagenicity of 2- and 3-carbon halogenated compounds in the Salmonella/mammalian-microsome test. *Environ. Mutag.*, 2, 59–66.

Sunahara, G., Perrin, I. & Marchesini, M. (1993) Carcinogenicity study on 3-monochloropropane-1,2-diol (3-MCPD) administered in drinking water to Fischer 344 rats. Unpublished report No. RE-SR93003 submitted to WHO by Nestec Ltd, Research & Development, Switzerland.

Toth, G.P., Wang, S.R., McCarthy, H., Tocco, D.R. & Smith, M.K. (1992) Effects of three male reproductive toxicants on rat cauda epididymal

sperm motion. *Reprod. Toxicol.*, 6, 507–515.

Tournaye H, Goossens E, Verheyen G, Frederickx V, De Block G, Devroey P, Van Steirteghem A. (2004). Preserving the reproductive potential of men and boys with cancer: current concepts and future prospects. Hum Reprod Update. 10(6):525-32.

Tritscher AM. (2004). Human health risk assessment of processing-related compounds in food.
Toxicol Lett 149(1-3):177-86.

Van Duuren, B.L., Goldschmidt, B.M., Katz, C., Seidman, J. & Paul, J.S. (1974) Carcinogenic activity of alkylating agents. *J. Natl Cancer Inst.*, 53, 695–700.

Vickery BH, Erickson GI, Bennett JP. (1974). Mechanism of antifertility action of low doses of alpha-chlorohydrin in the male rat. J Reprod Fertil. 38(1):1-10.

Weisburger, E.K., Ulland, B.M., Nam, J., Gart, J.J. & Weisburger, J.H. (1981) Carcinogenicity tests of certain environmental and industrial chemicals. *J. Natl Cancer Inst.*, 67, 75–88.

Woods, J. & Garside, D.A. (1996) An in vivo and in vitro investigation into the effects of alpha-chlorohydrin on sperm motility and correlation with fertility in the Han Wistar rat. *Reprod. Toxicol.*, 10, 199–207.

Yamada, T., Inoue, T., Sato, A., Yamagishi, K. & Sato, M. (1995) Effects of short-term administration of alpha-chlorohydrin on reproductive toxicity parameters in male Sprague-Dawley rats. *J. Toxicol. Sci.*, 20, 195–205.

Zeiger, E., Anderson, B., Haworth, S., Lawlor, T. & Mortelmans, K. (1988) *Salmonella* mutagenicity tests: IV. Results from the testing of 300 chemicals. *Environ. Mol. Mutag.*, 11 (Suppl. 12), 1–158.