201-14185A

High Production Volume (HPV) Challenge Program

Test Plan

For

ETHYL BROMIDE
(CAS# 74-96-4)

Prepared for:

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TEST PLAN MATRIX HPV SIDS DATA REQUIREMENTS/CRITICAL STUDIES: ETHYL BROMIDE

HPV Data Category	Test Endpoint		Data Available	Data Acceptable	Data to be Generated
Physical and Chemical Properties	Melting Point		Yes	Yes	No
	Boiling Point		Yes	Yes	No
	Vapor Pressure		Yes	Yes	No
	Partition Coefficient		Yes	Yes	No
	Water Solubility		Yes	Yes	No
Environmental Fate and Pathways	Photodegradation		Yes[1]	Yes	No
	Stability in Water		Yes[1]	Yes	No
	Biodegradation		Yes[1]	Yes	No
	Transport/Distribution		Yes[2]	Yes	No
Ecotoxicity	Acute toxicity to fish		Yes[1]	Yes	No
	Acute toxicity to aquatic invertebrates		Yes[1]	Yes	No
	Toxicity to Aquatic Plants		No	Waiver[4]	No
	Chronic aquatic invertebrate test		NR[3]	NR	No
	Terrestrial toxicity		NR[3]	NR	No
Human Health Effects	Acute toxicity		Yes	Yes	No
	Repeated Dose		Yes	Yes	No
	Genetic Toxicity	Gene Mut.	Yes	Yes	No
		Chrom. Ab	Yes	Yes	No
	Reproductive Toxicity		Yes[1]	Yes	No
	Developmental Toxicity		Yes[1]	Yes	No

Footnote 1: This SIDS requirement is fulfilled using acceptable data from Methyl Bromide, as a surrogate to Ethyl Bromide. See Test Plan for rationale.
Footnote 2: This information was generated using the EPIWIN model (v3.10).
Footnote 3: These SIDS data requirements are conditional and are not required for the Ethyl Bromide.
Footnote 4: A waiver is proposed for the aquatic plant toxicity study. See Test Plan for rationale.

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1.0 INTRODUCTION: Alkyl Bromides

Great Lakes Chemical Corporation has voluntarily committed to participate in the Environmental Protection Agency's (EPA's) high production volume chemicals (HPV) challenge program, and subsequently to the International Council of Chemical Associations (ICCA) HPV Chemical Initiative. These programs are undertaken to assess the health and environmental hazards, including physical chemical characteristics, for selected chemicals. Great Lakes Chemical Corporation is sponsoring ethyl bromide (bromoethane) for these HPV programs.

The objective of this test plan is to evaluate the available data and determine what additional data, if any, are needed to adequately characterize the human health and environmental hazards of ethyl bromide. This document includes an evaluation of all available data. In order to adequately assess the health effects, environmental fate and ecological effects of ethyl bromide it is recommended that surrogate data from methyl bromide, another halobromide compound, be considered in support of identified SIDS data requirements. Robust summaries of these data are appended. Based upon a thorough evaluation of all existing data for ethyl bromide and the use of surrogate data from methyl bromide, it is proposed that no additional studies be conducted.

2.0 Structure Activity Relationship Between Ethyl Bromide and Methyl Bromide:

The HPV Challenge Program endorses the development of chemical categories and/or use of surrogate data from a structurally similar chemical(s) as an acceptable mechanism to achieve an efficient completion of the program goals. EPA considers this an acceptable premise for chemicals whose physicochemical and toxicological properties are likely to be similar or follow a regular pattern as a result of structural similarity.

Alkyl bromides are a class of organic halogens having the general formula:

R - Br

In the most simple of these structures, each R represents a primary or secondary alkyl. In this case R equals either a methyl or an ethyl group.

Use of the bromides is widespread in industry. Methyl bromide is used in ionization chambers, for degreasing wool, for extracting oils from nuts, seed and flowers. It is an insect fumigant for mills, warehouses, vaults, ships, freight cars and is also a soil fumigant. It is a solvent for extracting vegetable oils. Ethyl bromide is an ethylating agent in organic syntheses and is used as a refrigerant and a solvent. In medicine its use is as an inhalation anesthetic (Merck, 1983, Montgomery, 2000).

These two chemicals appropriately belong in one study group-based on the very similar structures (Figure 1) and similar physical chemical characteristics of the two alkyl bromides (Table 1).

Table 1
Physical/Chemical Characteristics

	Methyl Bromide	Ethyl Bromide	Difference Between Ethyl and Methyl
CAS Number	74-83-9	74-96-4	
M.W.	95	109	14 daltons
Melting pt. ^{o}C	-94	-119	factor 1.3
Boiling pt. ^{o}C	3.6	38	factor 10
Solubility mg/L 25^{o}C	15,200 17,500**	9,000	factor 1.7
log P	1.19	1.61	factor 1.3
K_{Henry} atm-m^3/mol 25^{o}C	6.2 x 10^{-3}	7.5 x 10^{-3}	factor 1.2
Vapor pressure mm Hg 25^{o}C	1,620	467 - 475	factor 3.5
Physical State	colorless gas	volatile liquid	
Bioconcentration*	3.5	3-5	within same range
$t_{1/2}$ in river*	1.1 hours	6.6 hours	6
$t_{1/2}$ in lake*	4.2 days	3.9 days	same half life

Data from Howard & Meylan, (1997), unless otherwise indicated.
* data from EPIWIN, 2002.
** derived from EPA Drinking Water Health Advisory (1987), ref. Stenger (1978)

Environmental Fate
Methyl Bromide hydrolyzes in water forming methanol and hydrobromic acid. The estimated hydrolysis half-life in water at 25 ^{o}C and pH 7 is 20 days (Mabey and Mill, 1978). Castro and Belser (1981) reported a hydrolysis rate constant of 3 x 10^{-7}/sec or a half-life of 26.7 days. Methyl bromide forms a crystalline hydrate at 0 - 5 ^{o}C (Keith and Walters, 1992). When it was heated to 550 ^{o}C in the absence of oxygen, methane, hydrobromic acid, hydrogen, bromine, ethyl bromide, anthracene, pyrene and free radicals were produced (Chaigneau et al., 1966). The half lives in river and lake waters are 1 hour and 4 days, respectively.

Ethyl Bromide hydrolyzes in water forming ethyl alcohol and bromide ions. The estimated hydrolysis half-life at 25 ^{o}C and pH 7 is 30 days (Mabey and Mill, 1978). A strain of *Acinetobacter* isolated from activated sludge degraded ethyl bromide to ethanol and bromide ions (Janssen et al., 1987). *Methanococcus ssp.* and *Methanobacterium thermoautotrophicum* grown with H_2CO_2 in the presence of ethyl bromide produced methane and ethane (Belay and Daniels, 1987). In groundwater, under reducing conditions in the presence of hydrogen sulfide, ethyl bromide was converted to sulfur containing products (Schwarzenbach et al., 1985). The half lives in river and lake waters are 6 hours and 3.9 days, respectively.

Similarities in Transport/Distribution: Information on chemical transport and distribution for ethyl bromide and methyl bromide has been estimated using EPIWIN (v3.10) and fugacity modeling. The Henry's Law Constant for ethyl bromide is 7.5E-03 atm-m^3/mole @ 25 degrees C. The Henry's Law Constant for methyl bromide is 6.24E-03 atm-m^3/mole @ 25 degrees C. EPIWIN also predicts linear biodegradation with probabilities of 0.649 for ethyl and 0.656 for methyl bromide, indicating that both are readily degradable. The model also predicts similarities in the Bioconcentration Factor (BCF) with 3.5 estimated for ethyl bromide and between 3 and 5 for methyl bromide.

Finally, the fugacity model estimates the similarities for distribution in air, water, soil and sediment for ethyl and methyl bromide, and these values are indicated below:

Mass Amount	Ethyl Bromide	Methyl Bromide
Air	50.7%	53.2%
Water	43.7%	42.5%
Soil	5.47%	4.25%
Sediment	0.0978%	0.08%
Fugacity (atm)		
Air	4.92E-10	6.13E-10
Water	6.51E-8	6.21E-8
Soil	1.19E-7	1.37E-7
Sediment	5.2E-8	5.09E-8
Half-Lives (hr)		
Air	733.4	6386
Water	360	360
Soil	360	360
Sediment	1440	1440

Structures and Properties
Structures of the two bromides discussed in this document are presented in Figure 1. These structures are very similar except for the length of the chain. Each is composed of an alkyl group with bromide. The side groups are methyl in one case and ethyl in another.

Conclusion
The similarity of these two alkyl bromide structures is visually evident in Figure 1, as well as their physical/chemical properties that are listed in Table 1. The molecules are very close in size, with the difference being one methyl group. In addition, since ethyl bromide is a slightly larger molecule, it may not be as bioavailable or as bioaccessible as the gaseous methyl bromide. Note particularly that melting points, solubilities, partition coefficients and Henry's Law Constants are all different by *less than* a factor of 2. The hydrolysis products of ethyl bromide (ethanol and bromide ion) should be of less concern than the methanol and hydrobromic acid created during hydrolysis of methyl bromide. Bioconcentration of the two compounds is virtually the same and the half lives estimated in air, water and soil indicate these substances are eliminated quickly from the environment. EPIWIN (v3.10) models generated for each compound and the similarity in the fugacity predictions illustrate similar environmental fate and distribution pathways for these compounds. Evidence from the available toxicological studies in experimental animals and its therapeutic use in medicine, demonstrate that ethyl bromide is also less toxic than methyl bromide. For these reasons, the products should be categorized together for HPV investigation. Methyl bromide might well be a conservative surrogate for ethyl bromide and use of methyl bromide data in support of ethyl bromide, particularly with respect to environmental fate, seems justified.

Since EPA encourages the use of analogues and structurally similar chemicals as a source of scientific data on related chemical species, Great Lakes Chemical Corporation believes methyl bromide (CAS # 74-83-9) has similar physicochemical properties, and is therefore an acceptable surrogate source of data in support of ethyl bromide, where needed, under the HPV Challenge Program.

3.0 EVALUATION OF EXISTING DATA FOR ETHYL BROMIDE

The available data for ethyl bromide have been assessed in accordance with the Organization for Economic Cooperation and Development (OECD) HPV program and Screening Information Data Sets (SIDS)

prepared as robust summaries. Most of the toxicity data were generated using chemically pure ethyl bromide. Robust summaries of these files are appended as an IUCLID Export file.

Melting Point

The melting point has been determined to be -119 degrees C.

Recommendation: No additional testing is proposed.

Boiling Point

The boiling point has been determined to be 38.4 degrees C.

Recommendation: No additional testing is proposed.

Vapor Pressure

The vapor pressure for ethyl bromide is 467to 475 mmHg @ 25 degrees C.

Recommendation: No additional testing is proposed.

Partition Coefficient

The octanol/water partition coefficient for ethyl bromide is 1.61 Log Kow.

Recommendation: No additional testing is proposed.

Water Solubility

The water solubility for ethyl bromide is 9,000 mg/L @ 25 degrees C.

Recommendation: No additional testing is proposed.

Photodegradation

There are no photodegradation data for ethyl bromide. Estimates from a model of gas/particle partitioning of semivolatile organic compounds in the atmosphere estimated a half-life in air of 46 days, by reaction with photochemically-produced hydroxyl radicals.

Recommendation: No additional testing is proposed. See Data Evaluations for Methyl Bromide.

Stability in Water

Ethyl bromide hydrolyzes in water to form ethyl alcohol and bromide ions. The half-life at 25 degrees C and pH 7 is 30 days.

Recommendation: No additional testing is proposed. See Data Evaluations for Methyl Bromide.

Biodegradation

Biodegradation is the utilization of a chemical by microorganisms as source of energy and carbon. A strain of *Actinetobacter* isolated from activated sludge degraded ethyl bromide to ethanol and bromide ions (Janssen et al.. 1987). *Methanococcus sp.* and *Methanobacerium thermoautotrophicum* grown with H2CO2 in the presence of ethyl bromide produced methane and ethane (Belay and Daniels, 1987). Ethyl bromide is reduced to sulfur containing products in groundwater under reducing conditions in the presence of hydrogen sulfide (Schwarzenbach et al., 1985). The bioconcentration factor for ethyl bromide is between 3 and 5. The half-life in river and lake waters is 6 hours and 3.9 days, respectively.

Recommendation: No additional testing is proposed. See Data Evaluations for Methyl Bromide.

Transport/Distribution

Models for predicting bioconcentration and soil sorption have been developed and used for chemicals where water solubility is known. These models are useful for predicting the environmental transport using known pre-selected parameters, such as water solubility. Information on chemical transport and distribution has been estimated using the EPIWIN (v3.10) model and fugacity modeling. The Henry's Law Constant for ethyl bromide is 7.5E-03 atm-m^3/mole @ 25 degrees C. EPIWIN also predicts a linear biodegradation with a probability of 0.6, indicating that it is readily degradable. Further, from the Kow of 1.61 the model predicts a Bioconcentration Factor (BCF) of 3.5, with half-lives in air estimated at 733 hrs, water 360 hrs and soil 360 hours.

Recommendation: No additional testing is proposed.

Aquatic Toxicity

Aquatic toxicity testing is required to determine the concentration of a chemical that will produce mortality or growth inhibition in 50% of a specified population (LC50 and EC50, respectively). There are no specific aquatic toxicity tests for ethyl bromide. However, a 96 hour static fish toxicity test and 48 hour daphnia mortality/immobility test were conducted using methyl bromide. The 96 hr LC50 to Rainbow trout was 3.9 mg/L. The EC50 to Daphnia magna was 2.6 mg/L. An acute toxicity study to aquatic plants is not considered useful data based upon the demonstrated use of methyl bromide in the production of plants and vegetables for human consumption. No adverse effects upon any food crops have been demonstrated in the 40 plus years of agricultural use of methyl bromide in the production of these plants. Request that this data requirement be waived.

Recommendation: No additional testing is proposed. The extensive agriculture use history of methyl bromide illustrates that it has not produced any adverse effects (e.g. phytotoxicity) on target and non-target plants. It is recommended that this use history be used to support ethyl bromide as well, based upon their structural similarity. See Data Evaluations for Methyl Bromide.

Acute Toxicity

InhalationToxicity: The acute toxicity to rats and mice was examined in acute inhalation studies, and the LC50s were 4681 ppm (20.8 mg/L) and 2723 ppm (12.14 mg/L), respectively, following a 4 hour exposure.

Recommendation: No additional testing is proposed.

Repeated Dose Testing

Ethyl bromide was evaluated in several repeat dose inhalation studies in rats and mice. Exposures varied from 14 days to 14 weeks. Exposures were normally 6 hrs/day and 5 days/week. The 14 day exposure levels ranged from 250-4000 ppm; whilst the 14 week exposures ranged from 100-1600 ppm. Generally NOAELs of 400-500 ppm were demonstrated in both species. The major toxic symptoms were confined to the nasal turbinates, trachea and lungs in the short term 14 day studies. In the 14 week rat study adverse effects were observed in the brain, spinal cord, spleen, skeletal muscle, testes (M) and uterus (F). Mice in the 14 week inhalation study displayed similar effects in the uterus and skeletal muscle.

The carcinogenic potential of ethyl bromide examined in mice and rats in 2 year inhalation protocols provided evidence of oncogenicity in both species. Tumors observed in rats were brain gliomas and alveolar/bronchiolar adenomas in lungs. Tumors observed in mice included adenomas/adenocarcinomas and squamous cell carcinomas in the uterus (F) and an overall increase in lung pathology in dosed males.

Recommendation: No additional testing is proposed.

Mutagenicity Assays

Gene Mutation: Ethyl bromide was mutagenic in an Ames assay in *Salmonella typhimurium.*

Chromosomal Aberration: Ethyl bromide was mutagenic in an in vitro Sister chromatid exchange assay using Chinese Hamster Ovary cells in culture, with and without metabolic activation. In a separate in vitro chromosome aberration assay, also in Chinese Hamster Ovary cells, ethyl bromide was negative for producing chromosome aberrations in the presence and absence of metabolic activation.

Recommendation: No additional testing is proposed.

Reproductive Toxicity Studies

Effects on reproductive organs in male and female rats and mice have been examined in 14 week and 2 year inhalation toxicity studies. The only reproductive effect observed in both species was an increase in squamous cell carcinomas in the uterus in mice in a 2 year carcinogenicity study.

Although there are no reproductive toxicity studies, per se, for ethyl bromide, a rationale is presented in the Data Evaluations for Methyl Bromide for using the methyl bromide reproductive studies in lieu of additional studies for ethyl bromide. It is accepted that methyl bromide is more toxic than ethyl bromide and therefore, dose-response relationships would need to be adjusted accordingly.

Recommendation: No additional testing is proposed. See Data Evaluations for Methyl Bromide.

Developmental Toxicity Studies

Although there are no developmental toxicity studies, per se, for ethyl bromide, a rationale is presented in the Data Evaluations for Methyl Bromide for using the methyl bromide developmental studies in lieu of additional studies for ethyl bromide. It is accepted that methyl bromide is more toxic than ethyl bromide and therefore, dose-response relationships would need to be adjusted accordingly.

Recommendation: No additional testing is proposed. See Data Evaluations for Methyl Bromide.

4.0 EVALUATION OF EXISTING RELEVANT DATA FOR METHYL BROMIDE

When and where data are lacking for the HPV chemical, ethyl bromide, use of data from the surrogate chemical, methyl bromide, is not only scientifically justified, but encouraged. This position is bolstered by: (1) EPA's guidance on the category approach noted above under 1.0; and (2) its position presented before the OECD Working Party on Existing Chemicals (1999) that industry should minimize, as well as optimize, animal usage when fulfilling HPV data requirements. Therefore, data for CAS # 74-83-4, have been considered scientifically reliable data in support of existing SIDS data requirements for CAS #74-96-4.

The following data regarding environmental fate and biodegradation for methyl bromide are considered relevant for the assessment of ethyl bromide.

Biodegradation

Methyl bromide hydrolyzes in water forming methanol and hydrobromic acid. The estimated hydrolysis half-life in water at 25 ^{o}C and pH 7 is 20 days (Mabey and Mill, 1978). Castro and Belser (1981) reported a hydrolysis rate constant of 3 x 10^{-7}/sec or a half-life of 26.7 days. Methyl bromide forms a crystalline hydrate at 0 - 5 ^{o}C (Keith and Walters, 1992). When it was heated to 550 ^{o}C in the absence of oxygen, methane, hydrobromic acid, hydrogen, bromine, ethyl bromide, anthracene, pyrene and free radicals were produced (Chaigneau et al., 1966). The bioconcentration factor is 3.5 and half life in river and lake waters is 1 hour and 4 days, respectively.

The ready biodegradability, aerobic and anaerobic transformation in soil was tested in two different soil types, sandy loam and clay loam. These soils were derived from an agricultural site in California where methyl bromide had been used for several years as a soil fumigant in the production of food crops. The half-life in sandy loam soil, under aerobic conditions, was 35 hours (non-sterilized soil). Under anaerobic conditions the half-life in sandy loam soil was 144 hours (again using non-sterilized soil). The half-life for clay loam soil, under aerobic conditions was 3.8 hours (non-sterilized soil). Under anaerobic conditions the half-life in clay loam soil was 39 hours (using non-sterilized soil). The study further demonstrated that the level of microbial activity in both soil types was reduced. Methyl bromide was rapidly degraded within the first 2-4 hours due to chemical reaction with components in the soil. After 1-2 days a more gradual degradation was observed that was attributed to hydrolysis by the moisture in the soil.

> **Recommendation: This information regarding the biodegradation of methyl bromide in soil should be used in support of the biodegradation of ethyl bromide, and therefore, no additional testing is recommended.**

Photodegradation

Photohydrolysis of methyl bromide in water at three different pH values was measured over a period of approximately 28 days. Photohydrolysis followed a first-order rate of kinetics. The half-life (t ½) at pH 5 was 212 hrs, at pH 7 it was 208.8 hrs and at ph 9 it was 305.4 hours.

> **Recommendation: This information regarding the photohydrolysis of methyl bromide in water should be used, as needed, in support of the photohydrolysis of ethyl bromide.**

Hydrolysis

The hydrolysis rates of methyl bromide at 25 degrees C and 3 different pH values, were measured. The half-life (t ½) at pH 5 was 258.6 hrs, at pH 7 it was 255.8 hrs and at pH 9 it was 361 hours.

> **Recommendation: This information regarding the hydrolysis of methyl bromide in water should be used, as needed, in support of the hydrolysis of ethyl bromide.**

Acute Toxicity to Fish

Rainbow trout were exposed for 96 hours to five different concentrations of methyl bromide ranging from 1.3 to 7.7 mg/L. The 96 hr LC50 was 3.9 mg/L, indicating that it is toxic to rainbow trout. The NOEC is approximately 1.9 mg/L.

> **Recommendation: The information regarding the acute toxicity of methyl bromide to fish should be used in support of the toxicity of ethyl bromide to fish. The solubility of ethyl bromide is 9,000 mg/L versus methyl bromide which is 15,200 mg/L. No additional testing is recommended for ethyl bromide in view of the marginal increase in solubility for methyl bromide (e.g. < twice) compared to ethyl bromide, and the comparable bioconcentration factors (3.5 for methyl versus 3 to 5 for ethyl). The major component in the environment from either compound is inorganic bromine, and the source of this element is wide, varied, and ubiquitous.**

Acute Toxicity to Aquatic Invertebrates

In a 48 hour static test, Daphnia magna less than 24 hours old were added to test chambers containing methyl bromide and examined for mortality and immobility after 24 and 48 hours. The number of immobilized Daphnia was counted. The 48 hour EC50 was 2.6 mg/L, and the 48 hour no mortality/no immobility concentration was 1.2 mg/L. The NOEC was 1.2 mg/L.

Test results using Daphnia magna demonstrates methyl bromide is toxic to aquatic invertebrates.

> **Recommendation: This information regarding the acute toxicity of methyl bromide to aquatic invertebrates (Daphnia magna) should be used in support of the toxicity of ethyl bromide to similar species. The solubility of ethyl bromide is 9,000 mg/L versus methyl bromide which is 15,200 mg/L. No additional testing is recommended for ethyl bromide in view of the marginal increase in solubility for methyl bromide (e.g. < twice) compared to ethyl bromide, and the comparable bioconcentration factors (3.5 for methyl versus 3 to 5 for ethyl). The major component in the environment from either compound is inorganic bromine, and the source of this element is wide, varied, and ubiquitous.**

Acute Toxicity to Aquatic Plants

An acute toxicity study to aquatic plants is not considered useful data based upon the demonstrated use of methyl bromide in the production of plants and vegetables for human consumption. No adverse effects upon any food crops have been demonstrated in the 40 plus years of agricultural use of methyl bromide in their production and harvest.

> **Recommendation: Methyl bromide has been used for almost half a century in the fumigation and production of food crops for human consumption and animal feed purposes. The extensive use history of methyl bromide illustrates that it has not produced any adverse effects (e.g. phytotoxicity) on target and non-target plants. It is recommended that such use history be used to support ethyl bromide as well, based upon their structural similarity.**

Reproductive Toxicity

Methyl bromide has been examined by Morrissey et al. (1990) for the reproductive effects in rats and mice exposed for 13 weeks via inhalation (NTP, 1990). They examined the weights of testis, epididymis and cauda epididymis; cauda sperm motility and count; sperm head morphology; average estrous length; and relative frequency of different estrous stages. Some effects on increased testis weights were identified along with decrease in sperm motility. No effects were observed on estrous cycle length.

A two-generation study conducted in rats (American Biogenics Corp(1986), US EPA, 1988), also via inhalation, identified a NOAEL of 3 ppm. No adverse effects were observed on fertility, although a

decrease in body weight of parental rats and reduced growth of neonatal rats was observed at higher dose levels.

Hurtt and Working (1988) exposed male rats for 5 days to 200 ppm of methyl bromide (via inhalation) and then sacrificed them at various times from day 1 to 68 post-exposure. They measured plasma testosterone and testicular glutathione levels, effects on spermatogenesis and sperm quality and testicular weight and histology. No adverse effects were observed.

Recommendation: This information regarding the reproductive effects of methyl bromide to laboratory animals (rats and mice) should be used in support of the reproductive toxicity of ethyl bromide to similar species. Various endpoints of the effects on the reproductive system in rats and mice were also examined in repeated dose inhalation studies performed using ethyl bromide. The combination of these data support the conclusion that no additional reproductive testing is necessary for ethyl bromide.[Reference: IRIS (EPA), 2002 and US EPA Drinking Water Health Advisory, 1989]

Developmental Toxicity

No adverse developmental effects were observed in fetuses of rats exposed to methyl bromide via inhalation from days 1 through 19 of gestation (Hardin, et al., 1981; Sikov et al., 1980). Also no toxic effects were observed in the dams.

In a developmental toxicity study in rabbits (Hardin, et al., 1981; Sikov et al., 1980), inhalation exposure of 70 ppm on days 1 through 15 killed 24/25 pregnant dams by day 30. There were no adverse effects on the dams and no developmental effects observed at 20 ppm. In a separate developmental study, Breslin et al. (1990) exposed rabbits via inhalation to methyl bromide during gestation days 6-19. Maternal toxicity was evident at 80 ppm with reduced body weight gain and clinical signs of CNS toxicity. There was an increase in agenesis of the gall bladder and fused sternebrae at this level. There were no pre- or post-implantation losses or effects on litter size or fetal body weights, and the maternal and developmental NOAEL was estimated at 40 ppm for each.

Recommendation: This information regarding the developmental effects of methyl bromide to laboratory animals (rats and mice) should be used in support of the developmental toxicity of ethyl bromide to similar species. There are no specific developmental toxicity tests for ethyl bromide, as there are for methyl bromide. Based upon a similar consideration for use of reproductive studies, it is suggested that the developmental toxicity studies for methyl bromide be used to support the SIDS requirement for ethyl bromide. No additional Developmental toxicity testing is necessary for ethyl bromide.[Reference: IRIS (EPA), 2002 and US EPA Drinking Water Health Advisory, 1989]

5.0 CONCLUSIONS

As early as 1929 the US Public Health Service examined ethyl bromide and methyl bromide for their physiological and pathological effects in guinea pigs following repeated inhalation exposures. They observed that "the pathological changes due to ethyl bromide were similar in many respects to those described for methyl bromide." Further, "in arranging the compounds in order of decreasing toxicity, ethyl chloride was found to be the least toxic and methyl bromide the most toxic. Methyl chloride and ethyl bromide occupied intermediate positions on the scale."

The US EPA Integrated Risk Information System (IRIS) generated 6/12/02 stated that "bromomethane is structurally related to bromoethane." The contemporary toxicology data generated for ethyl and methyl bromide support these conclusions, viz. that methyl is more toxic than ethyl bromide and that they are similar in their biological effects in the laboratory assays conducted. Furthermore, almost the entire data bases for methyl and ethyl bromide are based upon inhalation exposure, owing to their gaseous state or volatile nature. Thus, no modifiers need to be considered in their environmental fate, bioavailability or effects in biological systems.

No additional environmental fate or ecological effects tests will be conducted, based upon scientifically reliable data from the surrogate chemical, methyl bromide. An acute toxicity study to aquatic plants for ethyl bromide is not considered necessary based upon the demonstrated use of methyl bromide in the production of plants and vegetables for human consumption. No adverse effects upon any food crops have been demonstrated in the 40 plus years of agricultural use of methyl bromide in the production of these crops.

Because bromomethane is structurally related and biologically similar to bromoethane, data from the more toxic compound (e.g. methyl) should be used, where necessary, as surrogate data for the less toxic and less bioavailable alkyl bromide (e.g. ethyl) in satisfying the SIDS data requirements for ethyl bromide. Based upon a thorough evaluation of all existing data for ethyl bromide and the use of surrogate data from methyl bromide, it is proposed that no additional studies be conducted.

References for SAR Analysis

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Figure 1

ethyl bromide

methyl bromide