AR 201-12939A

HIGH PRODUCTION VOLUME (HPV)

CHEMICAL CHALLENGE PROGRAM

TEST PLAN

For The

ALKYL ACETATE C6 - Cl3 CATEGORY

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EXECUTIVE SUMMARY

Under EPA's High Production Volume (HPV) Challenge Program ExxonMobil Chemical Company has committed to voluntarily compile a Screening Information Data Set (SIDS) on a category of chemicals defined as Alkyl Acetates C6 - C13. This category is supported by the basic screening data needed for an initial assessment of the physicochemical properties, environmental fate, and human and environmental effects of chemicals as defined by the Organization for Economic Cooperation and Development (OECD). The information used to complete the HPV SIDS endpoints comes from existing data.

ExxonMobil Chemical Company believes a category of Alkyl Acetates C6 - Cl3 is scientifically justifiable because their physicochemical and toxicological properties are very similar and follow a regular pattern as a result of the synthesis process. The structural similarities create a predictable pattern in the following parameters: physicochemical properties, environmental fate and environmental effects, and/or human health effects. The similarities are based on the following: a common structure (CH_3COOR), an incremental and constant change across the category where R is a branched alkyl group having carbon numbers C6, C7, C8, C9, C10, or Cl3 as the main constituent, a common functional ester group, and a likelihood of common precursors and breakdown products which result in structurally similar chemicals (e.g., acetic acid and intermediate-chain aliphatic alcohols).

The test data compiled for the category anchor studies proves adequate to support a screening-level hazard assessment for the category and its members (CAS numbers, 88230-35-7, 90438-79-2, 108419-32-5, 108419-33-6, 108419-34-7, and 108419-35-8). One can assess the untested endpoints by extrapolation between and among the category members.

The use of an Alkyl Acetate C6 - Cl3 category will: First, inform the public earlier about any hazards of Alkyl Acetates C6 - Cl 3. Second, the matrix of completed anchor study testing demonstrates the safety of the category without end-point tests for each chemical. Third, this reduction in testing resulted in fewer animals used to test this category of chemicals as opposed to doing each test on individual Alkyl Acetates C6 - c13.

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TEST PLAN FOR ALKYL ACETATES C6 - Cl3

I. INTRODUCTION

Under EPA's High Production Volume (HPV) Challenge Program ExxonMobil Chemical Company has committed to voluntarily compile a Screening Information Data Set (SIDS) on a category of chemicals defined as Alkyl Acetates C6 - C13. This category is supported by the basic screening data needed for an initial assessment of the physicochemical properties, environmental fate, and human and environmental effects of chemicals as defined by the Organization for Economic Cooperation and Development (OECD). The information used to complete the SIDS comes from existing data and fulfills an ExxonMobil obligation to the HPV Challenge Program.

ExxonMobil Chemical Company believes a category of Alkyl Acetates C6 - Cl3 is scientifically justifiable because their physicochemical and toxicological properties are very similar and follow a regular pattern as a result of the synthesis process. The structural similarities create a predictable pattern in the following parameters: physicochemical properties, environmental fate and environmental effects, and/or human health effects.

The test data compiled for the category proves adequate to support a screening-level hazard assessment for the category and its members (CAS numbers, 88230-35-7, 90438-79-2, 108419-32-5, 108419-33-6, 108419-34-7, and 108419-35-8). One can assess the untested endpoints by extrapolation between and among the category anchor studies that adequately demonstrate the relatively low toxicity of the Alkyl Acetates C6 - C13.

The use of an Alkyl Acetate C6 - Cl3 category will inform the public earlier about any hazards of Alkyl Acetates C6 - C13. Second, the matrix of completed anchor study testing demonstrates the safety of the category without end-point tests for each chemical. Third, this reduction in testing will result in fewer animals used to test this category of chemicals as opposed to doing each test on individual Alkyl Acetates C6 - C13.

II. CHEMICAL PROCESS AND DESCRIPTION

The Alkyl Acetate C6 - Cl 3 category, for the purposes of the Challenge Program, is a group of Alkyl Acetates whose physicochemical and toxicological properties are very similar and follow a regular pattern as a result of synthesis and structural similarity (Table 1). The production of the alkyl acetate family involves the reaction of aliphatic, monohydric alcohols with acetic acid to form the corresponding acetate esters.

$$ROH + CH_3COOH \rightarrow CH_3COOR + H_2O$$

The structural similarities create a predictable pattern in the following parameters: physicochemical properties, environmental fate and environmental effects, and/or human health effects. The similarities are based on the following:

- A common structure - CH_3COOR,
- An incremental and constant change across the category where R is a branched alkyl group having carbon numbers of C6, C7, C8, C9, Cl 0, or Cl 3 as the main constituent,
- A common functional ester group, and
- A likelihood of common precursors and breakdown products which result in structurally similar chemicals (e.g., acetic acid and intermediate-chain aliphatic alcohols).

Table 1. CAS Numbers and Descriptions

CAS Number	Chemical Name	Generic Name
88230-35-7	Hexanol, acetate, branched and linear	C6 branched and linear alkyl acetate ester
90438-79-2	Acetic acid, C6-8 branched alkyl esters	C6-C8 branched alkyl acetate ester
108419-32-5	Acetic acid, C7-9 branched alkyl esters*	C7-C9 branched alkyl acetate ester
108419-33-6	Acetic acid, C8-10 branched alkyl esters*	C8-C10 branched alkyl acetate ester
108419-34-7	Acetic acid, C9-11 branched alkyl esters*	C9-C11 branched alkyl acetate ester
108419-35-8	Acetic acid, Cl l-14 branched alkyl esters	Cl l-Cl4 branched alkyl acetate ester

* = Not currently HPV but included to facilitate category evaluation

In formulating the category, Alkyl Acetates C6 - Cl 3, robust summaries of SIDS endpoints are addressed for the anchor alkyl acetate studies.

Category, Alkyl Acetates C6 - C13, accomplishes the goal of the Challenge Program - to obtain screening level hazard information - through the strategic application of testing across the category. The testing strategy results show that these chemicals behave in a similar or predictable manner and (1) extrapolation can be used to assess the Alkyl Acetates for which limited endpoint test data are available, and (2) no additional screening-level testing will be necessary. There will be a minimal amount of data modeling to be performed in 2001.

Procedures to assess the reliability of selected data for inclusion in the HPV Challenge Program were based on the guidelines described by Klimisch et al, 1997.

III. TEST PLAN RATIONALE

A. Physicochemical Data

Physicochemical data (i.e., melting point, boiling point, vapor pressure, water solubility, and Kow) for selected chemical components in the C6 - Cl3 Alkyl Acetate category will be calculated using the EPIWIN© model (EPIWIN, 1999), as discussed in the EPA document titled "The Use of Structure-Activitv Relationships (SAR) in the High Production Volume Chemicals Challenge Program." These data will be presented as ranges, based on the chemical components selected to represent each individual Alkyl Acetate product. In addition, measured data for some of these endpoints will also be

provided for selected Alkyl Acetate products where readily available. Where possible, the measured and calculated data will be presented together for comparison purposes. Table 2 lists selected measured physicochemical data as they appear on the material safety data sheets for these products and are provided with this test plan to further support considering these products a distinct category under the HPV Chemical program.

Table 2. Selected Physical Properties of Alkyl Acetates C6 - Cl3

CAS NUMBER	CHEMICAL NAME	BOILING RANGE (° C)	VAPOR PRESSURE (mm Hg @ 20° C)	SPECIFIC GRAVITY	FLASH POINT (° C)
88230-35-7	Hexanol, acetate, branched and linear	164-176	1.6	0.87	57
90438-79-2	Acetic acid, C6-8 branched alkyl esters	176-200	1.3	0.87	66
108419-32-5	Acetic acid, C7-9 branched alkyl esters	186-215	0.8	0.87	77
108419-33-a	Acetic acid, C8-10 branched alkyl esters	205-235	0.15	0.87	90
108419-34-7	Acetic acid, C9-11 branched alkyl esters	220-250	0.07	0.87	100
108419-35-8	Acetic acid, Cl 1-14 branched alkyl esters	240-285	0.04	0.87	127

B. Human Health Effects

The structural similarity of the Alkyl Acetates C6 - Cl3 influences both their physicochemical (Table 2) and their toxicological properties (Table 3). As a chemical category, the Alkyl Acetates C6 - C13, have predictable, low-level environmental and health hazards.

ExxonMobil Chemical Company believes the category of Alkyl Acetates C6 - Cl3 is scientifically justifiable and the test data compiled for the category proves adequate to support a screening-level hazard assessment for the category and its members (CAS numbers, 88230-35-7, 90438-79-2, 108419-32-5, 108419-33-6, 108419-34-7, and 108419-35-8). One can assess the untested endpoints by extrapolation between and among the category members.

The initial metabolic hydrolysis of the Alkyl Acetates results in reversal of the synthesis reaction. Metabolism of the Alkyl Acetates is catalyzed by esterases to yield acetic acid

and the corresponding aliphatic alcohol. Alcohol residues liberated by esterases, would likely be broken down by mitochondrial beta-oxidation or by cytochrome P450 mediated omega and omega-minus-one oxidation (may be followed by beta-oxidation). The alcohol undergoes various oxidative steps to yield other alcohols, ketones, aldehydes, carboxylic acids and carbon dioxide (Mann, 1987). Because alcohols are the primary metabolites of Alkyl Acetates, data on alcohols are very useful to address the toxicologic properties of Alkyl Acetates. Data for monohydric, aliphatic alcohols show a systematic variation according to molecular weight in a manner similar to many other homologous series (Monick, 1968). The body handles aliphatic hydrocarbons in a similar manner via oxidative conversion to alcohols, ketones, and eventual elimination as carbon dioxide and carboxylic acids (Wislocki et al, 1980). The undegraded alcohols can be conjugated either directly or as a metabolite with glucuronic acid, sulfuric acid, or glycine and are rapidly excreted (Lington and Bevan, 1994). Acetyl residues liberated by the esterases would enter intermediary metabolism pathways, be broken down and excreted as carbon dioxide and water. Intermediate aldehydes could be reactive and bind with DNA and/or proteins. Glucuronidation and glutathione conjugation are possible means of rapid elimination (Mann, 1987).

Table 3. Alkyl Acetates C6 - Cl3 Data Matrix For Mammalian Toxicity Studies

CAS Number	88230- 35-7	90438-79-2	108419-32-5	108419-33-6	108419-34-7	108419-35-8
Branched Alkyl Acetate Ester	C6	C6-C8	C7-C9	C8-C10	C9-C11	C11-C14
ACUTE						
ORAL -RAT	XX	R	R	R	R	x x
DERMAL - RABBIT	xx	xx	xx	xx	xx	xx
GENOTOXICITY						
Genetic - Point Mutation	xx	xx	xx	RA	RA	x x
Genetic - Chromosome Aberration	xx	xx	xx	RA	RA	xx
REPEATED DOSE						
ORAL - Rat	xx 28-DAY Gavage	RA	xx OO-DAY Gavage	RA	RA	xx 90-DAY Gavage
REPRODUCTIVE I DEVELOPMENTAL						
Developmental Tox ORAL - Rat	RA	RA	x x	RA	RA	x x
Reproductive Tox	Read across to Developmental Toxicity Studies and Repeated Dose Toxicity Studies that included histopathology on male and female sex organs and accessory sex organs.					

XX Anchor Studies with Adequate Existing Data; Studies are reliable without restrictions (Robust Summaries presented).
RA Read Across Extrapolation.
R Referenced Supportive Internal Study Document (No Robust Summary Provided).

Table 4. Summary of Toxicology Data Endpoints for Alkyl Acetates C6 - Cl3 Anchor Studies

NAME	ORAL LD_{50} -RAT	DERMAL LD_{50} - RABBIT	ORAL REPEATED DOSE - Rat	DEVELOPMENT - Rat	AMES Test ± Activation	CHROMOSOMAL ABERRATION - In Vitro or In Vivo
Hexanol, acetate, branched and linear	>2 glkg and >10 g/kg	>2 g/kg and >3.16 g/kg	28-DAY Gavage NOAEL = 1000 mglkglday	RA	NEGATIVE	NEGATIVE CHROM ABS (CHO)
Acetic acid, C6-8 branched alkyl esters	>5 g/kg *	>3.16 g/kg	RA	RA	NEGATIVE	NEGATIVE CHROM ABS (CHO)
Acetic acid, C7-9 branched alkyl esters*	>5 glkg *	>3.16 g/kg	90-DAY Gavage NOAEL = 1000 mglkglday	DEV-TOX MATERNAL NOAEL = 500 mg/kg; PUP NOAEL = 500 mg/kg	NEGATIVE	INACTIVE CD-I MOUSE MICRO-NUCLEUS
Acetic acid, C8-10 branched alkyl esters*	>5 g/kg *	>3.16 g/kg	RA	RA	RA	RA
Acetic acid, C9-11 branched alkyl esters*	>5 g/kg *	>3.16 g/kg	RA	RA	RA	RA
Acetic acid, CII-14 branched alkyl esters	>5 g/kg	>3.16 g/kg	90-DAY Gavage NOAEL = 1000 mg/kg/day	DEV-TOX MATERNAL NOAEL = 500 mg/kg; PUP NOAEL = 2 5 0 0 mg/kg	NEGATIVE	INACTIVE CD-1 MOUSE MICRO-NUCLEUS

RA Read Across.
* Referenced Supportive Internal Study Document (No Robust Summary Provided)

C. Presentation of Alkyl Acetates C6 - Cl3 Category Data Associated with the Anchor Studies under the HPV Challenge Program

Acute Oral Toxicity

TEST	C6 branched and linear alkyl acetate ester	C6-C8 branched alkyl acetate ester	C7-C9 branched alkyl acetate ester	C8-C10 branched alkyl acetate ester	C9-C11 branched alkyl acetate ester	C11-C14 branched alkyl acetate ester
ACUTE ORAL - RAT	LD_{50}>10 g/kg (HL, 1963) LD_{50}>2 g/kg (EBSI, 1995a)	LD_{50}>5 g/kg (Biodyn, 1983a) *	LD_{50}>5 glkg (Biodyn, 1984a,) *	LD_{50}>5 g/kg (Biodyn, 1983b) *	LD_{50}>5 g/kg (Biodyn, 1983c) *	LD_{50}>5 g/kg (Biodyn. 1983d)

* References] Supportive Internal Study Document (No Robust summary Provi d)

All of the Alkyl Acetates C6 - Cl3 have a low order of toxicity via the oral route of exposure to rats. The LD_{50} for C6 branched and linear alkyl acetate ester anchor studies were >2 to >10 g/kg (EBSI, 1995a; HL, 1963; ~~EBSI 1 99~~%). The LD_{50} for Cl l-Cl4 branched alkyl acetate ester anchor study was greater than 5 g/kg (Biodyn, 1983d). The LD_{50}'s for the referenced supportive C6-C8, C7-C9, C8-Cl 0, and C9-C11 branched alkyl acetate esters were all > 5 g/kg (Biodyn, 1983a;

1984a; 1983b; 1983c). No evidence of systemic toxicity was seen in any of these studies.

Acute Dermal Toxicity

TEST	C 6 branched and linear alkyl acetate ester	C6-C8 branched alkyl acetate ester	C7-C9 branched alkyl acetate ester	C8-C10 branched al kyl acetate ester	CQ-Cl1 branched alkyl acetate ester	C11-C14 branched alkyl acetate ester
ACUTE DERMAL - RABBIT	LD_{50}>3.16 g/kg (HL,1963) LD_{50}>2 g/kg (EBSI, 1995b)	LD_{50}>3.16 g/kg (Biodyn, 1983e)	LD_{50}>3.16 g/kg (Biodyn, 1983f)	LD_{50}>3.16 g/kg (Biodyn, 1983g)	LD_{50}>3.16 g/kg (Biodyn, 1964b)	LD_{50}>3.16 g/kg (Biodyn, 1984c)

The Alkyl Acetates C6 - Cl 3 have a low order of toxicity via the dermal route of exposure. The rabbit dermal LD_{50} for the C6 branched and linear alkyl acetate ester anchor study was greater than 2 or 3.16 g/kg (EBSI, 1995b; HL, 1963). The rabbit dermal LD_{50} for Cl l-Cl4 branched alkyl acetate ester anchor study was greater than 3.16 g/kg (Biodyn, 1984c). The rabbit dermal LD_{50}'s for the C6-C8, C7-C9, C8-C10, and C9-C11 branched alkyl acetate esters were also greater than 3.16 g/kg (Biodyn, 1983e; 1983f; 1983g; 1984b).

Genotoxicity

TEST	C6 branched and linear alkyl acetate ester	C6-C8 branched alkyl acetate ester	C7-C9 branched alkyl acetate ester	C8-C10 branched alkyl acetate ester	C9-C11 branched alkyl acetate ester	C11-C14 branched alkyl acetate ester
AMES - S. typhimurium; TA98, 100, 1535, 1537.1538 ± Activation	NEGATIVE (EBSI, 1995c)	NEGATIVE (EBSI, 1997a)	NEGATIVE (EBSI, 1994a)	RA	RA	NEGATIVE (EBSI, 1994b)
Chromosomal Aberration - In Vitro or In Vivo	NEGATIVE CHROM ABS (CHO) (EBSI, 1995d)	NEGATIVE CHROM ABS (CHO) (EBSI, 1997b)	INACTIVE CD-I MOUSE MICRO-NUCLEUS (EBSI, 1994c)	RA	RA	INACTIVE CD-I MOUSE MICRO-NUCLEUS (EBSI, 1994d)

RA Read Across

The Alkyl Acetates C6 - Cl3 have shown no evidence of genotoxicity. Neither of the anchor studies, the C6 branched and linear alkyl acetate ester nor the Cl 1-Cl4 branched alkyl acetate ester were mutagenic in Ames assays using five strains of *Salmonella typhimurium*, with and without metabolic activation (EBSI, 199%; 1994b). The C6-C8 and C7-C9 branched alkyl acetate ester assays likewise were negative in the Ames assays (EBSI, 1997a; 1994a).

The clastogenicity of the anchor study, C6 branched and linear alkyl acetate ester was investigated in an in vitro chromosomal aberration assay in CHO cells

and was negative (EBSI, 1995d) as was the C6-C8 branched alkyl acetate ester study (EBSI, 1997b).

The clastogenicity of the Cl l-Cl4 branched alkyl acetate ester anchor study was investigated in the *in vivo* mouse micronucleus assay and was inactive for producing an increase in micronuclei formation in the bone marrow of CD-l mice (EBSI, 19944) as was the C7-C9 branched alkyl acetate ester study (EBSI, 1994c). Both mouse micronucleus assays showed evidence of cytotoxicity at the highest doses as shown by a decrease in the percentage of polychromatic erythrocytes compared to negative controls (EBSI, 1994c; EBSI, 19944).

Subchronic Toxicity

TEST	C6 branched and linear alkyl acetate ester	C7-C9 branched alkyl acetate ester	Cl 1 -C14 branched alkyl acetate ester
ORAL - Rat	28-DAY Gavage NOAEL = 1000 mglkglday (EBSI, 1995e)	OO-DAY Gavage NOAEL = 1000 mg/kg/day; NOEL = 100 mglkglday (Biodyn. 1985a)	OO-DAY Gavage NOAEL = 1000 mg/kg/day; NOEL = 100 mg/kg/day (Biodyn, 1985b)

An evaluation of the repeated dose anchor studies indicates a low toxicity concern for Alkyl Acetates C6 - Cl 3. Rats were exposed to 0, 100, 500 or 1000 mg/kg/day C6 branched and linear alkyl acetate ester for 28 days. No clinical signs of toxicity were observed at any time during the study. All animals survived to study termination and there were no treatment-related clinical, in-life, gross postmortem or microscopic findings (including adrenal glands, heart, kidneys, liver, lung, spleen, testes and ovaries). There were no adverse effects on body weight, food consumption, clinical laboratory parameters or organ weights. The no observable adverse effect level (NOAEL) was 1000 mglkglday (EBSI, 1995e).

A 90-day oral subchronic study was conducted in Sprague-Dawley rats with C7-C9 branched alkyl acetate ester at doses of 100, 500, and 1000 mg/kg of body weight administered by gavage. Liver weights were elevated at the 45-day interim sacrifice. Terminal liver and kidney weights were elevated in a dose-related manner. Organ weight changes were generally considered to be adaptive changes and did not indicate toxic effects. There were no abnormal necropsy observations or elevated serum chemistry values; thus, these increased organ weights were not treatment related. Microscopic evaluation of the kidneys revealed evidence of mild tubular nephropathy only in high-dose male rats that were consistent with alpha-2-u-globulin effects. Histopathology review of all other tissues from high-dose animals, including reproductive organs (testes, epididymides, prostate, seminal vesicles, ovaries, uterine horns, cervix, corpus of the uterus, and vagina) showed normal morphology. The lowest observable effect level was 500 mg/kg (increased liver/body weight ratio); however this is of minimal toxicological significance. The no observable adverse effect level (NOAEL) was 1000 mg/kg (Biodyn, 1985a).

A 90-day oral subchronic study was conducted in rats with Cl l-Cl4 branched alkyl acetate ester at doses of 100, 500, and 1000 mg/kg of body weight

administered by gavage. Terminal liver and kidney weights were elevated in a dose-related manner but were considered to be adaptive changes and do not indicate toxic effects. Microscopic evaluation of the kidneys revealed evidence of mild tubular nephropathy only in the high-dose male rats that was consistent with alpha-2-u-globulin effects not expected to occur in humans. Histopathology review of all other tissues from high-dose animals, including reproductive organs (testes, epididymides, prostate, seminal vesicles, ovaries, uterine horns, cervix, corpus of the uterus, and vagina) showed normal morphology. The no observable adverse effect level (NOAEL) was 1000 mglkg. (Biodyn, 1985b).

Developmental Toxicity

TEST	C7-C9 branched alkyl acetate ester	Cl 1 -C14 branched alkyl acetate ester
ORAL - Rat	DEV-TOX MATERNAL NOEL = 100 mglkg; PUP NOEL = 500 mglkg (Biodyn, 1985c)	DEV-TOX MATERNAL NOEL = 500 mg/kg; PUP NOEL = 2500 mglkg (Biodyn, 1985d)

The Alkyl Acetates C6 - Cl 3 anchor study products evaluated for developmental toxicity were C7-C9 and Cl l-Cl4 branched alkyl acetate ester. The C7-C9 branched alkyl acetate ester was administered at 100, 500, and 1000 mg/kg on gestation days 6-l 5 in a developmental toxicity study in rats. Maternal toxicity was seen at mid and high doses as evidenced by decreases in body weight. There was a slight increase in fetal malformations and embryotoxicity in the high-dose group only; no adverse fetal effects were observed in the mid- or low-dose groups. A maternal NOEL of 100 mg/kg and a developmental NOEL of 500 mg/kg were observed (Biodyn, 198%).

The Cl 1 -Cl4 branched alkyl acetate ester was administered at 500, 1300, and 2500 mg/kg on gestation days 6-l 5 in a developmental toxicity study in rats. Maternal toxicity was seen at mid and high doses as evidenced by decreases in body weight. There were no statistically significant deleterious effects on fetal survival, body weight, crown-rump length and no evidence of treatment-related malformations. A maternal NOAEL of 500 mg/kg and a developmental NOAEL of 2500 mglkg were observed (Biodyn, 1985d).

Reproductive Toxicity

The three repeated dose toxicity anchor studies (C6 branched and linear alkyl acetate ester, and C7-C9, Cl l-Cl4 branched alkyl acetate ester) and the two developmental toxicity anchor studies (C7-C9 and Cl 1-C14 branched alkyl acetate ester) prove adequate to support a screening-level hazard assessment for reproductive toxicity for Alkyl Acetates C6 - C13. This conclusion is based on the organ weights (ovaries and testes), gross and microscopic histopathology observations that showed the male and female sex organs and accessory sex organs were with in normal control ranges. There were no treatment-related histopathologic effects in the reproductive organs for any test animals in the repeated dose or developmental toxicity studies. According to the OECD SIDS

Guidelines, adequate developmental toxicology data coupled with subchronic toxicity data showing no effects on reproductive organs, fulfills the reproductive endpoint.

D. Aquatic Toxicity

Products ranging from the C6 branched and linear alkyl acetate ester to C9-C11 branched alkyl acetate ester are expected to produce a relatively narrow range of moderate acute aquatic toxicity to freshwater fish and invertebrates, and a similar narrow range of moderate toxicity to freshwater algae. This is based on results of studies for selected products in this range of alkyl acetate esters. In comparison, the Cl 1-C14 branched alkyl acetate is not expected to produce acute aquatic toxicity to freshwater fish and invertebrates, or toxicity to freshwater algae, based on results of studies for this product. The lack of toxicity is due to its comparatively lower water solubility, which limits the exposure of aquatic organisms to soluble fractions of this product.

Fish Acute Toxicity

TEST	C 6 branched and linear alkyl acetate ester	C6-C8 branched alkyl acetate ester	C7-C9 branched alkyl acetate ester	C8-C10 Branched alkyl acetate ester	C9-C11 branched alkyl acetate ester	C11-C14 branched alkyl acetate ester
FISH ACUTE TOXICITY (96-hour)	LL_{50}= 11.9 mg/L (EBSI, 1995f)	LC_{50}= 8.2 mg/L (EBSI, 1997c)	LC_{50}= 14.9 mg/L* (EBSI, 1985a)	RA	RA	LL_0= 5800 mg/L (EBSI, 1985b)

RA read across
* based on total carbon analysis

Acute experimental toxicity tests are reported for rainbow trout (*Oncorhynchus mykiss*) and fathead minnow (*Pimephales promelas*). Experimental values for C6 branched and linear alkyl acetate ester, C6-C8 branched alkyl acetate ester, and C7-C9 branched alkyl acetate ester show that they have the potential to cause acute toxicity (96-hour LL50 or LC50) in a range of approximately 8 to 15 mg/L. Although there are no data for C8-C10 branched alkyl acetate ester or C9-C11 branched alkyl acetate ester, their acute toxicities are expected to be similar to the existing fish acute toxicity data based on invertebrate acute toxicity test results, which show that these 5 products demonstrate a relatively narrow range of acute toxicity. In comparison, no mortality was observed with a fathead minnow when exposed to a saturated solution of a Cl l-Cl4 branched alkyl acetate ester prepared at a test material loading of 5800 mg/L.

Invertebrate Acute Toxicity

TEST	C 6 branched and linear alkyl acetate ester	C6-C8 branched alkyl acetate ester	C7-C9 branched alkyl acetate ester	C8-C10 branched alkyl acetate ester	C9-C11 branched alkyl acetate ester	CII-CI4 branched al kyl acetate ester

TEST	C6 branched and linear alkyl acetate ester	C6-C8 branched alkyl acetate ester	C7-C9 branched alkyl acetate ester	C8-C10 branched alkyl acetate ester	C9-C11 branched alkyl acetate ester	C11-C14 branched alkyl acetate ester
DAPHNID ACUTE TOXICITY (48-hour)	EL_{50}= 7.6 mg/L (EBSI, 1995g)	RA	EC_{50}= 29.4 mg/L* (EBSI, 1985c)	RA	EL_{50}= 6.7 mg/L (EBSI, 2000)	EL_0= 5829 mg/L (EBSI, 1985d)

RA read across
* based on total carbon analysis

Acute experimental toxicity tests for three alkyl acetate esters are reported for a Daphnid (*Daphnia* magna). The results show that these products have the potential to cause acute toxicity (48-hour EL50 or EC50) in a range of approximately 7 to 30 mg/L. In comparison, no effect was observed with the same organism exposed to a saturated solution of a Cl l-Cl4 branched alkyl acetate ester prepared at a test material loading of 5829 mg/L.

Alga Toxicity

TEST	C 6 branched and linear alkyl acetate ester	C6-C8 branched alkyl acetate ester	C7-C9 branched alkyl acetate ester	C8-C10 branched alkyl acetate ester	C9-C11 branched alkyl acetate ester	C11-C14 branched alkyl acetate ester
ALGA TOXICITY (96-hour)	EL_{50}b(1) = 40.1 mg/L; EL_{50}gr(2)= 32.1 mg/L; NOELRb= 31.0 mg/L; NOELRgr= 8.0 mg/L (EBSI, 1995h)	RA	EL_{50}b = 19.4 mg/L*; EL_{50}gr = 43.5 mg/L*; NOELRb= 31.0 mg/L*; NOELRgr= 8.0 mg/L* (EBSI, 1985e; EBSI, 1994e)	RA	RA	EL_0b = 5829 mg/L; EL0gr = 5829 mg/L; NOELRb= 5829 mg/L; NOELRgr= 5829 mg/L (EBSI, 1985f)

(1) biomass
(2) growth rate
RA read across
* based on total carbon analysis

Acute experimental toxicity tests are reported for an alga (*Selenastrum capricornutum*). Experimental values for C6 branched and linear alkyl acetate ester and C6-C8 branched alkyl acetate ester show that these products have the potential to cause acute toxicity (96-hour EL50 for biomass, b, and growth rate, gr) in a range of approximately 19 to 44 mg/L. Although there are no data for C6-C8 branched alkyl acetate ester, C8-Cl 0 branched alkyl acetate ester, or C9-C11 branched alkyl acetate ester, their acute toxicities are expected to be similar to the existing alga acute toxicity data based on invertebrate acute toxicity test results, which show that these 5 products demonstrate a relatively narrow range of acute toxicity. In comparison, no effect on biomass or growth rate was observed with the same organism when exposed to a saturated solution of a Cl l-Cl4 branched alkyl acetate ester prepared at a test material loading of 5829 mg/L.

E. Environmental Fate

Biodegradation data are available for four alkyl acetate ester products, which show that with the exception of the highest molecular weight product, these ester products are rapidly biodegraded. The Cl 1-C14 branched alkyl acetate ester has been shown to biodegrade at a moderate rate, which suggests that although it is not expected to degrade at a rate equivalent to the lighter molecular weight alkyl acetate ester products, it also will not persist in the environment.

Hydrolysis data developed for two alkyl acetate ester products suggest that the entire range of alkyl acetate ester products is stable in water. Although there is some information on photodegradation and fugacity, a complete data set will be developed to adequately characterize the alkyl acetate ester products. Chemical equilibrium models are used to calculate fugacity, which describes the potential of a chemical to be distributed in the environment. These data can only be calculated. Available information for selected component chemicals in the alkyl acetate ester category suggests that these products are expected to partition primarily to the air. Therefore, their fate in air is of environmental interest (this is discussed below under photodegradation). In addition, the majority of the component chemicals in these products have relatively low Kow values, which suggests that they will not tend to partition to suspended organic matter in air and precipitate to aquatic and terrestrial environmental compartments.

Biodegradation

TEST	C 6 branched and linear alkyl acetate ester	C6-C8 branched alkyl acetate ester	C7-C9 Branched alkyl acetate ester	C8-C10 branched alkyl acetate ester	C9-C11 branched alkyl acetate ester	CII-CI4 branched alkyl acetate ester
28-Day Aerobic Biodegradation Test	76.9% (EBSI, 1994f)	77.1% (EBSI, 1998)	RA	RA	84.7% (EBSI, 1996)	31.0%* (EBSI, 1985g)

RA read across
• data developed using an acclimated inoculum

C6 branched and linear alkyl acetate ester, C6-C8 branched alkyl acetate ester, and C9-C11 branched alkyl acetate ester have been shown to biodegrade rapidly using 28-day standard biodegradation test procedures. In comparison, Cl l-Cl4 branched alkyl acetate ester biodegrades at a moderate rate, which suggests that although it is not expected to degrade at a rate equivalent to the lighter alkyl acetate ester products, it will not persist in the environment.

Upon review of the available information, sufficient quality data were identified to accurately characterize the biodegradability of the products in this category, The data show that all products except the Cl l-Cl4 branched alkyl acetate ester are expected to biodegrade to an extent ranging from approximately 77 to 85% after 28 days. These data were developed using non acclimated inocula. The tests used various closed systems, which is required when assessing the biodegradability of volatile materials like

those in this category. The test systems were continuously stirred, which is also recommended when evaluating mixtures containing several chemicals, some of which may have minimal water-solubility. In comparison, the Cl l-Cl4 branched alkyl acetate ester demonstrated a lower extent of biodegradability, 31%, using an acclimated inoculum after the same period of time.

Photodegradation - Photolysis

Direct photochemical degradation occurs through the absorbance of solar radiation by a chemical substance. If the absorbed energy is high enough, then the resultant excited state of the chemical may undergo a transformation. Simple chemical structures can be examined to determine whether a chemical has the potential for direct photolysis in water. First order reaction rates can be calculated for some chemicals that have a potential for direct photolysis using the procedures of Zepp and Cline (Zepp, 1977). UV light absorption of the chemical components in this category will be evaluated to identify those having the potential to degrade in solution. For those compounds with a potential for direct photolysis in water, first order reaction rates will be calculated.

Photodegradation - Atmospheric Oxidation

Photodegradation can be measured (US EPA, 1999a) (EPA identifies OECD test guideline 113 as a test method) or estimated using models accepted by the EPA (US EPA, 1999b). An estimation method accepted by the EPA includes the calculation of atmospheric oxidation potential (AOP). Atmospheric oxidation as a result of hydroxyl radical attack is not direct photochemical degradation, but rather indirect degradation. AOPs can be calculated using a computer model. Alkyl Acetates, such as those in the Alkyl Acetate category, have the potential to volatilize to air. In air, these chemicals may undergo reaction with photosensitized oxygen in the form of ozone and hydroxyl radicals. The computer program AOPWIN (atmospheric oxidation program for Microsoft Windows) (EPIWIN, 1999) is used by OPPTS (Office of Pollution Prevention and Toxic Substances). This program calculates a chemical half-life based on an overall OH reaction rate constant, a 12-hr day, and a given OH- concentration. This calculation will be performed for the representative chemical components in the alkyl acetate ester category.

Stability in Water (Hydrolysis)

Hydrolysis of an organic chemical is the transformation process in which a water molecule or hydroxide ion reacts to form a new carbon-oxygen bond. Chemicals that have a potential to hydrolyze include alkyl halides, amides, carbamates, carboxylic acid esters and lactones, epoxides, phosphate esters, and sulfonic acid esters (Neely, 1985). Stability in water can be measured (US EPA, 1999a) (EPA identifies OECD test guideline 111 as a test method) or estimated using models accepted by the EPA (US EPA, 199913).

Upon review of the available information, sufficient quality data were identified to accurately characterize the hydrolysis potential of the products in this category. Results of two studies for the C6 branched and linear alkyl acetate ester and C6-C8 branched

alkyl acetate ester products indicate that these products are stable in water and are not subject to physically mediated hydrolysis at environmentally relevant pH values and over environmentally relevant time periods (EBSI, 1995i; EBSI, 1995j).

Chemical Transport and Distribution In The Environment (Fugacity Modeling)

Fugacity based multimedia modeling can provide basic information on the relative distribution of chemicals between selected environmental compartments (i.e., air, soil, sediment, suspended sediment, water, biota). The US EPA has acknowledged that computer modeling techniques are an appropriate approach to estimating chemical partitioning (fugacity is a calculated endpoint and is not measured). A widely used fugacity model is the EQC (Equilibrium Criterion) model (Mackay, 1996). EPA cites the use of this model in its document titled *Determining the Adequacy of Existing Data* (US EPA, 1999a), which was prepared as guidance for the HPV Program.

In its document, EPA states that it accepts Level I fugacity data as an estimate of chemical distribution values. The input data required to run a Level I model include basic physicochemical parameters; distribution is calculated as percent of chemical partitioned to 6 compartments (air, soil, water, suspended sediment, sediment, biota) within a unit world. Level I data are basic partitioning data that allow for comparisons between chemicals and indicate the compartment(s) to which a chemical is likely to partition.

The EQC Level I is a steady state, equilibrium model that utilizes the input of basic chemical properties including molecular weight, vapor pressure, and water solubility to calculate distribution within a standardized regional environment. This model will be used to calculate distribution values for representative chemical components identified in products in this category. A computer model, EPIWIN – version 3.02 (EPIWIN, 1999), will be used to calculate the properties needed to run the Level I EQC model.

IV. TEST PLAN SUMMARY

ExxonMobil Chemical believes that the Alkyl Acetate C6 - Cl 3 category of chemicals should be further examined in the following manner:

- Calculate physicochemical data as described in the EPA document titled, *The Use of Structure-Activify Relationships (SAR)* **in** *the High Production Volume Chemicals Challenge Program* for selected chemical components of Alkyl Acetate products in this category. Provide measured data for selected products where readily available.
- Prepare a technical discussion on the potential of Alkyl Acetate products in this category to photodegrade. Calculate AOP values for selected chemical components of alkyl acetate ester products in this category.
- Calculate fugacity data for selected chemical components of alkyl acetate ester products in this category.

ExxonMobil Chemical believes that the Alkyl Acetate C6 - Cl3 category of chemicals should be exempt from additional animal testing based on:

- available toxicologic data on Alkyl Acetates,
- established metabolic pathways for Alkyl Acetates,
- available toxicologic data on alkyl acetate metabolites, and
- well established structure-activity relationships.

ExxonMobil Chemical Company believes the thorough evaluation of the strategic anchor studies and the overall robustness of the screening data set for an Alkyl Acetates C6 - Cl3 category complies with the objectives of the HPV volunteer testing program. The category is supported by the basic data assessment of the physicochemical properties, environmental fate, and human and environmental effects of chemicals as defined by the Organization for Economic Cooperation and Development (OECD).

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