Supporting Documents for Initial Risk-Based Prioritization of High Production Volume Chemicals

Chemical/Category: **Alkyl Acetates C6 – C13 Category**

CAS No. 88230-35-7	**Hexanol, acetate, branched and linear**
CAS No. 90438-79-2	**Acetic acid, C6-8 branched alkyl esters**
CAS No. l08419-32-5*	**Acetic acid, C7-9 branched alkyl esters**
CAS No. l08419-33-6*	**Acetic acid, C8-l0 branched alkyl esters**
CAS No. l08419-34-7*	**Acetic acid, C9-11 branched alkyl esters**
CAS No. l08419-35-8*	**Acetic acid, C11-l4 branched alkyl esters**

(*Chemicals that were not HPV chemicals in 1990/1994)

Contents:

QUALITATIVE SCREENING-LEVEL RISK CHARACTERIZATION FOR
Alkyl Acetates C6 – C13 Category

Hexanol, acetate, branched and linear (C6-rich)	**CAS No. 88230-35-7**
Acetic acid, C6-8 branched alkyl esters (C7-rich)	**CAS No. 90438-79-2**
Acetic acid, C7-9 branched alkyl esters (C8-rich)	**CAS No. l08419-32-5***
Acetic acid, C8-10 branched alkyl esters (C9-rich)	**CAS No. l08419-33-6***
Acetic acid, C9-11 branched alkyl esters (C10-rich)	**CAS No. l08419-34-7***
Acetic acid, C11-14 branched alkyl esters (C13-rich)	**CAS No. l08419-35-8**

(*Supporting chemicals that were not HPV chemicals in 1990/1994)

1. Background

The High Production Volume (HPV) Challenge Program[1] is a voluntary initiative aimed at developing and making publicly available screening-level health and environmental effects information on chemicals manufactured in or imported into the United States (U.S.) in quantities greater than one million pounds per year. In the Challenge Program, producers and importers of HPV chemicals voluntarily sponsor chemicals; sponsorship entails the identification and initial assessment of the adequacy of existing toxicity data/information, conducting new testing if adequate data do not exist, and making both new and existing data and information available to the public. Each complete data submission contains data on 18 internationally agreed to "SIDS" (Screening Information Data Set[1,2]) endpoints that are screening-level indicators of potential hazards (toxicity) for humans or the environment and environmental fate.

The Environmental Protection Agency's Office of Pollution Prevention and Toxics (OPPT) is evaluating the data submitted in the HPV Challenge Program on approximately 1,400 sponsored chemicals. Data submitted to the Organisation for Economic Co-operation and Development (OECD) HPV Programme are also being evaluated. OPPT developed a screening-level hazard characterization that consists of an objective evaluation, conducted according to established EPA guidance[2,3], of the quality and completeness of the data set provided and is based primarily on hazard data provided by sponsors. The characterization does not draw conclusions regarding the completeness of all data generated with respect to a specific chemical substance or mixture. The OECD SIDS documents (SIDS Initial Assessment Profile; SIAP and SIDS Initial Assessment Report; SIAR) provide similar information. Under both the HPV Challenge and OECD HPV Programs, chemicals that have similar chemical structures, properties and biological activities may be grouped together and their data shared across the resulting category. Evaluation of chemical category formation and data extrapolation(s) among category members is performed in accord with established U.S. EPA[1] and OECD[4] guidance.

In 2006 and 2007, EPA received data on uses of and reasonably likely exposures to chemicals on the Toxic Substances Control Act (TSCA) Inventory of existing chemicals, submitted in accordance with the requirements of the Inventory Update Reporting (IUR) rule[5]. Information is collected every five years under IUR, promulgated under the authority of section 8(a) of TSCA. The most recent reports pertain to chemicals manufactured in (including imported into) the U.S. during calendar year 2005 in quantities of 25,000 pounds or more at a single site. Information is reported on the identity of the chemical manufactured or imported and the quantity, physical form, and number of persons reasonably likely to be exposed during manufacture of the chemical. For chemicals manufactured or imported in quantities of 300,000 pounds or more at a single site during calendar year 2005, additional information was reported on the industrial processing and uses of the chemical, the number of industrial processing sites and of employees reasonably likely to be exposed to the chemical at these sites, the consumer and commercial uses of the chemical and an indication whether the chemical is used in products intended for use by children under 14 years of age.

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[1] U.S. EPA. High Production Volume (HPV) Challenge Program; http://www.epa.gov/chemrtk/index.htm.
[2] U.S. EPA. HPV Challenge Program – Information Sources; http://www.epa.gov/chemrtk/pubs/general/guidocs.htm.
[3] U.S. EPA. Risk Assessment Guidelines; http://cfpub.epa.gov/ncea/raf/rafguid.cfm.
[4] OECD. Guidance Document on the Development and Use of Chemical Categories; http://www.oecd.org/document/7/0,2340,en_2649_34379_1947463_1_1_1_1,00.html.
[5] U.S. EPA – Basic IUR Information: http://www.epa.gov/opptintr/iur/pubs/guidance/basic-information.htm

For these qualitative screening-level risk characterization documents, EPA has reviewed the IUR data to evaluate exposure potential. In addition, exposure information that may have become available through prior Agency actions has been considered, as appropriate. The resulting exposure information has been combined with the screening-level hazard characterizations to develop this qualitative screening-level risk characterization[6,7]. These screening-level risk characterizations are technical documents intended to support subsequent decisions and actions by OPPT. Accordingly, the document is not written with the goal of informing the general public. The purpose of the qualitative screening-level risk characterization is two-fold: to support initial risk-based decisions to prioritize chemicals and inform risk management options and to identify data needs for individual chemicals or chemical categories.

2. Category Justification

The alkyl acetates category includes six chemicals (named above) that have a common structure consisting of an acetate ester functional group (CH_3COO-R) and a branched alkyl side chain (R). The alkyl side chain varies incrementally across the members of the category from six to 13 carbons as the main substituent. Each member typically consists of methyl-branched isomers of various chain lengths, the composition of which depends on the alcohol feedstock. For example, the C_{11}-C_{14} alkyl acetates identify the range of possible isomers, although the predominant one is a C_{13}-length side chain. Thus, the upper end of the category boundary is identified as the predominant isomer (C_{13}) in this range. The basis for the category is structural similarities and the predictable pattern in physicochemical and environmental fate properties, ecological and mammalian toxicity associated with the change in the number of carbons from the low of six to the high of 13. This category is considered acceptable and reasonable for the purposes of the HPV Challenge Program.

3. Physical-Chemical Properties and Environmental Fate

This report was prepared using the best available data from a number of sources, but draws no conclusions regarding whether additional relevant data may exist. The members of the alkyl acetates C6-C13 category are liquids at room temperature. Going from longer chain (predominantly C13) to shorter chain (C6) for the category members; they have moderate to high vapor pressure, low to moderate water solubility, and moderate to high volatility. Using the same descriptors for the category trend, they are moderately mobile in soil and water systems, are expected to degrade at moderate to rapid rates by biodegradation and by photolysis, and slow to negligible rates by hydrolysis. The persistence and bioaccumulation ranking for this category is low to moderate. With the exception of acetic acid, C11-14, the alkyl acetates are low for persistence (P1) and bioaccumulation (B1). Based on available data, acetic acid, C11-14 (108419-35-8) is ranked low for persistence (P1) and high for bioaccumulation (B3) and may biodegrade to moderately persistent (P2) and bioaccumulative (B2) branched alcohols.

4. Hazard Characterization

Aquatic Organism Toxicity: The evaluation of the available aquatic toxicity data for fish, aquatic invertebrates and aquatic plants indicates that the potential acute hazard of the members of the alkyl acetates C6 to C13 category to aquatic organisms ranges from low (hexanol, acetate C6 rich and acetic acid, C6-C8 branched alkyl esters) to moderate (acetic acid, C11-C14 branched alkyl esters). In addition, because the largest member of the category (acetic acid, C11 – C14 branched alkyl esters) may be persistent and bioaccumulative chronic aquatic toxicity has been identified as a data gap under the HPV Challenge Program.

Human Health Toxicity: The acute toxicity of the C6-C13 alkyl acetates is low via the oral and dermal routes. The category members are moderate skin irritants and may cause slight eye irritation. Repeated exposures to C6-C13 alkyl acetates via the oral route show low toxicity in experimental animals tested at high doses. The only notable effects observed were changes in the kidney of male rats that may be relevant to humans. There is no indication of toxicity to reproduction. Some development toxicity was observed at the highest tested dose. The category members

[6] U.S. EPA Guidelines for Exposure Assessment; http://cfpub.epa.gov/ncea/raf/recordisplay.cfm?deid=15263
[7] U.S. EPA. Risk Characterization Program; http://www.epa.gov/osa/spc/2riskchr.htm.

are not mutagenic and do not induce chromosomal aberrations. Based on the available data submitted in the HPV Challenge Program, the overall human health hazard is considered low.

5. Exposure Characterization

This exposure characterization was completed using available 2006 Inventory Update Rule (IUR) submissions. Data and information that are claimed Confidential Business Information (CBI) by the submitter were reviewed and considered by EPA in preparing this assessment but are not disclosed in this summary.

In addition, the following sources were reviewed to identify exposure and use information: the HPV Challenge Submission, OECD SIDS data, the Toxics Release Inventory (TRI), OSHA PEL documentation, various databases and public sources.

Production Volume Information for Each Member

Acetic Acid, C6 – C8 Branched Alkyl Esters (C7-rich) – Sponsored Chemical: Acetic acid, C6-8 branched alkyl esters was manufactured and/or imported in the United States in the range of 1,000,000 to 10,000,000 pounds in 2005.

Acetic Acid, C7 – C9 Branched Alkyl Esters(C8-rich) – Supporting Chemical: Acetic acid, C7-9 branched alkyl esters was manufactured and/or imported in the United States in the range of 500,000 to 1,000,000 pounds in 2005.

Acetic Acid, C9 – C11 Branched Alkyl Esters (C10-rich) – Supporting Chemical: Acetic acid, C9-11 branched alkyl esters was manufactured and/or imported in the United States in the range of 500,000 to 1,000,000 pounds in 2005.

Acetic Acid, C11 – C14 Branched Alkyl Esters (C13-rich) – Sponsored Chemical: Acetic acid, C11-14 branched alkyl esters was manufactured in the United States in the range of 10,000 to 500,000 pounds in 2005.

Information Applicable to All Category Members

IUR information for 2005 was submitted for five of the six category members; the exception being acetic acid, C8 – C10 branched alkyl esters. The available IUR submissions for one of the five members (hexanol, acetate, branched and linear; CAS No. 88230-35-7) reported a production volume of less than 500,000 pounds with no industrial, commercial, or consumer use information. Therefore, Exposure Characterizations are available for only four category members (two sponsored chemicals and two supporting chemicals).

According to information in the HPV Challenge submission, alkyl acetates are mainly used as solvents in lacquers, janitorial cleaning products and agricultural products. Limited workplace air sampling data suggest air concentrations below 10 mg/m^3 for C6 to C13 alkyl acetate aerosols.

Exposures to General Population and the Environment
None of the alkyl acetates are on the Toxics Release Inventory. Based on use information, EPA assumes for the purpose of this risk prioritization that there is potential for exposures to the general population and the environment. However, in this case, the category members are used as solvents in lacquers, janitorial cleaning products, and agricultural products. The potential for exposure to the general population and the environment from environmental releases is possible based on these uses. Searches of additional relevant information sources related to Voluntary Children's Chemical Evaluation Program (VCCEP) and HSDB did not provide any further information on this chemical. The IUR-based ranking for the general population and exposure to the environment from environmental releases of the chemicals in this category is high due to the assumption that there will be exposure to these chemicals.

As noted above in the Physical-Chemical Properties section, the ratings for all category members except for acetic acid, C11-14 show no concern for persistence or bioaccumulation in the environment. The C11-14 category member may biodegrade to moderately persistent and strongly bioaccumulative branched alcohols.

Exposure to Children
No information was provided on the IUR for exposure to children through using products that contain these chemicals. The HPV Challenge Program submission indicates that alkyl acetates (C6 to C13) are mainly used as solvents in lacquers, janitorial cleaning products, and agricultural products. Thus, EPA assumes that all members of this category are used in products to which children may be exposed.

Information Applicable to Most Category Members

Exposure to Workers
The National Occupational Exposure Survey (NOES), conducted from 1981 to 1983, did not provide information on the number of workers likely to be exposed to any category member. The 2005 IUR data submitted indicate that workers may be exposed to each of the category members. Based on IUR reporting, the maximum total number of workers likely to be exposed to each category member during manufacturing and industrial processing and use is less than 100. The vapor pressure value for each member of the category (see attached Hazard Characterization supporting document) are above 0.001 torr. OPPT has established 0.001 torr as a value above which worker exposures to vapors should be estimated for chemical assessments. Therefore, the vapor pressures of all category members could result in significant worker exposures to vapors if workers are proximal to the liquid. None of the members have an OSHA Permissible Exposure Limit.

> *Acetic Acid, C6 – C8 Branched Alkyl Esters (C7-rich):* There may be additional potentially exposed workers that are not included in this estimate since not all production volume has been accounted for. The IUR-based ranking for worker exposure is low.
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> *Acetic Acid, C7– C9 Branched Alkyl Esters (C8-rich), Acetic Acid, C9 – C11 Branched Alkyl Esters (C10-rich) and Acetic Acid, C11 – C14 Branched Alkyl:* There may be additional potentially exposed workers that are not included in this estimate since not all production volume has been accounted, and there is at least one use that contains a "Not Readily Obtainable" (NRO) response among the submissions. The IUR-based ranking for worker exposure is high based on uncertainty associated with the data.

Exposure to Commercial Workers and Consumers
Based on the vapor pressure of all category members as cited above, there could be significant exposures to vapors if commercial workers/consumers are near products containing the chemical.

> *Acetic Acid, C6 – C8 Branched Alkyl Esters (C7-rich) and Acetic Acid, C7– C9 Branched Alkyl Esters (C8-rich):* A very low number of workers were reported to be in jobs manufacturing these chemicals. It is unknown how many workers may be involved in jobs that are related to use of these chemicals or how many consumers may use these chemicals because that information was not reported on the IUR. These chemicals do not appear to be used in commercial/consumer products.
>
> *Acetic Acid, C9 – C11 Branched Alkyl Esters (C10-rich) and Acetic Acid, C11 – C14 Branched Alkyl Esters (C13-rich):* It is unknown how many workers may be involved in jobs that are related to use of these chemicals or how many consumers may use these chemicals because that information was not reported on the IUR. These chemicals appear to be used in commercial/consumer products.

6. Risk Characterization

The statements and rationale provided below are intended solely for the purpose of this screening-level and qualitative risk characterization and will be used for prioritizing substances for future work in the U.S. HPV Challenge Program.

6.1 Risk Statement and Rationale

Potential Risk to Aquatic Organisms from Environmental Releases

MEDIUM CONCERN for acetic acid, C_{11-14} branched alkyl esters: EPA assumes there is potential for exposure to aquatic organisms from environmental releases. This category member, which was an HPV in the 1990's but was reported at less than a million pounds in the 2006 IUR, has the potential to be both persistent in the environment and bioaccumulative in aquatic organisms. There is a data gap for potential chronic hazard to those organisms, leading to a concern for potential risk to aquatic organisms from environmental releases.

LOW CONCERN for the remaining category members: EPA assumes there is potential for exposure to aquatic organisms from environmental releases. The low acute aquatic hazard and the overall fate characteristics (e.g., not persistent or bioaccumulative) of these category members suggest a low concern for potential risk to aquatic organisms from environmental releases.

Potential Risk to General Population from Environmental Releases (LOW CONCERN – all category members): EPA assumes there is potential for exposure to the general population from environmental releases. The potential human health hazard is expected to be low due to minimal toxicity observed only at high doses in animal studies. Thus, although one category member (acetic acid, C_{11-14} branched alkyl esters) may be persistent/bioaccumulative in the environment, the low human health hazard suggests a low concern for potential risk to the general population from environmental releases for all the category members.

Potential Risk to Workers (LOW CONCERN – all category members): There is a potential for exposure in the workplace for most of the category members; however, the low hazard profile for all six category members suggests a low concern for potential risk to workers

Potential Risk to Commercial Workers and Consumers from Known Uses (LOW CONCERN – all category members): There is potential for commercial workers/consumer exposures resulting from the stated uses of the category members; however, the low hazard profile for all six category members suggests a low concern for potential risk to both groups.

Potential Risk to Children (LOW CONCERN – all category members): The available exposure/use information suggests there is a potential for exposure to children. There is uncertainty (see below) regarding the identity of the category members in products available to children; however, the low hazard profile for all six category members suggests a low concern for the potential risk to children.

6.2 Uncertainties

The alkyl acetates C6 – C13 category may have minor uses that were not reported in IUR. There is also uncertainty regarding the exposure/use information for the category members pertaining to whether these substances may be found in products to which children may be exposed. In addition, there is uncertainty as to the extent of possible exposure to the environment and the general population from environmental releases. Finally, little data was provided regarding the specific composition of the category members other than the carbon number range and the descriptor "branched." This introduces some uncertainty into this screening-level assessment. Ideally, the number and identity of components and their typical percentages increase the confidence in determining the overall hazard of these compounds.

6.3 Data Needs

There is a need to fill the data gap for chronic aquatic toxicity for acetic acid C11-14, branched alkyl ester.

SCREENING-LEVEL HAZARD CHARACTERIZATION OF HIGH PRODUCTION VOLUME CHEMICALS

CHEMICAL CATEGORY NAME
Alkyl Acetates C6 to C13

SPONSORED CHEMICALS

Hexanol, acetate, branched and linear (C6-rich)	**CAS No. 88230-35-7**
Acetic acid, C6-8 branched alkyl esters (C7-rich)	**CAS No. 90438-79-2**
Acetic acid, C11-l4 branched alkyl esters (C13-rich)	**CAS No. 108419-35-8**

SUPPORTING CHEMICALS

Acetic acid, C7-9 branched alkyl esters (C8-rich)	**CAS No. 108419-32-5**
Acetic acid, C8-l0 branched alkyl esters (C9-rich)	**CAS No. 108419-33-6**
Acetic acid, C9-11 branched alkyl esters (C10-rich)	**CAS No. 108419-34-7**

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SCREENING-LEVEL HAZARD CHARACTERIZATION OF HIGH PRODUCTION VOLUME CHEMICALS

The High Production Volume (HPV) Challenge Program[8] is a voluntary initiative aimed at developing and making publicly available screening-level health and environmental effects information on chemicals manufactured in or imported into the United States in quantities greater than one million pounds per year. In the Challenge Program, producers and importers of HPV chemicals voluntarily sponsor chemicals; sponsorship entails the identification and initial assessment of the adequacy of existing toxicity data/information, conducting new testing if adequate data do not exist, and making both new and existing data and information available to the public. Each complete data submission contains data on 18 internationally agreed to "SIDS" (Screening Information Data Set[1,9]) endpoints that are screening-level indicators of potential hazards (toxicity) for humans or the environment.

The Environmental Protection Agency's Office of Pollution Prevention and Toxics (OPPT) is evaluating the data submitted in the HPV Challenge Program on approximately 1400 sponsored chemicals. OPPT is using a hazard-based screening process to prioritize review of the submissions. The hazard-based screening process consists of two tiers described below briefly and in more detail on the Hazard Characterization website[10].

Tier 1 is a computerized sorting process whereby key elements of a submitted data set are compared to established criteria to "bin" chemicals/categories for OPPT review. This is an automated process performed on the data as submitted by the sponsor. It does not include evaluation of the quality or completeness of the data.

In Tier 2, a screening-level hazard characterization is developed by EPA that consists of an objective evaluation of the quality and completeness of the data set provided in the Challenge Program submissions. The evaluation is performed according to established EPA guidance[2,11] and is based primarily on hazard data provided by sponsors. EPA may also include additional or updated hazard information of which EPA, sponsors or other parties have become aware. The hazard characterization may also identify data gaps that will become the basis for a subsequent data needs assessment where deemed necessary. Under the HPV Challenge Program, chemicals that have similar chemical structures, properties and biological activities may be grouped together and their data shared across the resulting category. This approach often significantly reduces the need for conducting tests for all endpoints for all category members. As part of Tier 2, evaluation of chemical category rationale and composition and data extrapolation(s) among category members is performed in accord with established EPA[2] and OECD[12] guidance.

The screening-level hazard characterizations that emerge from Tier 2 are important contributors to OPPT's existing chemicals review process. These hazard characterizations are technical documents intended to support subsequent decisions and actions by OPPT. Accordingly, the documents are not written with the goal of informing the general public. However, they do provide a vehicle for public access to a concise assessment of the raw technical data on HPV chemicals and provide information previously not readily available to the public. The public, including sponsors, may offer comments on the hazard characterization documents.

The screening-level hazard characterizations, as the name indicates, do not evaluate the potential risks of a chemical or a chemical category, but will serve as a starting point for such reviews. In 2007, EPA received data on uses of and exposures to high-volume TSCA existing chemicals, submitted in accordance with the requirements of the Inventory Update Reporting (IUR) rule. For the chemicals in the HPV Challenge Program, EPA will review the IUR data to evaluate exposure potential. The resulting exposure information will then be combined with the screening-level hazard characterizations to develop screening-level risk characterizations[4,13]. The screening-level risk characterizations will inform EPA on the need for further work on individual chemicals or categories. Efforts are currently underway to consider how best to utilize these screening-level risk characterizations as part of a risk-based decision-making process on HPV chemicals which applies the results of the successful U.S. High Production Volume Challenge Program and the IUR to support judgments concerning the need, if any, for further action.

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[8] U.S. EPA. High Production Volume (HPV) Challenge Program; http://www.epa.gov/chemrtk/index.htm.
[9] U.S. EPA. HPV Challenge Program – Information Sources; http://www.epa.gov/chemrtk/pubs/general/guidocs.htm.
[10] U.S. EPA. HPV Chemicals Hazard Characterization website (http://www.epa.gov/hpvis/abouthc.html).
[11] U.S. EPA. Risk Assessment Guidelines; http://cfpub.epa.gov/ncea/raf/rafguid.cfm.
[12] OECD. Guidance on the Development and Use of Chemical Categories; http://www.oecd.org/dataoecd/60/47/1947509.pdf.
[13] U.S. EPA. Risk Characterization Program; http://www.epa.gov/osa/spc/2riskchr.htm.

SCREENING-LEVEL HAZARD CHARACTERIZATION
Alkyl Acetates C6 to C13 Category

Introduction

The sponsor, ExxonMobil Chemical Company, submitted a Test Plan and Robust Summaries to EPA for the Alkyl Acetates C6 to C13 category on December 21, 2000. EPA posted the submission on the ChemRTK HPV Challenge website on February 7, 2001 (http://www.epa.gov/chemrtk/pubs/summaries/alkylace/c12939tc.htm). EPA comments on the original submission were posted to the website on June 6, 2001. Public comments were also received and posted to the website. The sponsor submitted updated/revised documents on August 24, 2005, which were posted to the ChemRTK website on August 31, 2005. The Alkyl Acetates C6 to C13 category consists of the following six mixtures:

Sponsored Chemicals:

Hexanol, acetate, branched and linear (C6-rich)	CAS No. 88230-35-7
Acetic acid, C6-8 branched alkyl esters (C7-rich)	CAS No. 90438-79-2
Acetic acid, C11-l4 branched alkyl esters (C13-rich)	CAS No. 108419-35-8

Supporting Chemicals:

Acetic acid, C7-9 branched alkyl esters (C8-rich)	CAS No. 108419-32-5
Acetic acid, C8-l0 branched alkyl esters (C9-rich)	CAS No. l08419-33-6
Acetic acid, C9-11 branched alkyl esters (C10-rich)	CAS No. l08419-34-7

This screening-level hazard characterization is based primarily on the review of the test plan and robust summaries of studies submitted by the sponsor(s) under the HPV Challenge Program. In preparing the hazard characterization, EPA considered its own comments and public comments on the original submission as well as the sponsor's responses to comments and revisions made to the submission. Structure(s) of the sponsored chemical(s) is included in the appendix. The screening-level hazard characterization for environmental and human health toxicity is based largely on SIDS endpoints and is described according to established EPA or OECD effect level definitions and hazard assessment practices.

Category Justification

The alkyl acetates category includes six chemicals (named above) that have a common structure consisting of an acetate ester functional group (CH_3COO-R) and a branched alkyl side chain (R). The alkyl side chain varies incrementally across the members of the category from six to 13 carbons as the main substituent. Each member typically consists of methyl-branched isomers of various chain lengths, the composition of which depends on the alcohol feedstock. For example, the C_{11}-C_{14} alkyl acetates identify the range of possible isomers, although the predominant one is a C_{13}-length side chain. Thus, the upper end of the category boundary is identified as the predominant isomer (C_{13}) in this range. Based on these structural similarities as well as a predictable pattern in physicochemical and environmental fate properties, environmental effects and mammalian toxicity, the chemicals in this category can be grouped and evaluated together. Data for the tested category members and supporting chemicals are extrapolated to provide estimates of similar properties for the untested members.

EPA agreed with the sponsor's support of the category, that the available data tend to be similar and follow a predictable pattern across the category members. EPA notes that although the C11-C14 branched alkyl acetate esters show less biodegradation and aquatic toxicity compared to the other members of the category, this reflects the predictable change in certain test-related properties such as water solubility and represents a natural break-point within the category.

Justification for Supporting Chemicals

The sponsor provided additional data for the following supporting substances to support the endpoints indicated:

Acetic acid, C7-9 branched alkyl esters (predominantly C8), data submitted for acute toxicity, repeated-dose toxicity, reproductive toxicity, developmental toxicity and genetic toxicity.

Acetic acid, C8-l0 branched alkyl esters (predominantly C9), data submitted for acute toxicity.

Acetic acid, C9-11 branched alkyl esters (predominantly C10) , data submitted for ready biodegradation, aquatic toxicity, acute toxicity,

The supporting substances have similar chemical structures and their component composition provide a reasonable attempt to bridge the gap between the C6-8 and C11-14 sponsored chemicals in the category.

Summary-Conclusion

The members of the Alkyl Acetate C6-C13 category are liquids at room temperature. They have moderate to high vapor pressure, low to moderate water solubility, and moderate to high volatility. They are moderately mobile in soil and water systems. They are expected to degrade at moderate to rapid rates by biodegradation and by photolysis, and slow to negligible rates by hydrolysis. The persistence and bioaccumulation ranking for this category is low to moderate. With the exception of acetic acid, C11-14, the alkyl acetates are low for persistence (P1) and bioaccumulation (B1). Based on available data, acetic acid, C11-14 (108419-35-8) is ranked low for persistence (P1) and high for bioaccumulation (B3) and may biodegrade to moderately persistent (P2) and bioaccumulative (B2) branched alcohols.

The evaluation of the available aquatic toxicity data for fish, aquatic invertebrates and aquatic plants indicates that the potential acute hazard of the members of the Alkyl Acetates C6 to C13 Category to aquatic organisms is likely to be moderate.

The acute oral dermal toxicity of the members of this category is low. The category members, hexanol, acetate, branched and linear and C11-14 branched alkyl acetate esters are mild to moderate skin irritants and mild eye irritants. Repeated oral exposures to hexanol, acetate, branched and linear, C7-9 branched alkyl acetate ester and C11-14 branched alkyl acetate esters were minimally toxic to rats. For the C7-9 branched alkyl acetate ester and C11-14 branched alkyl acetate ester, mild tubular nephropathy in the high-dose male rats consistent with $alpha_{2\mu}$-globulin effect was the only notable effect[14]. Histopathological evaluation of all other tissues and organs including reproductive organs was normal when tested at the limit doses of 1000 mg/kg-bw/day. Developmental toxicity characterized as a slight increase in fetal malformations and embryo toxicity, was observed following exposure of pregnant rats to C7-9 branched alkyl acetate esters (1000 mg/kg-bw/day). Exposure of pregnant rats to C11-14 branched alkyl acetate ester showed pronounced maternal toxicity at high doses; but no statistically significant effects on fetal survival, body weight and crown-rump length were noted. There were no treatment-related malformations. The category members, hexanol, acetate, branched and linear, C6-8 branched alkyl acetate esters, C7-9 branched alkyl acetate ester, and C11-14 branched alkyl acetate ester, did not show mutagenic potential when tested in bacterial cells. Hexanol, acetate, branched and linear and C6-8 branched alkyl acetate ester did not induce chromosomal aberrations in *in vitro* and C7-9 branched alkyl acetate ester and C11-14 branched alkyl acetate ester did not increase the mean number of micronucleated polychromatic erythrocytes *in vivo*.

The potential health hazard of the C6 to C13 alkyl acetates C6 to C13 category is low.

Chronic aquatic toxicity has been identified as a data gap for acetic acid, C11-C14 alkyl esters under the HPV Challenge Program. In addition, although not a data gap *per se,* little data was provided regarding the specific

[14] The presence of nephropathy in association with the hyaline droplet accumulation in male rats suggests that the nephropathy in the males is occurring by an $alpha_{2\mu}$-globulin-mediated mechanism which appears to be unique to male rats and the response is probably not relevant to humans for purposes of risk assessment. EPA's Risk Assessment Forum has outlined the key events and the data that are necessary to demonstrate this mode of action ($Alpha_{2\mu}$-Globulin: Association with Chemically Induced Renal Toxicity and Neoplasia in the Rat, EPA/625/3-91/019F). One of the key events, $alpha_{2u}$-globulin accumulation, has not been demonstrated. Therefore, the nephropathy is assumed to be relevant to human health.

composition of the category members other than the carbon number range and the descriptor "branched." This introduces some uncertainty into this screening-level hazard assessment. Ideally, the number and identity of components and their typical percentages increase the confidence in determining the overall hazard of these compounds.

1. Physical-Chemical Properties and Environmental Fate

This report was prepared using the best available data from a number of sources, including information from the HPV test plan and robust summaries for the category (ExxonMobil, 2000) and estimations using EPIWIN (U.S. EPA, 2007).

The alkyl acetates, C6-C13 category are complex mixtures of linear and branched hexanol acetate, and the branched alkyl acetates with carbon numbers C6 to C13. Basic physical-chemical and environmental fate properties of these compounds are listed in Tables 1a and 1b, respectively. The structures of all category members are in the Appendix.

Physical-Chemical Properties Characterization
The members of the C6-C13 Alkyl Acetate category are clear, colorless liquids with moderate-to-high volatility and low-to-moderate water solubility. Both the vapor pressure and the water solubility decrease with an increase in the alkyl carbon chain length.

Environmental Fate Characterization
The alkyl acetates, C6-C13 category are moderately mobile in soil and water systems. They are expected to degrade at moderate to rapid rates by biodegradation and by photolysis, and slow to negligible rates by hydrolysis. The persistence and bioaccumulation ranking for this category is low to moderate. With the exception of acetic acid, C11-14, the alkyl acetates are low for persistence (P1) and bioaccumulation (B1). Using data from the acetic acid, C11-14-branched alkyl esters, C13-rich (108419-35-8) mixture, (31% biodegradation after 28 days, measured, and estimated BCF = 9021), substances in this sub-category are rated P1B3. However, it is also likely that branched alcohols are formed as biodegradation products, and these products may be more persistent than the parent. Based on estimated biodegradability and estimated BCF, these alcohols are rated P2B2.

Table 1a. Physical Chemical Properties of Alkyl Acetate C6-C13 Category[a]						
Chemical Name	Hexanol, acetate, branched and linear	Acetic acid, C6-8-branched alkyl esters	Acetic acid, C7-9-branched alkyl esters, C8-rich **(Supporting chemical)**	Acetic acid, C8-10-branched alkyl esters, C9-rich **(Supporting chemical)**	Acetic acid, C9-11-branched alkyl esters, C10-rich **(Supporting chemical)**	Acetic acid, C11-14-branched alkyl esters, C13-rich
CAS Reg. No.	88230-35-7	90438-79-2	108419-32-5	108419-33-6	108419-34-7	108419-35-8
Melting point ºC	-59	-50	-30	-20	-8.8	-2
Boiling point ºC	**164-176 (m)**	**176-200 (m)**	**186-215 (m)**	**205-235 (m)**	**220-250 (m)**	**240-285 (m)**
Vapor pressure mm Hg (25 ºC)	1.45	0.51	0.70	0.26	0.1	0.01
Log K_{ow}	2.83	3.32	3.86[b]	4.15	4.65	6.05
Water solubility (mg/L)	309	102	45	14.5	4.7	0.2
Henry's law constant (atm-m^3/mol)[b]	$8.9x10^{-4}$	$1.0x10^{-3}$	$3.5x10^{-3}$	$4.4x10^{-3}$	$5.6x10^{-3}$	0.016

[a] Data from ExxonMobil Chemical, 2000 and U.S.EPA 2007; **(m)** denotes measured value, all others are estimated.
[b] Estimated value is from EPA.

Table 1b. Environmental Fate Properties of Alkyl Acetate C6-C13 Category[a]						
Chemical Name	Hexanol, acetate, branched and linear	Acetic acid, C6-8-branched alkyl esters	Acetic acid, C7-9-branched alkyl esters, C8-rich **(Supporting chemical)**	Acetic acid, C8-10-branched alkyl esters, C9-rich **(Supporting chemical)**	Acetic acid, C9-11-branched alkyl esters, C10-rich **(Supporting chemical)**	Acetic acid, C11-14-branched alkyl esters, C13-rich
CAS Reg. No.	88230-35-7	90438-79-2	108419-32-5	108419-33-6	108419-34-7	108419-35-8
Photodegradation half-life (hours)	17.3	14.5	12.5	10.5	9.3	6.5
Biodegradation	**76.9% after 28 days (m)**	**77.1% after 28 days (m)**	No Data		**84.7% after 28 days (m)**	**31% after 28 days (m)**
Hydrolysis half-life[b]	Stable at pHs 4 & 7; 13 days @ pH 9 & 25 ºC[b] 2.1 years pH 7 78 days pH 8	16 days at pH 9 and 20 ºC[b] 2.1 years pH 7 78 days pH 8	2.1 years pH 7 78 days pH 8	2.1 years pH 7 78 days pH 8	2.1 years pH 7 78 days pH 8	2.1 years pH 7 78 days pH 8
K_{oc}[b]	71	131	190	350	646	3730
BCF	30	63	131[b]	316	754	9021[b]
Persistence[c]	P1 (low)	P1 (low)	P1 (low)	P1 (low)	P1 (low)	P1 (low)
Bioaccumulation[c]	B1 (low)	B1 (low)	B1 (low)	B1 (low)	B1 (low)	B3 (high)

[a] Data from ExxonMobil Chemical, 2000 unless otherwise noted. **(m)** denotes measured values, all others are estimated.

[b] USEPA, 2007. Note that the two BCF values calculated by EPA differed from those calculated by the sponsor, which were 151 and 325, for the C7-9 and C11-14 category members, respectively.

[c] Persistence and bioaccumulation are qualitatively characterized according to criteria set forth in the PMN program (FR, 1999).

[d] Branched alcohol biodegradation products from Acetic acid, C11-14-branched alkyl esters, C13-rich (108419-35-8) moderate persistence and moderate bioaccumulation (P2B2)

2. Environmental Effects – Aquatic Toxicity

A summary of aquatic toxicity data submitted for SIDS endpoints is provided in Table 2. The table also indicates where data for tested category members are read-across (RA) to untested members of the category. All data presented below are from the submission by the sponsor (ExxonMobil, 2000) unless otherwise noted.

Acute Toxicity to Fish

Hexanol, acetate, branched and linear (C6-rich, CAS No. 88230-35-7)
Rainbow trout (*Oncorhynchus mykiss,* 15/concentration) were exposed to the test substance as water accommodated fractions (WAFs) under semi static conditions for 96 hours. The nominal concentrations were 0, 0.5, 1.3, 3.2, 8.0 and 20 mg/L (measured as Total Organic Carbon, or TOC). Mortality was seen at 8 mg/L (1/15 fish) and 20 mg/L where 100% fish died.
96-h LC_{50} = 11.9 mg/L (expressed as Total Organic Carbon)

Acetic acid, C6-8 branched alkyl esters (C7-rich) (CAS No. 90438-79-2)
Rainbow trout (*Oncorhynchus mykiss,* 10/concentration) were exposed to the test substance as water accommodated fractions (WAFs) under static conditions for 96 hours. The nominal concentrations were 0, 2.0, 4.5, 10.0, 23.0 and 50.0 mg/L (measured concentrations: not detectable, 1.2, 1.49, 5.39, 21.1 and 43.6 mg/L respectively). Mortality was seen at 5.39 mg/L and above.
96-h LC_{50} = 8.18 mg/L

Acetic acid, C7-9 branched alkyl esters (C8-rich) (CAS No. 108419-32-5, supporting chemical)
Fathead minnows (*Pimephales promelas,* 20/concentration) were exposed to the test substance as water accommodated fractions (WAFs) under flow-through conditions for 96 hours. Nominal concentrations were 0, 4.4, 8.8, 17.5, 35.0 and 70.0% WAF, which measured as 0, 1.39, 2.71, 4.90, 9.91 and 19.86 mg/L of total carbon. Mortality was seen only at 19.86 mg/L at which all fish died.
96-h LC_{50} = 14.9 mg/L (expressed as Total Carbon)

Acetic acid, C11-l4 branched alkyl esters (C13-rich) (CAS No. 108419-35-8)
Fathead minnows (*Pimephales promelas*, 20/concentration) were exposed to the test substance as water accommodated fractions (WAFs) under flow-through conditions for 96 hours. The loading rates were 0, 6.25, 125, 25, 50, and 100% WAF and no analytical measurements were made on the WAFs. No effects were noted at any of the WAF loading rates. The sponsor reported the 96-hour LC_0 (no deaths observed) to be 5800 mg/L – the estimated highest concentration tested - based on nominal loading levels. EPA does not consider the loading rate as the no effect concentration when the concentration exceeds the water solubility of the substance. Assuming exposure concentration in the WAF is the water solubility limit (saturation) for C11-C14 methyl-branched alkyl acetate ester, the no effect concentration would be approximately 0.2 mg/L.
No effects at saturation

Acute Toxicity to Aquatic Invertebrates

Hexanol, acetate, branched and linear (C6-rich, CAS No. 88230-35-7)
Daphnia magna (20/concentration) were exposed to the test substance as water accommodated fractions (WAFs) under static conditions for 48 hours at nominal concentrations of 0, 0.1, 0.5, 1 .0, 5.0 and 10.0 mg/L. Although the robust summary states that samples were analyzed for Total Organic Carbon, no measured values were listed. Mortality was 1, 2, 1, 3, 5 and 14 at 0, 0.1, 0.5, 1 .0, 5.0 and 10.0 mg/L, respectively.
48-h EC_{50} = 7.6 mg/L (expressed as nominal organic carbon loading rates)

Acetic acid, C7-9 branched alkyl esters (C8-rich) (CAS No. 108419-32-5, supporting chemical)
Daphnia magna (20/concentration) were exposed to the test substance as water accommodated fractions (WAFs) under flow-through conditions for 48 hours at nominal concentrations of 0, 6.25, 12.5, 25, 50 and 100% WAF which were measured as 0, 1.87, 4.13, 10.24, 20.21, and 39.95 mg/L total carbon, respectively. Treatment-related mortality was observed at the two highest concentrations (3/20 and 17/20 for 20.21 and 39.95 mg/L, respectively)

48-h EC_{50} = 29.4 mg/L (expressed as Total Organic Carbon)

Acetic acid, C9-C11 branched alkyl esters (C10-rich) (CAS No. 108419-34-7, supporting chemical)
Daphnia magna (20/concentration), were exposed to the test substance as water accommodated fractions (WAFs) under static conditions for 48 hours at nominal concentrations of 0, 1.3, 3.2, 8.0, 20.0 and 50.0 mg/L (measured concentrations: not detectable, 0.44, 1.3, 2.1, 1.9 and 2.2 mg/L, respectively). Mortality was 0, 0, 20%, 55%, 95%, and 100%, respectively at 0, 0.44, 1.3, 2.1, 1.9 and 2.2 mg/L.
48-h EC_{50} = 1.8 mg/L

Acetic acid, C11-l4 branched alkyl esters (C13-rich) (CAS No. 108419-35-8)
Daphnia magna (40/concentration), were exposed to the test substance as water accommodated fractions (WAFs) under static conditions for 48 hours at nominal concentrations. The loading rates were 0, 6.25, 125, 25, 50, and 100% and no analytical measurements were made on the WAFs. No effects were noted at any of the WAF loading rates. The sponsor reported the 96-hour LC_0 (no deaths observed) to be 5829 mg/L – the estimated highest concentration tested - based on nominal loading levels. EPA does not consider the loading rate as the no effect concentration when the concentration exceeds the water solubility of the substance. Assuming exposure concentration in the WAF is the water solubility limit (saturation) for C11-C14 methyl-branched alkyl acetate ester, the no effect concentration would be approximately 0.2 mg/L.
No effects at saturation

Toxicity to Aquatic Plants

Hexanol, acetate, branched and linear (C6-rich, CAS No. 88230-35-7)
Green algae (*Selenastrum capricornutum*) were exposed to the test substance as water accommodated fractions (WAFs) under static conditions for 96 hours at nominal concentrations of 0, 8, 31, 62, 125 and 250 mg/L reported as loading rates. Although samples were analyzed for test substance, the measurement was for dissolved organic carbon only and the results were not reported in the submitted robust summary. Both growth rate and biomass were inhibited at the top three concentrations.
96-h EC_{50} (biomass) = 40.1 (expressed as nominal organic carbon loading rates)
96-h EC_{50} (growth) = 32.1 mg/L (expressed as nominal organic carbon loading rates)

Acetic acid, C9-C11 branched alkyl esters (C10-rich) (CAS No. 108419-34-7, supporting chemical)
Green algae (*Pseudokirchneriella subcapitata*) were exposed to the test substance as water accommodated fractions (WAFs) under static conditions for 72 hours at nominal concentrations of 0, 64.5, 130, 254, 522 and 1021 mg/L as carbon loading levels; but measured concentrations at the start of the study were 0, 4.8, 5.0, 5.2, 5.2, and 5.6 mg/L, respectively. Essentially, these values reflect the approximate water solubility limit (4.7 mg/L) and show there was no essential difference across test groups in terms of starting concentration. There were no effects at this concentration.
No effects at saturation

Acetic acid, C11-l4 branched alkyl esters (C13-rich) (CAS No. 108419-35-8)
Green algae (*Selenastrum capricornutum*) were exposed to the test substance as water accommodated fractions (WAFs) under static conditions for 96 hours. The loading rates were 0, 6.25, 125, 25, 50, and 100% WAF and measured values (as Total Carbon) were reported as 0, 0.058, 0.219, 0.492, and 0.873 mg/L. No effects were noted at any of the WAF loading rates. The sponsor reported the 96-hour LC_0 (no inhibition of algal growth) to be 5829 mg/L – the estimated highest concentration tested - based on nominal loading levels. Assuming exposure concentration in the WAF is the water solubility limit (saturation) for C11-C14 methyl-branched alkyl acetate ester, the no effect concentration would be approximately 0.2 mg/L.
No effects at saturation

Conclusion: The evaluation of the available aquatic toxicity data for fish, aquatic invertebrates and aquatic plants indicates that the potential acute hazard of the members of the Alkyl Acetates C6 to C13 Category to aquatic organisms is likely to be moderate. This is because the reported values in the most of the studies were expressed as carbon load and so the actual chemical concentrations are not known but are probably lower than the total carbon values. It is uncertain how much lower, but it is probably less than an order of magnitude. The largest (in terms of molecular weight) member of the category (the C11-C14) showed no effects at the water solubility estimate of 0.2

mg/L, but because of its persistence and other chemical/physical properties, as stated in the Agency comments in 2001, chronic aquatic toxicity has been identified as a data gap for acetic acid, C11-C14 alkyl esters under the HPV Challenge Program.

Table 2. Summary of Environmental Effects – Aquatic Toxicity Data

Endpoints	Hexanol, acetate, branched and linear (C6-rich) (88230-35-7)	Acetic acid, C6-C8 branched alkyl esters (C7-rich) (90438-79-2)	Acetic acid, C7-C9 branched alkyl esters (C8-rich) (supporting chemical) (l08419-32-5)	Acetic acid, C8-C10 branched alkyl esters (C9-rich) (supporting chemical) (108419-33-6)	Acetic acid, C9-C11 branched alkyl esters (C10-rich) (supporting chemical) (108419-34-7)	Acetic Acid, C11-C14 branched alkyl esters (C13-rich) (108419-35-8)
Fish 96-h LC_{50} (mg/L)	**11.9 (m)** (expressed as total carbon)	**8.18 (m)**	**14.9 (m)** (expressed as total carbon)	—	—	**NES (m)**
Aquatic Invertebrates 48-h EC_{50} (mg/L)	**7.6 (m)** (expressed as total carbon)	No data 7.6 (RA)	**29.4 (m)** (expressed as total carbon)	—	**1.8 (m)**	**NES (m)**
Aquatic Plants 72-h EC_{50} (mg/L) **(growth)** **(biomass)**	**32.1 (m)** **40.1 (m)** (expressed as total carbon)	No data 32.1 40.1 (RA)	—	—	**NES (m)**	**NES (m)**

(m) = measured data (i.e., derived from testing); (RA) = Read Across; NES = No effects at saturation;
— indicates endpoint not addressed for this substance.

2. Human Health Effects

A summary of health effects data submitted for SIDS endpoints is provided in Table 3. The table also indicates where data for tested category members are read-across (RA) to untested members of the category. All data presented below are from the submission by the sponsor (ExxonMobil, 2000) unless otherwise noted.

Acute Oral Toxicity

Hexanol, acetate, branched and linear (C6-rich, CAS No. 88230-35-7)
Acetic acid, C8-C10 branched alkyl esters (C9-rich) (CAS No. 108419-33-6, supporting chemical)
Acetic acid, C11-l4 branched alkyl esters (C13-rich) (CAS No. 108419-35-8)
Acute oral toxicity to rats is low.
LD_{50} > 2000 – 5000 mg/kg-bw

Acute Dermal Toxicity

Hexanol, acetate, branched and linear (C6-rich, CAS No. 88230-35-7)
Acetic acid, C6-8 branched alkyl esters (C7-rich) (CAS No. 90438-79-2)
Acetic acid, C7-9 branched alkyl esters (C8-rich) (CAS No. 108419-32-5, supporting chemical)
Acetic acid, C8-C10 branched alkyl esters (C9-rich) (CAS No. 108419-33-6, supporting chemical)

Acetic acid, C9-C11 branched alkyl esters (C10-rich) (CAS No. 108419-34-7, supporting chemical)
Acetic acid, C11-l4 branched alkyl esters (C13-rich) (CAS No. 108419-35-8)
Acute dermal toxicity to rabbits is low.
LD_{50} > 2000 – 3160 mg/kg-bw

Repeated-Dose Toxicity

Hexanol, acetate, branched and linear (C6-rich, CAS No. 88230-35-7)
Crl:CD BR rats were administered the test substance in corn oil via gavage at 0, 100, 500 and 1000 mg/kg-bw/day for 28 days. No adverse effects were noted on body weight, food consumption, clinical laboratory parameters, organ weights or gross or microscopic examination.
LOAEL > 1000 mg/kg-bw/day
NOAEL = 1000 mg/kg-bw/day (based on no effects at the highest dose tested)

Acetic acid, C7-9 branched alkyl esters (C8-rich) (CAS No. 108419-32-5, supporting chemical)
Sprague-Dawley rats were administered the test substance via gavage at 0, 100, 500 or 1000 mg/kg-bw/day, 5 days/week for 13 weeks. There was no treatment-related mortality; clinical signs included oral and dermal irritation. There were no effects on body weight, food consumption, hematology or clinical chemistry parameters. At study termination, there was a dose-related increase in liver and kidney weights; however, microscopic evaluation of liver did not show any corresponding findings. Microscopic evaluation of kidneys showed evidence of mild tubular nephropathy in the high-dose male rats consistent with alpha$_{2\mu}$-globulin effect[15]. Histopathological evaluation of all other tissues and organs was normal.
LOAEL = 1000 mg/kg-bw/day (based on nephropathy in males)
NOAEL = 500 mg/kg-bw/day

Acetic acid, C11-l4 branched alkyl esters (C13-rich) (CAS No. 108419-35-8)
Sprague-Dawley rats were administered the test substance via gavage at 0, 100, 500 or 1000 mg/kg-bw/day, 5 days/week for 13 weeks. There was no treatment-related mortality; clinical signs included oral and dermal irritation. There were no effects on body weight, food consumption, hematology or clinical chemistry parameters. At study termination, there was a dose-related increase in liver and kidney weights; however, this was considered to be an adaptive response. There was no correlation between increased liver weight and corresponding microscopic findings. Microscopic evaluation of kidneys showed evidence of mild tubular nephropathy in the high-dose male rats consistent with alpha$_{2\mu}$-globulin effect[1]. Histopathological evaluation of all other tissues and organs was normal.
LOAEL =1000 mg/kg-bw/day (based on nephropathy in males)
NOAEL = 500 mg/kg-bw/day

Reproductive Toxicity

Acetic acid, C7-9 branched alkyl esters (C8-rich) (CAS No. 108419-32-5, supporting chemical)
In the repeated-dose toxicity study with C7-9 branched alkyl acetate esters described previously, histopathological examination of reproductive organs—testes, epididymides, prostate, seminal vesicles, ovaries, uterine horns, cervix and corpus of the uterus and vagina—showed no effects at study termination.

[15] The presence of nephropathy in association with the hyaline droplet accumulation in male rats suggests that the nephropathy in the males is occurring by an alpha$_{2\mu}$-globulin-mediated mechanism which appears to be unique to male rats and the response is probably not relevant to humans for purposes of risk assessment. EPA's Risk Assessment Forum has outlined the key events and the data that are necessary to demonstrate this mode of action (Alpha$_{2\mu}$-Globulin: Association with Chemically Induced Renal Toxicity and Neoplasia in the Rat, EPA/625/3-91/019F). One of the key events, alpha$_{2u}$-globulin accumulation, has not been demonstrated. Therefore, the nephropathy is assumed to be relevant to human health.

Acetic acid, C11-l4 branched alkyl esters (C13-rich) (CAS No. 108419-35-8)
In the repeated-dose study with C11-14 branched alkyl acetate esters described previously, histopathological examination of reproductive organs—testes, epididymides, prostate, seminal vesicles, ovaries, uterine horns, cervix and corpus of the uterus and vagina—showed no effects at study termination.

Developmental Toxicity

Acetic acid, C7-9 branched alkyl esters (C8-rich) (CAS No. 108419-32-5, supporting chemical)
Female Sprague-Dawley rats were administered the test substance via gavage at 0, 100, 500 or 1000 mg/kg-bw/day during days 6 – 15 of gestation. Maternal toxicity was observed (decreased body weight and food consumption) at 500 and 1000 mg/kg-bw/day. Slight increases in fetal malformations and embryotoxicity were seen at 1000 mg/kg-bw/day. No adverse fetal effects were seen at the 100 and 500 mg/kg-bw/day.
LOAEL (maternal toxicity) = 500 mg/kg-bw/day (based on decreased body weight and food consumption)
NOAEL (maternal toxicity) = 100 mg/kg-bw/day
LOAEL (developmental toxicity) = 1000 mg/kg-bw/day (based on fetal malformations and embryotoxicity)
NOAEL (developmental toxicity) = 500 mg/kg-bw/day

Acetic acid, C11-l4 branched alkyl esters (C13-rich) (CAS No. 108419-35-8)
Female Sprague-Dawley rats were administered the test substance via gavage at 0, 500, 1300 or 2500 mg/kg-bw/day during days 6 – 15 of gestation. Maternal toxicity was observed (decreased body weight) at 1300 and 2500 mg/kg-bw/day. No marked effects on fetal survival or body weight were seen. There was no evidence of treatment-related malformations.
LOAEL (maternal toxicity) = 1300 mg/kg-bw/day (based on decreased body weight)
NOAEL (maternal toxicity) = 500 mg/kg-bw/day
LOAEL (developmental toxicity) > 2500 mg/kg-bw/day
NOAEL (developmental toxicity) = 2500 mg/kg-bw/day (based on no effects at the highest dose tested)

Genetic Toxicity – Gene Mutation

In vitro
Hexanol, acetate, branched and linear (C6-rich) (CAS No. 88230-35-7)
Acetic acid, C6-8 branched alkyl esters (C7-rich) (CAS No. 90438-79-2)
Acetic acid, C7-9 branched alkyl esters (C8-rich) (CAS No. 108419-32-5, supporting chemical)
Acetic acid, C11-l4 branched alkyl esters (C13-rich) (CAS No. 108419-35-8)
In separately conducted Ames assays, five strains of *Salmonella typhimurium* were exposed to the test substances listed above at concentrations up to 600 - 10,000 µg/plate (highest concentrations tested) in the presence and absence of metabolic activation. At the highest concentration cytotoxicity was seen. The category members did not induce significant increases in revertant colonies.
The category members listed above were not mutagenic in these assays.

Genetic Toxicity – Chromosomal Aberrations

In vitro
Hexanol, acetate, branched and linear (C6-rich, CAS No. 88230-35-7)
Chinese hamster ovary cells were exposed to the test substance at concentrations up to 250 – 550 µg/mL with and without metabolic activation. Appropriate responses were seen for positive, negative and solvent controls.
Hexanol, acetate, branched and linear did not induce chromosomal aberrations in this assay.

Acetic acid, C6-8 branched alkyl esters (C7-rich) (CAS No. 90438-79-2)
Chinese hamster ovary cells were exposed to the test substance at concentrations up to 40 – 240 µg/mL with and without metabolic activation. Appropriate responses were seen for positive, negative and solvent controls.
C6-C8 branched alkyl acetate ester did not induce chromosomal aberrations in this assay.

In vivo

Acetic acid, C7-9 branched alkyl esters (C8-rich) (CAS No. 108419-32-5, supporting chemical)
In a bone marrow micronucleus assay, CD-1 mice were administered the test substance as a single dose via gavage up to 2500 mg/kg-bw. Animals were sacrificed at 24, 48 and 72 hours, bone marrow was aspirated and slides were prepared, stained and evaluated for the presence of micronuclei. Appropriate responses were seen for positive, negative and solvent controls. No marked increase in the mean number of micronucleated polychromatic erythrocytes in the bone marrow.

Acetic acid, C7-9 branched alkyl esters (C8-rich) did not increase micronuclei in this assay.
Acetic acid, C11-l4 branched alkyl esters (C13-rich) (CAS No. 108419-35-8)
In a bone marrow micronucleus assay, CD-1 mice were administered the test substance as a single dose by gavage up to 2500 mg/kg-bw. Animals were sacrificed at 24, 48 and 72 hours, bone marrow was aspirated and slides were prepared, stained and evaluated for the presence of micronuclei. Appropriate responses were seen for positive, negative and solvent controls. Although C11-C14 branched alkyl acetate esters was toxic to bone marrow showing a decrease in the mean percent of polychromatic erythrocytes at the 48-hour sampling time, it did not induce statistically significant increase in the mean number of micronucleated polychromatic erythrocytes.
C11-C14 branched alkyl acetate esters did not increase micronuclei in this assay.

Additional Information

Eye Irritation

Hexanol, acetate, branched and linear (C6-rich, CAS No. 88230-35-7)
Acetic acid, C11-l4 branched alkyl esters (C13-rich) (CAS No. 108419-35-8)
The test substances were instilled into the conjunctival sacs of New Zealand White rabbits and observed at 1, 4 and 24 hours post-dosing and at 2, 3, 4 and 7 days (in separate studies). Ocular irritation was most prominent at the 1-hour observation period. Irritation was confined to the conjunctivae with moderate redness, chemosis and discharge and corneal ulceration in one animal. Signs of irritation completely subsided in all animals by day 7.
The category chemicals cause mild reversible eye irritation in these assays.

Skin Irritation

Hexanol, acetate, branched and linear (C6-rich, CAS No. 88230-35-7)
Acetic acid, C11-l4 branched alkyl esters (C13-rich) (CAS No. 108419-35-8)
In separate assays, New Zealand White rabbits were dermally administered the test substances under semi-occlusive conditions for 4 hours. The animals were observed and scored for irritation at 1, 24, 48 and 72 hours and 7 days post-dosing. All animals displayed erythema and/or edema in the first 72 hours. All animals were cleared of irritation by day 7. The category members listed above are mild (CAS No. 108419-35-8) to moderate (CAS No. 88230-35-7) skin irritants.
The category chemicals listed above cause mild to moderate skin irritation in these assays.

Conclusion: The acute oral dermal toxicity of the members of this category is low. The category members, hexanol, acetate, branched and linear and C11-14 branched alkyl acetate esters are mild to moderate skin irritants and mild eye irritants. Repeated oral exposures to hexanol, acetate, branched and linear, C7-9 branched alkyl acetate ester and C11-14 branched alkyl acetate esters were minimally toxic to rats. For the C7-9 branched alkyl acetate ester and C11-14 branched alkyl acetate ester, mild tubular nephropathy in the high-dose male rats consistent with alpha$_{2\mu}$-globulin effect was the only notable effect[16]. Histopathological evaluation of all other tissues and

[16] The presence of nephropathy in association with the hyaline droplet accumulation in male rats suggests that the nephropathy in the males is occurring by an alpha$_{2\mu}$-globulin-mediated mechanism which appears to be unique to male rats and the response is probably not relevant to humans for purposes of risk assessment. EPA's Risk Assessment Forum has outlined the key events and the data that are necessary to demonstrate this mode of action (Alpha$_{2\mu}$-Globulin: Association with Chemically Induced Renal Toxicity and Neoplasia in the Rat, EPA/625/3-91/019F). One of the key events, alpha$_{2u}$-globulin accumulation, has not been demonstrated. Therefore, the nephropathy is assumed to be relevant to human health.

organs including reproductive organs was normal when tested at the limit doses of 1000 mg/kg-bw/day. Developmental toxicity characterized as a slight increase in fetal malformations and embryo toxicity was observed following exposure of pregnant rats to C7-9 branched alkyl acetate esters (1000 mg/kg-bw/day). Exposure of pregnant of rats to C11-14 branched alkyl acetate ester showed pronounced maternal toxicity at high doses; but no statistically significant effects on fetal survival, body weight and crown-rump length were noted. There were no treatment-related malformations. The category members, hexanol, acetate, branched and linear, C6-8 branched alkyl acetate esters, C7-9 branched alkyl acetate ester, and C11-14 branched alkyl acetate ester, did not show mutagenic potential when tested in bacterial cells. Hexanol, acetate, branched and linear and C6-8 branched alkyl acetate ester did not induce chromosomal aberrations in *in vitro* and C7-9 branched alkyl acetate ester and C11-14 branched alkyl acetate ester did not increase the mean number of micronucleated polychromatic erythrocytes *in vivo*.

Table 3. Summary of Human Health Data

Endpoints	Hexanol, acetate, branched and linear (C6-rich) (88230-35-7)	Acetic acid, C6-C8 branched alkyl esters (C7-rich) (90438-79-2)	Acetic acid, C7-C9 branched alkyl esters (C8-rich) (supporting chemical) (108419-32-5)	Acetic acid, C8-C10 branched alkyl esters (C9-rich) (supporting chemical) (108419-33-6)	Acetic acid, C9-C11 branched alkyl esters (C10-rich) (supporting chemical) (108419-34-7)	Acetic acid, C11-C14 branched alkyl acetate esters (C13-rich) (108419-35-8)
Acute Oral Toxicity LD_{50} (mg/kg-bw)	**> 2000**	No Data > 5000 (RA)	—	**> 5000**	—	**> 3000**
Acute Dermal Toxicity LD_{50} (mg/kg-bw)	**> 2000**	**> 3160**	**> 3160**	**> 3160**	**> 3160**	**> 3160**
Repeated-Dose Toxicity NOAEL/ LOAEL (mg/kg-bw/day)	**NOAEL = 1000** **LOAEL > 1000**	No Data NOAEL = 500 LOAEL = 1000 (RA)	**NOAEL = 500** **LOAEL = 1000**	—	—	**NOAEL = 500** **LOAEL = 1000**
Reproductive Toxicity NOAEL/ LOAEL (mg/kg-bw/day)	No Data No effects on male and female reproductive organs from the 90-day study (RA)	No Data No effects on male and female reproductive organs from the 90-day study (RA)	**No effects on male and female reproductive organs from the above 90-day study**	—	—	**No effects on male and female reproductive organs from the above 90-day study**
Developmental Toxicity NOAEL/ LOAEL (mg/kg-bw/day)				—	—	
Maternal	No Data NOAEL = 100 LOAEL = 500	No Data NOAEL = 100 LOAEL = 500	**NOAEL = 100** **LOAEL = 500**			**NOAEL = 500** **LOAEL = 1300**
Developmental	NOAEL = 500 LOAEL = 1000 (RA)	NOAEL = 500 LOAEL = 1000 (RA)	**NOAEL = 500** **LOAEL = 1000**			**NOAEL = 2500** **LOAEL > 2500**
Genetic Toxicity – Gene Mutation *In vitro*	**Negative**	**Negative**	**Negative**	—	—	**Negative**
Genetic Toxicity – Chromosomal Aberrations *In vitro*	**Negative**	**Negative**	—	—	—	No Data Negative (RA)
Genetic Toxicity – Chromosomal Aberrations *In vivo*	No Data Negative (RA)	No Data Negative (RA)	**Negative**	—	—	**Negative**
Eye Irritation	**Mild**	No Data Mild	—	—	—	**Mild**
Skin Irritation	**Moderate**	No Data Mild to moderate (RA)	—	—	—	**Mild**

Measured data in bold text; (RA) = read across; — indicates endpoint not addressed for this substance.

3. Hazard Characterization

The members of the Alkyl Acetate C6-C13 category are liquids at room temperature. They have moderate to high vapor pressure, low to moderate water solubility, and moderate to high volatility. They are moderately mobile in soil and water systems. They are expected to degrade at moderate to rapid rates by biodegradation and by photolysis, and slow to negligible rates by hydrolysis. The persistence and bioaccumulation ranking for this category is low to moderate. With the exception of acetic acid, C11-14, the alkyl acetates are low for persistence (P1) and bioaccumulation (B1). Based on available data, acetic acid, C11-14 (108419-35-8) is ranked low for persistence (P1) and high for bioaccumulation (B3) and may biodegrade to moderately persistent (P2) and bioaccumulative (B2) branched alcohols.

The evaluation of the available aquatic toxicity data for fish, aquatic invertebrates and aquatic plants indicates that the potential acute hazard of the members of the Alkyl Acetates C6 to C13 Category to aquatic organisms is likely to be moderate.

The acute oral dermal toxicity of the members of this category is low. The category members, hexanol, acetate, branched and linear and C11-14 branched alkyl acetate esters are mild to moderate skin irritants and mild eye irritants. Repeated oral exposures to hexanol, acetate, branched and linear, C7-9 branched alkyl acetate ester and C11-14 branched alkyl acetate esters were minimally toxic to rats. For the C7-9 branched alkyl acetate ester and C11-14 branched alkyl acetate ester, mild tubular nephropathy in the high-dose male rats consistent with alpha$_{2\mu}$-globulin effect was the only notable effect[17]. Histopathological evaluation of all other tissues and organs including reproductive organs was normal when tested at the limit doses of 1000 mg/kg-bw/day. Developmental toxicity characterized as a slight increase in fetal malformations and embryo toxicity, was observed following exposure of pregnant rats to C7-9 branched alkyl acetate esters (1000 mg/kg-bw/day). Exposure of pregnant rats to C11-14 branched alkyl acetate ester showed pronounced maternal toxicity at high doses; but no statistically significant effects on fetal survival, body weight and crown-rump length were noted. There were no treatment-related malformations. The category members, hexanol, acetate, branched and linear, C6-8 branched alkyl acetate esters, C7-9 branched alkyl acetate ester, and C11-14 branched alkyl acetate ester, did not show mutagenic potential when tested in bacterial cells. Hexanol, acetate, branched and linear and C6-8 branched alkyl acetate ester did not induce chromosomal aberrations in *in vitro* and C7-9 branched alkyl acetate ester and C11-14 branched alkyl acetate ester did not increase the mean number of micronucleated polychromatic erythrocytes *in vivo*.

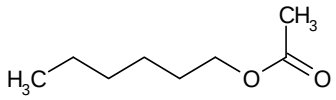
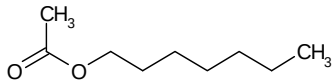
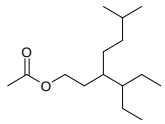
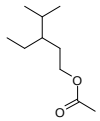
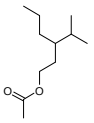
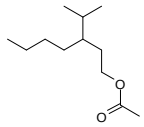
The potential health hazard of the C6 to C13 alkyl acetates C6 to C13 category is low.

4. Data Gaps

Chronic aquatic toxicity has been identified as a data gap for acetic acid, C11-C14 alkyl esters under the HPV Challenge Program. In addition, although not a data gap *per se,* little data was provided regarding the specific composition of the category members other than the carbon number range and the descriptor "branched." This introduces some uncertainty into this screening-level hazard assessment. Ideally, the number and identity of components and their typical percentages increase the confidence in determining the overall hazard of these compounds.

[17] The presence of nephropathy in association with the hyaline droplet accumulation in male rats suggests that the nephropathy in the males is occurring by an alpha$_{2\mu}$-globulin-mediated mechanism which appears to be unique to male rats and the response is probably not relevant to humans for purposes of risk assessment. EPA's Risk Assessment Forum has outlined the key events and the data that are necessary to demonstrate this mode of action (Alpha$_{2\mu}$-Globulin: Association with Chemically Induced Renal Toxicity and Neoplasia in the Rat, EPA/625/3-91/019F). One of the key events, alpha$_{2u}$-globulin accumulation, has not been demonstrated. Therefore, the nephropathy is assumed to be relevant to human health.

Appendix

Alkyl Acetates C6 to C13		
CAS No.	**Chemical Name**	**Structure (Representative structures, branching may vary[a])**
SPONSORED CHEMICALS		
88230-35-7	Hexanol, acetate, branched and linear (C6-rich)	 $C_8H_{16}O_2$
90438-79-2	Acetic acid, C6-8 branched alkyl esters (C7-rich)	 $C_9H_{18}O_2$
108419-35-8	Acetic acid, C11-l4 branched alkyl esters (C13-rich)	 $C_{15}H_{30}O_2$
SUPPORTING CHEMICALS		
108419-32-5	Acetic acid, C7-9 branched alkyl esters (C8-rich)	 $C_{10}H_{20}O_2$
L08419-33-6	Acetic acid, C8-l0 branched alkyl esters (C9-rich)	 $C_{11}H_{22}O_2$
L08419-34-7	Acetic acid, C9-11 branched alkyl esters (C10-rich)	 $C_{12}H_{24}O_2$

[a] Principle constituents that are typical for each member of this class.

References

ExxonMobil Chemical, 2000. Robust Summaries & Test Plans: Alkyl Acetate C6-C13 Category HPV Test Plan, submitted by ExxonMobil Chemical Company, http://www.epa.gov/chemrtk/pubs/summaries/alkylace/c12939tc.htm

FR 1999, Category for Persistent, Bioaccumulative, and Toxic New Chemical Substances. *Federal Register* 64, Number 213 (November 4, 1999) Page 60194-60204

USEPA, 2007. EPI v3.12 PC-Computer software developed by EPA's Office of Pollution Prevention Toxics and Syracuse Research Corporation. http://www.epa.gov/opptintr/exposure/pubs/episuite.htm

Exposure Characterization for HPV Challenge Chemical

Acetic Acid, C_{6-8} Branched Alkyl Esters

CAS #90438-79-2

March 14, 2008

Prepared by

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Washington, DC 20460-0001

Exposure Characterization for HPV Challenge Chemical

Acetic acid, C_{6-8} branched alkyl esters **(CAS #90438-79-2)**

Non-CBI Executive Summary

This chemical has some public use and exposure information in the HPV Challenge Program submission. The information indicates that alkyl acetates (C6 to C13) are mainly used as solvents in lacquers, janitorial cleaning products, and agricultural products (Clayton, 1994). Limited workplace air sampling data suggest air concentrations below 10 mg/m^3 for C6 to C13 alkyl acetate aerosols.

Acetic acid, C_{6-8} branched alkyl esters (CAS #90438-79-2) was manufactured in the United States in calendar year 2005 (USEPA, 2006). This chemical has an aggregated volume produced and/or imported in the range of 1,000,000 to 10,000,000 pounds. Persons submitting Inventory Update Reporting (IUR) information in 2006 asserted that some of the information was confidential business information (CBI) and therefore cannot be disclosed. Data and information that are CBI have been excluded from this summary.

Exposure was characterized using both public, non-confidential sources and one or more IUR submissions available at the time the exposure characterization was written. If additional information warrants an update of the exposure characterization, the update will be posted on the EPA website.

A SIDS dossier has not been prepared for this chemical (SIDS, 2007).

Exposures to Workers

This chemical has a vapor pressure of 0.78 torr at 25°C (USEPA, 2007b). OPPT has established 1.0 x 10e-3 torr as a value above which worker exposures to vapors should be estimated for chemical assessments. Therefore, this chemical's vapor pressure could result in worker exposures to vapors if workers are near the chemical. This chemical does not have an OSHA Permissible Exposure Limit (NIOSH, 2007). The National Occupational Exposure Survey (NOES), conducted from 1981 to 1983, did not provide information on the number of workers likely to be exposed for this chemical.

Differences between numbers of workers estimated by IUR submitters and by the NOES are attributable to many factors, including time, scope, and method of the estimates. For example, NOES estimates are for all workplaces while IUR are for industrial workplaces only, and NOES used a survey and extrapolation method while IUR submitters simply provide their best estimates based on available information for the specific reporting year.

Based on IUR reporting, the maximum total number of workers likely to be exposed to this chemical during manufacturing and industrial processing and use is less than 100. The IUR based ranking for worker exposure is low.

Exposures to General Population and the Environment

The chemical is not on the Toxics Release Inventory (USEPA, 2007a). Chemicals used as solvents in lacquers, janitorial cleaning products, and agricultural products are expected to result in environmental releases. The potential for exposures to the general population and the environment is possible based on these uses. Searches of additional relevant information sources related to Voluntary Children's Chemical Evaluation Program (VCCEP) and HSDB did not provide any further information on this chemical. Based on the totality of the information considered and expert judgment, EPA assumes, for the purposes of this risk based prioritization, that the potential for exposure to the general population and the environment is high.

Persistence and bioaccumulation ratings for this chemical are P_1 (low) and B_1 (low). These ratings indicate that this chemical will not persist long in the environment and that it will be slow to bioaccumulate in environmental media.

Exposure to Commercial Workers and Consumers

This chemical has a vapor pressure of 0.78 torr at 25^{o} C which could result in potential exposure to vapor if commercial workers or consumers are near the products containing the chemical. (USEPA, 2007b). The likelihood that this chemical is used in commercial/consumer products is low based on IUR data.

Exposure to Children

No information was provided on the IUR for exposure to children through using products that contain this chemical. The HPV Challenge Program submission information indicates that alkyl acetates (C6 to C13) are mainly used as solvents in lacquers, janitorial cleaning products, and agricultural products (Clayton, 1994). There is a moderate likelihood that this chemical is used in products intended to be used by children but there is uncertainty in the IUR data.

References

Clayton G and Clayton F (eds.) (1994). Patty's Industrial Hygiene and Toxicology. Vol. 2D, 4th Edition, John Wiley & Sons, New York, USA.

ExxonMobil 2005, Alkyl Acetate C6 to C13 Category Analysis Report for the U.S. High Production Volume Chemical Challenge Program. August 24, 2005

MSDS obtained from DuPont. (downloaded on October 29, 2007)
http://msds.dupont.com/msds/pdfs/EN/PEN_09004a2f80006301.pdf

NIOSH, 2007. OSHA PEL Project Documentation. Accessed August, 2007. http://www.cdc.gov/niosh/pel88/npelcas.html.

SIDS 2007, United Nations Environment Programme (UNEP) Chemicals Screening Information Dataset (SIDS) for High Volume Chemicals. Accessed October 2007. http://www.chem.unep.ch/irptc/sids/oecdsids/sidspub.html

USEPA, 2006. 2006 Partial Updating of TSCA Chemical Inventory.

USEPA, 2007a. Toxic Release Inventory. Accessed August, 2007. http://www.epa.gov/tri/.

USEPA, 2007b, Physical/Chemical and Environmental Fate Characterization for High Production Volume Chemicals Chemical Name: Acetic Acid, C6-8 Branched Alkyl Esters

Exposure Characterization for HPV Challenge Chemical

Acetic Acid, C_{7-9} Branched Alkyl Esters

CAS #108419-32-5

March 14, 2008

Prepared by

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Exposure Characterization for HPV Challenge Chemical

Acetic acid, C_{7-9} branched alkyl esters **(CAS 108419-32-5)**

Non-CBI Executive Summary

This chemical has some public use and exposure information in the HPV Challenge Program submission. The information indicates that alkyl acetates (C6 to C13) are mainly used as solvents in lacquers, janitorial cleaning products, and agricultural products (Clayton, 1994). Limited workplace air sampling data suggest air concentrations below 10 mg/m^3 for C6 to C13 alkyl acetate aerosols.

Acetic acid, C_{7-9} branched alkyl esters (CAS #108419-32-5) was manufactured in the United States in calendar year 2005 (USEPA, 2006). This chemical has an aggregated volume produced and/ or imported in the range of 500,000 to 1,000,000 pounds. Persons submitting Inventory Update Reporting (IUR) information in 2006 asserted that some of the information was confidential business information (CBI) and therefore cannot be disclosed. Data and information that are CBI have been excluded from this summary.

Exposure was characterized using both public, non-confidential sources and one or more IUR submissions available at the time the exposure characterization was written. If additional information warrants an update of the exposure characterization, the update will be posted on the EPA website.

A SIDS dossier has not been prepared for this chemical (SIDS, 2007).

Exposures to Workers

This chemical has a vapor pressure of 0.78 torr at 25°C (USEPA, 2007b). OPPT has established 1.0 x 10e-3 torr as a value above which worker exposures to vapors should be estimated for chemical assessments. Therefore, this chemical's vapor pressure could result in worker exposures to vapors if workers are proximal to the liquid. This chemical does not have an OSHA Permissible Exposure Limit (NIOSH, 2007). The National Occupational Exposure Survey (NOES), conducted from 1981 to 1983, did not provide information on the number of workers likely to be exposed for this chemical. Based on IUR reporting, the maximum total number of workers likely to be exposed to this chemical during manufacturing and industrial processing and use is less than 100. There may be additional potentially exposed workers that are not included in this estimate since not all production volume has been accounted, and there is at least one use that contains a "Not Readily Obtainable" (NRO) response among the submissions.

Differences between numbers of workers estimated by IUR submitters and by the NOES are attributable to many factors, including time, scope, and method of the estimates. For example, NOES estimates are for all workplaces while IUR are for industrial workplaces only, and NOES

used a survey and extrapolation method while IUR submitters simply provide their best estimates based on available information for the specific reporting year.

The IUR based ranking for worker exposure is high based on the uncertainty associated with the data.

Exposure to General Population and the Environment

The chemical is not on the Toxic Release Inventory (USEPA, 2007a). Chemicals used as solvents in lacquers, janitorial cleaning products, and agricultural products are expected to result in environmental releases. The potential for exposures to the general population and the environment is possible based on these uses. Searches of additional relevant information sources related to the Voluntary Children's Chemical Evaluation Program (VCCEP) and HSDB did not provide any further information on this chemical. Therefore, based on the totality of the information considered and expert judgment, EPA assumes, for purposes of this risk based prioritization that the potential for general population and/or environmental exposure to this chemical is high.

Persistence and bioaccumulation ratings for this chemical are P_1 (low) and B_1 (low). These ratings indicate that this chemical will not persist long in the environment and that it will be slow to bioaccumulate in environmental media.

Exposure to Commercial Workers and Consumers

This chemical has a vapor pressure of 0.78 torr at 25°C which could result in exposures to vapor if commercial workers and consumers are near the products containing the chemical (USEPA, 2007b). However, the likelihood that this chemical is used in commercial/consumer products is low based on IUR data.

Exposure to Children

No information was provided on the IUR for exposure to children through using products that contain this chemical. The HPV Challenge Program submission information indicates that alkyl acetates (C6 to C13) are mainly used as solvents in lacquers, janitorial cleaning products, and agricultural products (Clayton, 1994). There is a moderate likelihood that this chemical is used in products intended to be used by children but there is uncertainty in the IUR data.

References

Clayton G and Clayton F (eds.) (1994). Patty's Industrial Hygiene and Toxicology. Vol. 2D, 4th Edition, John Wiley & Sons, New York, USA.

ExxonMobil 2005, Alkyl Acetate C6 to C13 Category Analysis Report for the U.S. High Production Volume Chemical Challenge Program. August 24, 2005

MSDS obtained from DuPont. (additional citation will be added here by CEB)

NIOSH, 2007. OSHA PEL Project Documentation. Accessed August, 2007. http://www.cdc.gov/niosh/pel88/npelcas.html.

SIDS 2007, United Nations Environment Programme (UNEP) Chemicals Screening Information Dataset (SIDS) for High Volume Chemicals. Accessed October 2007. http://www.chem.unep.ch/irptc/sids/oecdsids/sidspub.html

USEPA, 2006. 2006 Partial Updating of TSCA Chemical Inventory.

USEPA, 2007a. Toxic Release Inventory. Accessed August, 2007. http://www.epa.gov/tri/.

USEPA 2007b, Physical/Chemical and Environmental Fate Characterization for High Production Volume Chemicals Chemical Name: Acetic Acid, C7-9 Branched Alkyl Esters

Exposure Characterization for HPV Challenge Chemical

Acetic Acid, C_{9-11} Branched Alkyl Esters

CAS #108419-34-7

March 14, 2008

Prepared by

Exposure Assessment Branch
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Exposure Characterization for HPV Challenge Chemical

Acetic acid, $C_{9\text{-}11}$ branched alkyl esters **(CAS 108419-34-7)**

Non-CBI Executive Summary

This chemical has some public use and exposure information in the HPV Challenge Program submission. The information indicates that alkyl acetates (C6 to C13) are mainly used as solvents in lacquers, janitorial cleaning products, and agricultural products (Clayton, 1994). Limited workplace air sampling data suggest air concentrations below 10 mg/m^3 for C6 to C13 alkyl acetate aerosols.

Acetic acid, $C_{9\text{-}11}$ branched alkyl esters (CAS #108419-34-7) was manufactured in the United States in calendar year 2005 (USEPA, 2006). This chemical has an aggregated volume produced and/or imported in the range of 500,000 to 1,000,000 pounds. Persons submitting Inventory Update Reporting (IUR) information in 2006 asserted that some of the information was confidential business information (CBI) and therefore cannot be disclosed. Data and information that are CBI have been excluded from this summary.

Exposure was characterized using both public, non-confidential sources and one or more IUR submissions available at the time the exposure characterization was written. If additional information warrants an update of the exposure characterization, the update will be posted on the EPA website.

SIDS dossier has not been prepared for this chemical (SIDS, 2007).

Exposures to Workers

This chemical has a vapor pressure of 0.1 torr at 25°C (USEPA, 2007b). OPPT has established 1.0 x 10e-3 torr as a value above which worker exposures to vapors should be estimated for chemical assessments. Therefore, this chemical's vapor pressure could result in worker exposures to vapors if workers are proximal to the liquid. This chemical does not have an OSHA Permissible Exposure Limit (NIOSH, 2007). The National Occupational Exposure Survey (NOES), conducted from 1981 to 1983, did not provide information on the number of workers likely to be exposed for this chemical. Based on IUR reporting, the maximum total number of workers likely to be exposed to this chemical during manufacturing and industrial processing and use is less than 100. There may be additional potentially exposed workers that are not included in this estimate since not all production volume has been accounted, and there is at least one use that contains a "Not Readily Obtainable" (NRO) response among the submissions.

Differences between numbers of workers estimated by IUR submitters and by the NOES are attributable to many factors, including time, scope, and method of the estimates. For example, NOES estimates are for all workplaces while IUR are for industrial workplaces only, and NOES

used a survey and extrapolation method while IUR submitters simply provide their best estimates based on available information for the specific reporting year.

The IUR based ranking for worker exposure is high based on the uncertainty associated with the data.

Exposures to General Population and the Environment

The chemical is not on the Toxics Release Inventory (USEPA, 2007a). Chemicals used as solvents in lacquers, janitorial cleaning products, and agricultural products are expected to result in environmental releases. The potential for exposures to the general population and the environment is possible based on these uses. Searches of additional relevant information sources related to Voluntary Children's Chemical Evaluation Program (VCCEP) and HSDB did not provide any further information on this chemical. Therefore, based on the totality of the information considered and expert judgment, EPA assumes, for purposes of this risk based prioritization that the potential for general population and/or environmental exposure to this chemical is high.

Persistence and bioaccumulation ratings for this chemical are P_1 (low) and B_1 (low). These ratings indicate that this chemical will not persist long in the environment and that it will be slow to bioaccumulate in environmental media.

Exposure to Commercial Workers and Consumers

This chemical has a vapor pressure of 0.1 torr at 25^{o} C which could result in potential exposure to vapor if commercial workers or consumers are near to the products containing the chemical. It is unknown how many commercial workers and consumers may be exposed or how many consumers may use the chemical because that information was not reported on the IUR.

Exposure to Children

No information was provided in the IUR for exposure to children through using products that contain this chemical. The HPV Challenge Program submission information indicates that alkyl acetates (C6 to C13) are mainly used as solvents in lacquers, janitorial cleaning products, and agricultural products (Clayton, 1994). There is a moderate likelihood that this chemical is used in products intended to be used by children but there is uncertainty in the IUR data.

References

Clayton G and Clayton F (eds.) (1994). Patty's Industrial Hygiene and Toxicology. Vol. 2D, 4th Edition, John Wiley & Sons, New York, USA.

ExxonMobil 2005, Alkyl Acetate C6 to C13 Category Analysis Report for the U.S. High Production Volume Chemical Challenge Program. August 24, 2005

MSDS obtained from Esso Imperial Oil (downloaded October 29, 2007)

http://www.msds.exxonmobil.com/psims/psims.aspx?brand=iol
Product Trade Name : EXXATE 1000 solvent

NIOSH, 2007. OSHA PEL Project Documentation. Accessed August, 2007. http://www.cdc.gov/niosh/pel88/npelcas.html.

SIDS 2007, United Nations Environment Programme (UNEP) Chemicals Screening Information Dataset (SIDS) for High Volume Chemicals. Accessed October 2007. http://www.chem.unep.ch/irptc/sids/oecdsids/sidspub.html

USEPA, 2006. 2006 Partial Updating of TSCA Chemical Inventory.

USEPA, 2007a. Toxic Release Inventory. Accessed August, 2007, http://www.epa.gov/tri/.

USEPA 2007b, Physical/Chemical and Environmental Fate Characterization for High Production Volume Chemicals Chemical Name: Acetic Acid, C9-11 Branched Alkyl Esters

Exposure Characterization for HPV Challenge Chemical

Acetic Acid, C_{11-14} Branched Alkyl Esters

CAS #108419-35-8

March 14, 2008

Prepared by

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Exposure Characterization for HPV Challenge Chemical

Acetic acid, C_{11-14} branched alkyl esters **(CAS 108419-35-8)**

Non-CBI Executive Summary

This chemical has some public use and exposure information in the HPV Challenge Program submission. The information indicates that alkyl acetates (C6 to C13) are mainly used as solvents in lacquers, janitorial cleaning products, and agricultural products (Clayton, 1994). Limited workplace air sampling data suggest air concentrations below 10 mg/m^3 for C6 to C13 alkyl acetate aerosols.

Acetic acid, C_{11-14} branched alkyl esters was manufactured in the United States in amounts greater than 25,000 lb in 2005 (USEPA, 2006). This chemical has a production volume in the range of 10,000 to 500,000 lb. Persons submitting Inventory Update Reporting information in 2006 asserted that some of the information was confidential and therefore cannot be disclosed. Data and information that are CBI have been excluded from this summary.

Exposure was characterized using both public, non-confidential sources and one or more IUR submissions available at the time the exposure characterization was written. If additional information warrants an update of the exposure characterization, the update will be posted on the EPA website.

A SIDS dossier has not been prepared for this chemical (SIDS, 2007).

Exposures to Workers

This chemical has a vapor pressure of 0.01 torr at 25°C (USEPA, 2007b). This chemical does not have an OSHA Permissible Exposure Limit (NIOSH, 2007). OPPT has established 1.0 x 10e-3 torr as a value above which worker exposures to vapors should be estimated for chemical assessments. Therefore, this chemical's vapor pressure could result in worker exposures to vapors if workers are proximal to the liquid. The National Occupational Exposure Survey (NOES), conducted from 1981 to 1983, did not provide information on the number of workers likely to be exposed for this chemical. Based on IUR reporting, the maximum total number of workers likely to be exposed to this chemical during manufacturing and industrial processing and use is less than 100. There may be additional potentially exposed workers that are not included in this estimate since not all production volume has been accounted, and there is at least one use that contains a "Not Readily Obtainable" (NRO) response among the submissions.

Differences between numbers of workers estimated by IUR submitters and by the NOES are attributable to many factors, including time, scope, and method of the estimates. For example, NOES estimates are for all workplaces while IUR are for industrial workplaces only, and NOES used a survey and extrapolation method while IUR submitters simply provide their best estimates based on available information for the specific reporting year.

The IUR based ranking for worker exposure is high based on the uncertainty associated with the data.

Exposure to General Population and the Environment

The chemical is not on the Toxic Release Inventory (USEPA, 2007a). Chemicals used as solvents in lacquers, janitorial cleaning products, and agricultural products are expected to result in environmental releases. The potential for exposures to the general population and the environment is likely based on these uses. Searches of additional relevant information sources related to Voluntary Children's Chemical Evaluation Program (VCCEP) and HSDB did not provide any further information on this chemical. Therefore, based on the totality of the information considered and expert judgment, EPA assumes, for purposes of this risk based prioritization that the potential for general population and/or environmental exposure to this chemical is high.

Persistence and bioaccumulation ratings for this chemical are moderate (P_2 /B_3). Based on available data, acetic acid, C11-14 (108419-35-8) may biodegrade to moderately persistent and strongly bioaccumulative branched alcohols.

Exposure to Commercial Workers and Consumers

This chemical has a vapor pressure of 0.01 torr at 25^{o} C which could result in exposures to vapor if commercial workers and consumers are near the products containing the chemical (USEPA, 2007b). It is unknown how many commercial workers may be exposed or how many consumers may use the chemical because that information was not reported in the IUR. The likelihood that this chemical is used in commercial/consumer products is high based on uncertainty associated with the IUR data.

Exposure to Children

No information was provided on the IUR for exposure to children through using products that contain this chemical. The HPV Challenge Program submission information indicates that alkyl acetates (C6 to C13) are mainly used as solvents in lacquers, janitorial cleaning products, and agricultural products (Clayton, 1994). There is a moderate likelihood that this chemical is used in products intended to be used by children but there is uncertainty in the IUR data.

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