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

Diesters Category

Sponsored Chemicals

Maleic acid, bis(1,3-dimethylbutyl) ester (CASRN 105-52-2)
(CA Index Name: 2-Butenedioic acid (2Z)-, 1,4-bis(1,3-dimethylbutyl) ester)
(9th CI Name: 2-Butenedioic acid (2Z)-, bis(1,3-dimethylbutyl) ester)

Maleic acid, bis(2-ethylhexyl) ester (CASRN 142-16-5)
(CA Index Name: 2-Butenedioic acid (2Z)-, 1,4-bis(2-ethylhexyl) ester)
(9th CI Name: 2-Butenedioic acid (2Z)-, bis(2-ethylhexyl) ester)

Adipic acid, diisopropyl ester (CASRN 6938-94-9)
(CA Index Name: Hexanedioic acid, 1,6-bis(1-methylethyl) ester)
(9th CI Name: Hexanedioic acid, bis(1-methylethyl) ester)

Adipic acid, diisooctyl ester (CASRN 1330-86-5)
(CA Index Name: Hexanedioic acid, 1,6-diisooctyl ester)
(9th CI Name: Hexanedioic acid, diisooctyl ester)

Adipic acid, bis(1-methylheptyl)ester (CASRN 108-63-4)
(CA Index Name: Hexanedioic acid, 1,6-bis(1-methylheptyl) ester)
(9th CI Name: Hexanedioic acid, bis(1-methylheptyl) ester)

Adipic acid, diisononyl ester (CASRN 33703-08-1)
(CA Index Name: Hexanedioic acid, 1,6-diisononyl ester)
(9th CI Name: Hexanedioic acid, diisononyl ester)

Adipic acid, diisodecyl ester (CASRN 27178-16-1)
(CA Index Name: Hexanedioic acid, 1,6-diisodecyl ester)
(9th CI Name: Hexanedioic acid, diisodecyl ester)

Adipic acid, ditridecyl ester (CASRN 16958-92-2)
(CA Index Name: Hexanedioic acid, 1,6-ditridecyl ester)
(9th CI Name: Hexanedioic acid, ditridecyl ester)

Azelaic acid, bis(2-ethylhexyl) ester (CASRN 103-24-2)
(CA Index Name: Nonanedioic acid, 1,9-bis(2-ethylhexyl) ester)
(9th CI Name: Nonanedioic acid, bis(2-ethylhexyl) ester)

Azelaic acid, diisodecyl ester (CASRN 28472-97-1)
(CA Index Name: Nonanedioic acid, 1,9-diisodecyl ester)
(9th CI Name: Nonanedioic acid, diisodecyl ester)

Sebacic acid, dimethyl ester (CASRN 106-79-6)
(CA Index Name: Decanedioic acid, 1,10-dimethyl ester)
(9th CI Name: Decanedioic acid, dimethyl ester)

Sebacic acid, bis(2-ethylhexyl) ester (CASRN 122-62-3)
(CA Index Name: Decanedioic acid, 1,10-bis(2-ethylhexyl) ester)
(9th CI Name: Decanedioic acid, bis(2-ethylhexyl) ester)

Supporting Chemicals

Maleic acid, dibutyl ester (CASRN 105-76-0)
(CA Index Name: 2-Butenedioic acid (2Z)-, 1,4-dibutyl ester)
(9th CI Name: 2-Butenedioic acid (2Z)-, dibutyl ester)

Adipic acid, dibutyl ester (CASRN 105-99-7)
(CA Index Name: Hexanedioic acid, 1,6-dibutyl ester)
(9th CI Name: Hexanedioic acid, dibutyl ester)

Adipic acid, di-C7-9 branched and linear alkyl ester (CASRN 68515-75-3)
(9th CI and CA Index Name: Hexanedioic acid, di-C7-9-branched and linear alkyl esters)

Adipic acid, bis(2-ethylhexyl) ester (CASRN 103-23-1)
(CA Index Name: Hexanedioic acid, 1,6-bis(2-ethylhexyl) ester)
(9th CI Name: Hexanedioic acid, bis(2-ethylhexyl) ester)

Contents:

BACKGROUND

Screening-level hazard, exposure and risk characterizations for high production volume chemicals (HPV) are important contributions to the chemicals cooperation work being done in North America[1] through the EPA Chemical Assessment and Management Program (ChAMP)[2]. These screening-level characterizations are developed by EPA for individual chemicals or chemical categories to support initial Risk-Based Prioritizations (RBPs) for HPV chemicals. These screening-level characterizations are technical documents intended primarily to inform the Agency's internal decision-making process. Accordingly, they are written for assessment professionals and assume a degree of technical understanding. Each of the support documents is described below.

The Risk-Based Prioritizations are found in an accompanying document and are written for a general audience. They present EPA's initial thinking regarding the potential risks presented by these chemicals and future possible actions that may be needed.

Hazard Characterizations for HPV Chemicals

EPA's screening-level hazard characterizations are based primarily on the review of the summaries of studies and other information submitted by the chemical sponsor(s) under the HPV Challenge Program[3]. These studies included in the scope of the HPV Challenge comprise the Screening Information Data Set (SIDS) of the Organization for Economic Cooperation and Development (OECD)[4], an internationally recognized battery of tests that provides the basic data necessary to make an initial evaluation of a chemical's hazards and fate. In preparing the initial hazard characterizations, EPA also consulted a variety of reliable sources[5] for additional relevant information and 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. In order to determine whether any new hazard information was developed since the time of an HPV submission, EPA also searched publicly available databases[6] for information entered from one year prior to the HPV submission through May 2008. The screening-level hazard characterization is performed according to established EPA guidance[7]. A more detailed description of the hazard characterization process is available on the EPA website[8].

With respect to chemicals for which internationally-accepted OECD SIDS Initial Assessment Profiles (SIAP) and Initial Assessment Reports (SIAR) were available, EPA did not generate its own screening-level hazard characterization, but did check for and incorporate updated information in the risk characterization.

Exposure Characterizations for HPV Chemicals

EPA recently received exposure-related data on chemicals submitted in accordance with the requirements of Inventory Update Reporting (IUR)[9]. The 2006 IUR submissions pertain to chemicals manufactured in

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[1] U.S. EPA – U.S. Commitments to North American Chemicals Cooperation: http://www.epa.gov/hpv/pubs/general/sppframework.htm.
[2] U.S. EPA – ChAMP information: http://www.epa.gov/champ/.
[3] U.S. EPA – HPV Challenge Program information: http://www.epa.gov/hpv.
[4] U.S. EPA – Technical Guidance Document, OECD SIDS Manual Sections 3.4 and 3.5: http://www.epa.gov/chemrtk/pubs/general/sidsappb.htm.
[5] U.S. EPA – Public Database Hazard Information: http://www.epa.gov/hpvis/hazardinfo.htm
[6] U.S. EPA – Public Database Update Information: http://www.epa.gov/chemrtk/hpvis/updateinfo.htm.
[7] U.S. EPA – Risk Assessment Guidelines: http://cfpub.epa.gov/ncea/raf/rafguid.cfm.
[8] U.S. EPA – About HPV Chemical Hazard Characterizations: http://www.epa.gov/hpvis/abouthc.htm.
[9] U.S. EPA – Basic IUR Information: http://www.epa.gov/opptintr/iur/pubs/guidance/basic-information.htm.

(including imported into) the U.S. during calendar year 2005 in quantities of 25,000 pounds or more at a single site. The reports include the identity, the quantity, and the physical form of the chemical manufactured or imported, and the number of workers 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, additional reported information includes: the industrial processing and uses of the chemical; the number of industrial processing sites and workers reasonably likely to be exposed to the chemical at those sites; the consumer and commercial uses of the chemical; and an indication whether the chemical was used in products intended for use by children under 14 years of age.

EPA's screening-level exposure characterizations are based largely on the information submitted under the IUR reporting, although other exposure information submitted to the Agency (for example, in HPV submissions) or readily available through a limited set of publicly accessible databases[10] was also considered. The screening-level exposure characterizations identify a potential (high, medium, or low) that each of five populations – the environment, the general population, workers, consumers, and children – might be exposed to the chemical. In most cases, this potential doesn't address the quantity, frequency, or duration of exposure, but refers only to the likelihood that an exposure could occur.

In many instances EPA is not able to fully disclose to the public all the IUR exposure-related data reviewed or relied upon in the development of the screening-level documents because some of the material was claimed as confidential business information (CBI) when it was submitted to the Agency. These CBI claims do limit the Agency's ability to be completely transparent in presenting some underlying exposure and use data for chemicals in public documents. EPA does consider all data, including data considered to be CBI, in the screening-level exposure and risk characterization process, and endeavors whenever possible to broadly characterize supporting materials claimed as confidential in ways that do not disclose actual CBI.

Risk Characterizations for HPV Chemicals

EPA combines the information from the screening-level exposure characterization with the screening-level hazard characterization to develop a qualitative screening-level risk characterization, as described in the Agency's guidance on drafting risk characterizations[11]. These screening-level risk characterizations are technical documents intended to support subsequent priority-setting decisions and actions by OPPT. The purpose of the qualitative screening-level risk characterization is two-fold: to support initial risk-based decisions to prioritize chemicals, identify potential concerns, and inform risk management options; and to identify data needs for individual chemicals or chemical categories.

These initial characterization and prioritization documents do not constitute a final Agency determination as to risk, nor do they determine whether sufficient data are available to characterize risk. Recommended actions reflect EPA's relative judgment regarding this chemical or chemical category in comparison with others evaluated under this program, as well as the uncertainties presented by gaps that may exist in the available data.

[10] U.S. EPA – Summary of Public Databases Routinely Searched: http://www.epa.gov/chemrtk/hpvis/pubdtsum.htm.
[11] U.S. EPA – Risk Characterization Program: http://www.epa.gov/osa/spc/2riskchr.htm

QUALITATIVE SCREENING-LEVEL RISK CHARACTERIZATION OF HIGH PRODUCTION VOLUME CHEMICALS

CHEMICAL CATEGORY NAME
Diesters

SPONSORED CHEMICALS

Maleic acid, bis(1,3-dimethylbutyl)ester (CAS No. 105-52-2)
(9th CI Name: 2-Butenedioic acid (2Z)-, bis(1,3-dimethylbutyl) ester)
Maleic acid, bis(2-ethylhexyl)ester (CAS No. 142-16-5)
(9th CI Name: 2-Butenedioic (2Z)-, bis(2-ethylhexyl) ester)
Adipic acid, diisopropyl ester (CAS No. 6938-94-9)
(9th CI Name: Hexanedioic acid, bis(1-methylethyl) ester)
Adipic acid, diisooctyl ester (CAS No. 1330-86-5)
(9th CI Name: Hexanedioic acid, diisooctyl ester)
Adipic acid, bis(1-methylheptyl)ester (CAS No. 108-63-4)
(9th CI Name: Hexanedioic acid, bis(1-methylheptyl) ester)
Adipic acid, diisononyl ester (CAS No. 33703-08-1)
(9th CI Name: Hexanedioic acid, diisononyl ester)
Adipic acid, diisodecyl ester (CAS No. 27178-16-1)
(9th CI Name: Hexanedioic acid, diisodecyl ester)
Adipic acid, ditridecyl ester (CAS No. 16958-92-2)
(9th CI Name: Hexanedioic acid, ditridecyl ester)
Azelaic acid, bis(2-ethylhexyl)ester (CAS No. 103-24-2)
(9th CI Name: Nonanedioic acid, bis(2-ethylhexyl) ester)
Azelaic acid, diisodecyl ester (CAS No. 28472-97-1)
(9th CI Name: Nonanedioic acid, diisodecyl ester)
Sebacic acid, dimethyl ester (CAS No. 106-79-6)
(9th CI Name: Decanedioic acid, dimethyl ester)
Sebacic acid, bis(2-ethylhexyl)ester (CAS No. 122-62-3)
(9th CI Name: Decanedioic acid, bis(2-ethylhexyl) ester)

SUPPORTING CHEMICALS

Maleic acid, dibutyl ester (CAS No. 105-76-0)
(9th CI Name: 2-Butanedioic acid (2Z)-, dibutyl ester)
Adipic acid, dibutyl ester (CAS No. 105-99-7)
(9th CI Name: Hexanedioic acid, dibutyl ester)
Adipic acid, di-C7-9 branched and linear alkyl ester (CAS NO. 68515-75-3)
(9th CI Name: Hexanedioic acid, di-C7-9 branched and linear alkyl esters)
Adipic acid, bis(2-ethylhexyl) ester (CAS No. 103-23-1)
(9th CI Name: Hexanedioic acid, bis(2-ethylhexyl) ester)

September 2008

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QUALITATIVE SCREENING-LEVEL RISK CHARACTERIZATION FOR Diesters Category

1. Category Justification

The sponsor submitted the diesters category in response to EPA's comments on the original aliphatic esters category. The original category contained 45 category members divided into five groups (monoesters, diesters, glycol esters, sorbitan esters, and polyol esters). The twelve chemicals in the diesters category include diesters of maleic (C4), adipic (C6), azelaic (C9), and sebacic (C10) acids. Total carbon numbers for the category members range from C12 to C32. The sponsor justified the category based on structural and molecular weight similarities and carbon numbers. EPA considered this grouping acceptable for the purposes of the HPV Challenge Program and further accepts this category for prioritization in the Chemical Assessment and Management Program (ChAMP).

Supporting chemicals of the category include maleic acid, dibutyl ester (C12); adipic acid, dibutyl ester (14); adipic acid, di-C7-9 branched and linear alkyl ester (C20-C24); and adipic acid, bis(2-ethylhexyl) ester (C22). EPA agreed that these chemicals are appropriate supporting chemicals based on similarities in chemical structure and physical-chemical properties. In addition to supporting the Diesters Category for the endpoints listed above, maleic acid, dibutyl ester (C12); adipic acid, di-C7-9 branched and linear alkyl ester (C20-C24); and adipic acid, bis(2-ethylhexyl) ester (C22) each have a full hazard, exposure and risk characterization because they are part of EPA's commitment under the Security and Prosperity Partnership.

2. Physical-Chemical Properties and Environmental Fate

Most members of the diester category are colorless to pale straw-colored liquids at room temperature. Vapor pressure and water solubility of esters in this category range from negligible to moderate.

The environmental fate parameters of category members are dependent on the number of carbons in the parent diacid and the total number of carbons in the ester. In general, members of the diester category partition primarily to sediment, soil, and water. They are moderately volatile from water and moist soil surfaces. Soil mobility ranges from minimal to high, with higher molecular weight compounds tending to be less mobile. Atmospheric photodegradation ranges from slow to moderate. All members of the diester category undergo hydrolysis at rates that are considered slow to negligible.

Ready biodegradability tests conducted on category members and supporting compounds indicate that the potential for these compounds to persist in the environment is low (P1). Estimated BCF values suggest that members of the category have a low potential to bioaccumulate (B1). Although a high BCF was estimated for maleic acid, bis(1,3-dimethylbutyl) ester, its potential for bioconcentration is expected to be low (B1) due to metabolism by biota.

3. Hazard Characterization

Aquatic Organism Toxicity: The aquatic toxicity data for category members with low solubility were generated using Water Accommodated Fractions or dispersion by propeller techniques. The evaluation of available toxicity data indicates that the potential acute hazard to fish is moderate for the maleic acid esters and the C12 adipic acid and sebacic acid esters (based on C14 supporting chemical data) and low for esters above C20 (due to low water solubility). The potential acute hazard of the diester category members to aquatic invertebrates is low and to aquatic plants is moderate in the C12 to C20 range and low above C20. The potential chronic toxicity hazard of the C22 and above diester category members is low.

Human Health Toxicity: The acute toxicity of the category members is low for the oral and dermal routes. Systemic toxicity in the oral and dermal repeated dose toxicity studies for category members and for the C12 and C20 supporting chemicals in rats and dogs is low. Oral prenatal developmental toxicity studies for the category members and for the C20 supporting chemical in rats showed low developmental and maternal toxicity. A prenatal developmental toxicity study on the C22 supporting chemical, that included an assessment of postnatal growth and development, also showed low developmental and maternal toxicity, as well as low reproductive toxicity. A combined repeated-dose/reproductive/developmental toxicity screening study in rats with the C12 supporting chemical showed low maternal toxicity and no developmental or reproductive toxicity. A one-generation reproductive toxicity study on the C22 supporting chemical showed no reproductive toxicity. Likewise, numerous repeated-dose toxicity studies in rats on the category members as well as several supporting chemicals with examination of various reproductive organs and endpoints all showed no evidence of reproductive toxicity, with the exception of one study, which showed low reproductive toxicity. The tested category members or supporting chemicals did not induce gene mutation or chromosomal aberrations. Data indicate that maleic acid, dibutyl ester is a strong sensitizer. IARC has classified the supporting chemical adipic acid, bis (2-ethylhexyl) ester into Group 3 (substances not classifiable as to its carcinogenicity to humans).

4. Exposure Characterization

Eleven of the diesters category chemicals have aggregated production and/or import volumes in the range of 26.5 million to 162 million pounds. The aggregated volumes exclude two of the thirteen chemicals, adipic acid, bis(1-methylheptyl) ester (CAS# 108-63-4) and adipic acid, dibutyl ester (CAS# 105-99-7), which do not have Inventory Update Reporting (IUR) submissions. Non-confidential information in the IUR indicates that these chemicals were manufactured and/or imported at various companies and sites. Non-confidential IUR information indicates that many of the chemicals in the diesters category are used as lubricants in the manufacturing of certain industrial sectors specified in the IUR form as "other basic organic chemicals" and "all other chemical products and preparations," and as intermediates or functional fluids in various manufacturing processes. Ten of the eleven chemicals with IUR submissions are indicated to have uses in commercial settings or consumer uses. Information submitted as part of the HPV Challenge Program indicates that diesters chemicals have widespread applications as lubricants, solvents and plasticizers.

Potential Exposures to the General Population and the Environment: Based on the information considered, including information found from non-confidential public sources, EPA identifies, for the purposes of risk-based prioritization, a high potential that the general population and the environment might be exposed. The Hazardous Substances Data Bank (HSDB) information for some of these chemicals states that there might be potential releases to the environment from various waste streams.

Persistence and bioaccumulation ratings for these chemicals are P1 and B1. These ratings indicate that these chemicals are not persistent in the environment; and are not bioaccumulative.

Potential Exposures to Workers: Based on the information considered including IUR data, HPV Test Plan and SIDS, and in combination with the Agency's professional judgment, EPA identifies, for the purposes of risk-based prioritization, a medium relative ranking for potential worker exposure. The medium relative ranking is based on the vapor pressure and physical forms of these chemicals, potential dermal exposure during industrial processing and use activities and commercial uses, the number of workers potentially exposed, and the relatively high aggregated production volumes for all chemicals in this category.

Potential Exposures to Consumers: EPA identifies, for the purposes of risk-based prioritization, a high potential that consumers might be exposed based on the use of products containing these chemicals. Ten of the eleven chemicals with IUR submissions are indicated to have uses in commercial settings or consumer uses. The non-confidential consumer uses for many of these chemicals are: rubber and plastic products, and electrical and electronic products. There is also potential for exposure to consumers based on information from public data sources.

Potential Exposures to Children: EPA identifies, for the purposes of risk-based prioritization, a high potential that children might be exposed based on the use of products containing these chemicals. Information on three of these chemicals, including maleic acid, bis(2-ethylhexyl) ester (CAS# 142-16-5), adipic acid, diisononyl ester (CAS# 33703-08-1) indicated uses in products intended to be used by children. Reports for three chemicals, including adipic acid, diisodecyl ester (CAS# 27178-16-1), azelaic acid, bis(2-ethylhexyl) ester (CAS# 103-24-2), and sebacic acid, bis(2-ethylhexyl) ester (CAS# 122-62-3), indicated that such information was Not Readily Obtainable.

5. Risk Characterization

The statements and rationale provided below are intended solely for the purpose of this qualitative screening-level risk characterization and will be used for prioritizing substances for future work in the Chemical Assessment Management Program (ChAMP).

Risk Statement and Rationale

Potential Risk to Aquatic Organisms from Environmental Releases (LOW/MEDIUM CONCERN). EPA identifies a high potential that aquatic organisms might be exposed from environmental releases. Chemicals in the diesters category have low persistence and low bioaccumulation. For fish, these characteristics, in combination with the moderate acute toxicity for the maleic acid esters and the C12 adipic acid and sebacic acid esters (based on C14 supporting chemical data) indicates a medium concern for potential risks from the C12-C20 category members; and, the potential exposure in combination with the low acute toxicity for esters above C20 indicates a low concern for potential risks. For aquatic invertebrates, these characteristics, in combination with the low acute toxicity for the diester category members indicates a low concern for potential risks. For aquatic plants, the potential exposure in combination with the moderate acute toxicity to the C12 to C20 range indicates a medium concern for potential risks; the potential exposure in combination with the low acute and chronic toxicity above C20 indicates a low concern for potential risks.

Potential Risk to the General Population from Environmental Releases (LOW CONCERN). EPA identifies high potential that the general population might be exposed from environmental releases. The potential human health hazard is expected to be low due to the lack of specific toxicity to animals following exposure to high doses. The low hazard and the environmental fate characteristics of low persistence and low bioaccumulation together suggest a low concern for potential risk to the general population from environmental releases.

Potential Risk to Workers (LOW CONCERN). EPA identifies a medium relative ranking for potential worker exposure. The potential human health hazard is expected to be low due to the lack of specific toxicity to animals following exposure to high doses. Therefore, taken together, the available information suggests a low concern for potential risks to workers.

Potential Risk to Consumers from Known Uses (LOW CONCERN). EPA identifies a high potential that consumers might be exposed based on the use of products containing these chemicals. The potential human health hazard is expected to be low due to the lack of specific toxicity to animals following exposure to high doses. Taken together, the available information suggests a low concern for potential risks to consumers.

Potential Risk to Children (LOW CONCERN). EPA identifies a high potential that children might be exposed through the use of products specifically intended to be used by children, as well as through the use of some consumer products. Animal toxicity data that assessed postnatal growth and development indicated a low concern for potential toxicity for the C22 and C12 supporting chemicals. Taken together, the available information suggests a low concern for potential risks to children for the category members.

SCREENING LEVEL HAZARD CHARACTERIZATION OF HIGH PRODUCTION VOLUME CHEMICALS

CHEMICAL CATEGORY NAME

Diesters

SPONSORED CHEMICALS

Maleic acid, bis(1,3-dimethylbutyl)ester (CAS No. 105-52-2)
(9th CI Name: 2-Butenedioic acid (2Z)-, bis(1,3-dimethylbutyl) ester)

Maleic acid, bis(2-ethylhexyl)ester (CAS No. 142-16-5)
(9th CI Name: 2-Butenedioic (2Z)-, bis(2-ethylhexyl) ester)

Adipic acid, diisopropyl ester (CAS No. 6938-94-9)
(9th CI Name: Hexanedioic acid, bis(1-methylethyl) ester]

Adipic acid, diisooctyl ester (CAS No. 1330-86-5)
(9th CI Name: Hexanedioic acid, diisooctyl ester)

Adipic acid, bis(1-methylheptyl)ester (CAS No. 108-63-4)
(9th CI Name: Hexanedioic acid, bis(1-methylheptyl) ester)

Adipic acid, diisononyl ester (CAS No. 33703-08-1)
(9th CI Name: Hexanedioic acid, diisononyl ester)

Adipic acid, diisodecyl ester (CAS No. 27178-16-1)
(9th CI Name: Hexanedioic acid, diisodecyl ester)

Adipic acid, ditridecyl ester (CAS No. 16958-92-2)
(9th CI Name: Hexanedioic acid, ditridecyl ester)

Azelaic acid, bis(2-ethylhexyl)ester (CAS No. 103-24-2)
(9th CI Name: Nonanedioic acid, bis(2-ethylhexyl) ester)

Azelaic acid, diisodecyl ester (CAS No. 28472-97-1)
(9th CI Name: Nonanedioic acid, diisodecyl ester)

Sebacic acid, dimethyl ester (CAS No. 106-79-6)
(9th CI Name: Decanedioic acid, dimethyl ester)

Sebacic acid, bis(2-ethylhexyl)ester (CAS No. 122-62-3)
(9th CI Name: Decanedioic acid, bis(2-ethylhexyl) ester)

SUPPORTING CHEMICALS

Maleic acid, dibutyl ester (CAS No. 105-76-0)
(9th CI Name: 2-Butanedioic acid (2Z)-, dibutyl ester)

Adipic acid, dibutyl ester (CAS No. 105-99-7)
(9th CI Name: Hexanedioic acid, dibutyl ester)

Adipic acid, di-C7-9 branched and linear alkyl ester (CAS No. 68515-75-3)
(9th CI Name: Hexanedioic acid, di-C7-9 branched and linear alkyl esters)

Adipic acid, bis(2-ethylhexyl) ester (CAS No. 103-23-1)
(9th CI Name: Hexanedioic acid, bis(2-ethylhexyl) ester)

September 2008

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SCREENING LEVEL HAZARD CHARACTERIZATION
Diesters Category

Introduction

The sponsor, the American Chemistry Council's Aliphatic Esters Panel, submitted a Test Plan and Robust Summaries to EPA for the Aliphatic Esters category on December 20, 2001. EPA posted the submission on the ChemRTK Web site on February 20, 2002 (http://www.epa.gov/chemrtk/pubs/summaries/alipestr/c13466tc.htm). EPA comments on the original submission were posted to the website on August 28, 2002. The sponsor submitted updated/revised documents for five separate aliphatic ester categories based on EPA's comments on the original submission. The sponsor submitted the Diesters category on November 14, 2003 that was posted to the ChemRTK website on January 6, 2004. EPA comments on the Diesters category revision were posted to the website on May 1, 2006. The Diesters category consists of the following compounds:

Sponsored Chemicals

Maleic acid, bis(1,3-dimethylbutyl)ester	CAS No. 105-52-2
Maleic acid, bis(2-ethylhexyl)ester	CAS No. 142-16-5
Adipic acid, diisopropyl ester	CAS No. 6938-94-9
Adipic acid, diisooctyl ester	CAS No. 1330-86-5
Adipic acid, bis(1-methylheptyl)ester	CAS No. 108-63-4
Adipic acid, diisononyl ester	CAS No. 33703-08-1
Adipic acid, diisodecyl ester	CAS No. 27178-16-1
Adipic acid, ditridecyl ester	CAS No. 16958-92-2
Azelaic acid, bis(2-ethylhexyl)ester	CAS No. 103-24-2
Azelaic acid, diisodecyl ester	CAS No. 28472-97-1
Sebacic acid, dimethyl ester	CAS No. 106-79-6
Sebacic acid, bis(2-ethylhexyl)ester	CAS No. 122-62-3

Supporting Chemicals

Maleic acid, dibutyl ester	CAS No. 105-76-0
Adipic acid, dibutyl ester	CAS No. 105-99-7
Adipic acid,di-C7-9 branched and linear alkyl ester	CAS No. 68515-75-3
Adipic acid, bis(2-ethylhexyl) ester	CAS No. 103-23-1

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. In order to determine whether any new hazard information was developed since the time of the HPV submission, a search of the following databases was made from 2002 to July 2008: the NLM databases (ChemID to locate available data sources including Medline/PubMed, Toxline, HSDB, ATSDR, EPA SRS, etc.), STN/CAS online databases (Registry file for locators, ChemAbs for toxicology data, RTECS, Merck, etc.) and Science Direct. The structures of the sponsored chemical(s) are included in Appendix 1. Summary tables of SIDS endpoint data are included in the document. 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 sponsor submitted the diesters category in response to EPA's comments on the original aliphatic esters category. The original category contained 45 category members divided into five groups (monoesters, diesters, glycol esters, sorbitan esters, and polyol esters). The twelve chemicals in the diesters category include diesters of maleic (C4), adipic (C6), azelaic (C9), and sebacic (C10) acids. Total carbon numbers for the category members

range from C12 to C32. The sponsor justified the category based on structural and molecular weight similarities and carbon numbers. Representative structures of diesters category members are depicted in the appendix.

In the revised submission, the sponsor included adipic acid, bis[2-(2-butoxyethoxy)ethyl]ester (CAS No. 141-17-3) as an additional category member. However, EPA considered that the chemical structure and physical-chemical properties of this chemical are different from the other category members. In addition, the sponsor did not submit toxicity data to compare it with the other category members. EPA requested further justification or removal of this chemical from the category. The sponsor did not submit the requested information to justify the inclusion of this chemical in the category, therefore, EPA did not consider this chemical in this hazard characterization document.

Supporting Chemicals Justification

The sponsor provided data using the following supporting substances for several SIDS endpoints:

Supporting Chemicals	CAS No.	Endpoint(s) Supporting
Maleic acid, dibutyl ester	105-76-0	Aquatic toxicity to fish, daphnia and algae; Repeated-dose/reproductive/developmental and genetic toxicity
Adipic acid, dibutyl ester	105-99-7	Aquatic toxicity to fish, daphnia and algae
Adipic acid, di-C7-9 branched and linear alkyl ester	68515-75-3	Repeated-dose/reproductive/developmental toxicity and genetic toxicity
Adipic acid, bis(2-ethylhexyl) ester	103-23-1	Biodegradation; Chronic aquatic toxicity to daphnia; Reproductive/developmental toxicity, genetic toxicity, and carcinogenicity

EPA agreed that these chemicals, which range in carbon number from C12 to C22, are appropriate supporting chemicals based on similarities in chemical structure and physical-chemical properties. Maleic acid, dibutyl ester, adipic acid, dibutyl ester, and adipic acid bis(2-ethylhexyl) ester were assessed under the OECD HPV Chemicals Programme and the assessments have been published on the UNEP websites (http://www.chem.unep.ch/irptc/sids/OECDSIDS/105760.pdf) and (http://www.chem.unep.ch/irptc/sids/OECDSIDS/105997.pdf) and (http://www.chem.unep.ch/irptc/sids/OECDSIDS/103231.pdf). Adipic acid, di-C7-9 branched and linear alkyl ester was submitted to the U.S. EPA HPV Chemicals Program (http://www.epa.gov/chemrtk/pubs/summaries/hexanedi/c14079tc.htm). In addition to supporting the Diesters Category for the endpoints listed above, maleic acid, dibutyl ester (C12); adipic acid, di-C7-9 branched and linear alkyl ester (C20-C24); and adipic acid, bis(2-ethylhexyl) ester (C22) each have a full hazard, exposure and risk characterization because they are part of EPA's commitment under the Security and Prosperity Partnership.

Hazard Characterization

Most members of the diester category are colorless to pale straw-colored liquids at room temperature. Vapor pressure and water solubility of esters in this category range from negligible to moderate.

The environmental fate parameters of category members are dependent on the number of carbons in the parent diacid and the total number of carbons in the ester. In general, members of the diester category partition primarily to sediment, soil, and water. They are moderately volatile from water and moist soil surfaces. Soil mobility ranges from minimal to high, with higher molecular weight compounds tending to be less mobile. Atmospheric photodegradation ranges from slow to moderate. All members of the diester category undergo hydrolysis at rates that are considered slow to negligible.

Ready biodegradability tests conducted on category members and supporting compounds indicate that the potential for these compounds to persist in the environment is low (P1). Estimated BCF values suggest that members of the category have a low potential to bioaccumulate (B1). Although a high BCF was estimated for maleic acid, bis(1,3-dimethylbutyl) ester, its potential for bioconcentration is expected to be low (B1) due to metabolism by biota.

The aquatic toxicity data for category members with low solubility were generated using Water Accommodated Fractions or dispersion by propeller techniques. The evaluation of available toxicity data indicates that the potential acute hazard to fish is moderate for the maleic acid esters and the C12 adipic acid and sebacic acid esters (based on C14 supporting chemical data) and low for esters above C20 (due to low water solubility). The potential acute hazard of the diester category members to aquatic invertebrates is low and to aquatic plants is moderate in the C12 to C20 range and low above C20. The potential chronic toxicity hazard of the diester category members at and above C22 is low, based on supporting chemical data.

The acute toxicity of the category members is low for the oral and dermal routes. Systemic toxicity in the oral and dermal repeated-dose toxicity studies for category members and for the C12 and C20 supporting chemicals in rats and dogs is low. Oral prenatal developmental toxicity studies for the category members and for the C20 supporting chemical in rats showed low developmental and maternal toxicity. A prenatal developmental toxicity study on the C22 supporting chemical, that included an assessment of postnatal growth and development, also showed low developmental and maternal toxicity, as well as low reproductive toxicity. Likewise, a combined repeated-dose/reproductive/developmental toxicity screening study in rats on the C12 supporting chemical showed low maternal toxicity, and no developmental or reproductive toxicity. A one-generation reproductive toxicity study on the C22 supporting chemical showed no reproductive toxicity. Likewise, numerous repeated-dose toxicity studies in rats on the category members as well as several supporting chemicals with examination of various reproductive organs and endpoints all showed no evidence of reproductive toxicity, with the exception of one study, which showed low reproductive toxicity. The tested category members or supporting chemicals did not induce gene mutation or chromosomal aberrations. Data indicate that the supporting chemicial, maleic acid, dibutyl ester, is a strong sensitizer. IARC has classified the supporting chemical, adipic acid, bis (2-ethylhexyl) ester, into Group 3 (substances not classifiable as to its carcinogenicity to humans).

Melting point, vapor pressure and water solubility for certain category members (see section 1) and chronic aquatic toxicity of maleic acid, bis(1,3-dimethyl butyl) ester were identified as data gaps under the HPV Challenge Program.

1. Physical-Chemical Properties and Environmental Fate

The physical-chemical properties of compounds in the diester category are summarized in Table 1a, while their environmental fate properties are given in Table 1b. The structures of the compounds are provided in the Appendix.

Physical-Chemical Properties Characterization

Members of the diester category are generally colorless to pale straw-colored liquids at room temperature although some constituents may be solid materials. The maleic acid esters in this category have moderate vapor pressure and low water solubility. The vapor pressure and water solubility of adipic acid esters in this category range from negligible to moderate. The two azelaic acid esters have low vapor pressure and negligible water solubility and the two sebacic acid esters have low to moderate vapor pressure and moderate water solubility.

The estimated melting point data provided for adipic acid, bis(1-methylheptyl) ester; adipic acid ditridecyl ester; and azelaic acid, diisodecyl ester are not adequate for the purposes of the HPV Challenge Program. Only measured data are acceptable for melting point values above 0°C.

Estimated vapor pressure values are not acceptable under the HPV Challenge Program for compounds with values greater than 1.5×10^{-5} Pa at room temperature. Therefore, the estimated data provided by the submitter for maleic acid, bis(1,3-dimethylbutyl)ester; maleic acid, bis (2-ethylhexyl) ester; adipic acid, diisopropyl ester; adipic acid, bis (1-methylheptyl)ester; adipic acid, ditridecyl ester; azelaic acid, diisodecyl ester; sebacic acid, dimethyl ester; and sebacic acid, bis (2ethylhexyl) ester are not adequate for the purposes of the HPV Challenge Program.

Estimated water solubilities greater than 1 ppb are not acceptable for the purposes of the HPV Challenge Program. Therefore, the estimated data provided for maleic acid, bis(1,3-dimethylbutyl)ester; adipic acid, diisopropyl ester; adipic acid, dibutyl ester; and adipic acid, bis(1-methylheptyl) ester are not adequate for the purposes of the HPV Challenge Program.

Environmental Fate Characterization

The environmental fate parameters for the members of the diesters category are dependent both on the number of carbons in the parent diacid and the total number of carbons in the ester. Members of the diester category are expected to partition primarily to sediment, soil, and water, according to the results of a Level III fugacity model that assumes equal emissions to air, water, and soil. Lower molecular weight compounds tend to partition to soil and water, while the higher molecular weight compounds typically partition to the sediment compartment. All members of the diester category are considered moderately volatile from water and moist soil surfaces. The rate of hydrolysis is considered slow to negligible at environmental pH.

The maleic acid esters (unsaturated C_4-parent diacid) have a minimal to moderate soil mobility, with lower mobility resulting as the molecular weight increases. In the atmosphere, indirect photooxidation by the hydroxyl radical ranges from slow to moderate, with the larger ester being more rapidly photodegraded.

Soil mobility of the adipic acid esters (saturated C_6-parent diacid) decreases from high to minimal as the total number of carbons in the ester increases. In the atmosphere, indirect photooxidation by the hydroxyl radical ranges from slow to moderate, with the larger ester being more rapidly photodegraded. The soil mobility of the two azelaic acid esters (saturated C_9-parent diacid) included in the category is minimal. In the atmosphere, they are moderately photodegraded by the hydroxyl radical.

The two sebacic acid esters (saturated C_{10}-parent diacid) have a minimal to moderate mobility in soil, with mobility decreasing as the total number of carbons in the ester increases. In the atmosphere, indirect photooxidation by the hydroxyl radical ranges from slow to moderate, with the larger ester being more rapidly photodegraded.

Ready biodegradability tests conducted on category members and supporting chemicals indicate that the potential for these compounds to persist in the environment is low (P1). Estimated BCF values suggest that members of the category have a low potential to bioaccumulate (B1). Although a high BCF was estimated for maleic acid, bis(1,3-dimethylbutyl) ester, its potential for bioconcentration is expected to be low (B1) due to metabolism by biota.

Table 1a. Physical-Chemical Properties of the Diester Category[1]

Chemical	CAS No.	Molecular Weight	Physical State	Melting Point	Boiling Point	Vapor Pressure (mm Hg)	Water Solubility (mg/L)	Henry's Law Constant[2]	Log K_{ow}
Maleic acid, dibutyl ester (C12) (Supporting Chemical)	105-76-0	228	Liquid	**-60°C (measured)**	**277–280°C at 988 hPa (measured)**	**<7.5 x 10-3 at 20°C (measured)**	**173 at 20°C (measured)**	9.7×10^{-8} atm m^3/mol (estimated)	**3.38 (measured)**
Maleic acid, bis(1,3-dimethylbutyl) ester (C16)	105-52-2	284	Liquid	-28.3°C (estimated)	292.1°C (estimated)	Data Gap 0.003 at 25°C (estimated)	Data Gap 0.2 at 25°C (estimated)	1.5×10^{-6} atm·m^3/mol (estimated)	5.8 (estimated)
Maleic acid, bis(2-ethylhexyl) ester (C20)	142-16-5	341	Liquid	**-60°C (measured)**	**164°C at 10 mmHg (measured)** 360°C (estimated)	Data Gap 7.2×10^{-5} at 25°C (estimated)	0.001 at 25°C (estimated)	2.2×10^{-6} atm·m^3/mol (estimated)	7.9 (estimated)
Adipic acid, diisopropyl ester (C12)	6938-94-9	230	Liquid	**-1°C (measured)**	**120°C at 6.5 mm Hg (measured)** 241°C (estimated)	Data Gap 0.04 at 25°C (estimated)	Data Gap 55.6 at 25°C (estimated)	1.3×10^{-6} atm·m^3/mol (estimated)	3.2 (estimated)
Adipic acid, dibutyl ester (C14) (Supporting Chemical)	105-99-7	258	Liquid	**-32°C (measured)**	**165°C at 10 mm Hg (measured)** 294°C (estimated)	0.003 at 25°C (estimated)	4.2 at 25°C (estimated)	9.3×10^{-7} atm m^3/mol (estimated)	4.33 (estimated)
Adipic acid, di-C_7-C_9 branched and linear alkyl ester (C20-24) (Supporting Chemical)	68515-75-3	356-413	Viscous liquid or solid	No Data[3]	**224°C at 9.75 mmHg (measured)**	**9.75 at 224°C (measured)** 0.09 at 25°C (estimated)	**< 0.048 at 25°C (measured)**	1.8×10^{-5} atm m^3/mol (estimated)	**> 6.48 (measured)**
Adipic acid, diisooctyl ester (C22)	1330-86-5	370	Colorless or amber liquid	**-70°C (measured)**	**205–220°C at 4 mm Hg (measured)** 379°C (estimated)	**< 0.12 at 150°C (measured)** 2.6×10^{-5} at 25°C (estimated)	0.00054 at 25°C (estimated)	2.1×10^{-5} atm·m^3/mol (estimated)	8.12 (estimated)

Table 1a. Physical-Chemical Properties of the Diester Category[1]

Chemical	CAS No.	Molecular Weight	Physical State	Melting Point	Boiling Point	Vapor Pressure (mm Hg)	Water Solubility (mg/L)	Henry's Law Constant[2]	Log K_{ow}
Adipic acid, bis(1-methylheptyl) ester (C22)	108-63-4	370	Liquid	Data Gap 9.0°C (estimated)	**175°C at 2 mm Hg (measured)** 379°C (estimated)	Data Gap 2.7×10^{-5} at 25°C (estimated)	Data Gap 0.005 at 25°C (estimated)	4.1×10^{-5} atm·m^3/mol (estimated)	8.1 (estimated)
Adipic acid, bis(2-ethylhexyl) ester (C22) (Supporting Chemical)	103-23-1	371	Colorless or pale amber liquid[4]	**-67.8°C (measured)**	**417°C (measured)**	**1.58 ´ 10^{-2} at 100°C (measured)** **8.5×10^{-7} at 20°C (measured)[5]**	**0.0032 (measured)**	1.3×10^{-5} atm m^3/mol (estimated)	8.12 (estimated)
Adipic acid, diisononyl ester (C24)	33703-08-1	399	Liquid	**-60°C (measured)**	**233°C at 5 mm Hg (measured)** 416°C (estimated)	**0.9 at 200°C (measured)** 2.2×10^{-5} at 25°C (estimated)	**0.00022 at 20°C (measured)**	2.9×10^{-5} atm·m^3/mol (estimated)	9.24 (estimated)
Adipic acid, diisodecyl ester (C26)	27178-16-1	427	Liquid	**-71°C (measured)**	**239–246°C at 4 mm Hg (measured)** 426°C (estimated)	**0.0013 at 20°C (measured)**	**4.4×10^{-5} at 20°C (measured)**	8.5×10^{-5} atm·m^3/mol (estimated)	10.1 (estimated)
Adipic acid, ditridecyl ester (C32)	16958-92-2	511	Solid	Data Gap 140.5°C (estimated)	509.2°C (estimated)	Data Gap 1.4×10^{-7} at 25°C (estimated)	3.4×10^{-9} at 25°C (estimated)	4.7×10^{-4} atm·m^3/mol (estimated)	No Data[6]

Table 1a. Physical-Chemical Properties of the Diester Category[1]

Chemical	CAS No.	Molecular Weight	Physical State	Melting Point	Boiling Point	Vapor Pressure (mm Hg)	Water Solubility (mg/L)	Henry's Law Constant[2]	Log K_{ow}
Azelaic acid, bis(2-ethylhexyl) ester (C25)	103-24-2	413	Colorless liquid[2]	**-78°C (measured)**	**237°C at 5 mm Hg (measured)** 414°C (estimated)	**5 at 237°C (measured)** 1.66×10^{-5} at 25°C (estimated)	Insoluble in water[2] 1.6×10^{-5} at 25°C (estimated)	6.0×10^{-5} atm·m^3/mol (estimated)	9.6 (estimated)
Azelaic acid, diisodecyl ester (C29)	28472-97-1	469	Solid	Data Gap 82.6°C (estimated)	460.4°C (estimated)	Data Gap 7.6×10^{-8} at 25°C (estimated)	1.5×10^{-7} at 25°C (estimated)	2.4×10^{-4} atm·m^3/mol (estimated)	No Data[6]
Sebacic acid, dimethyl ester (C12)	106-79-6	230	Viscous liquid or solid	**38°C (measured)**	**175°C at 22 mm Hg (measured)** 260°C (estimated)	Data Gap 0.01 at 25°C (estimated)	**120 (measured)**	5.1×10^{-7} atm·m^3/mol (estimated)	3.4 (estimated)
Sebacic acid, bis (2-ethylhexyl) ester (C26)	122-62-3	427	Pale straw-colored liquid[2]	**-48°C (measured)**	**212°C at 1 mmHg (measured) 256°C at 5 mmHg (measured)** 422°C (estimated)	Data Gap 2.0×10^{-6} at 25°C (estimated)	**0.02% at 20°C (measured)[2]**	8.5×10^{-5} atm·m^3/mol (estimated)	**3.74 (measured)**

[1]American Chemistry Council Aliphatic Esters Panel. 2003. Robust Summary for the Aliphatic Esters Category. http://www.epa.gov/chemrtk/pubs/summaries/alipestr/c13466tc.htm.

[2]US EPA. 2008. Estimation Programs Interface Suite™ for Microsoft® Windows, v3.20. United States Environmental Protection Agency, Washington, DC, USA. http://www.epa.gov/opptintr/exposure/pubs/episuite.htm.

[3]The substance is a complex mixture; the melting point will change depending on composition and therefore a value was not estimated.

[4]HSDB. 2008. Hazardous Substances Data Bank. As cited in records for di-2-ethylhexyl maleate, diisooctyl adipate, di-2-ethylhexyl azelate, bis(2-ethylhexyl) sebacate, bis(2- ethylhexyl) adipate, accessed June 3, 2008. http://toxnet.nlm.nih.gov/.

[5]From OECD SIDS Dossier for adipic acid, bis(2-ethylhexyl) ester. http://www.chem.unep.ch/irptc/sids/OECDSIDS/103231.pdf.

[6]The estimated value provided by the sponsor is greater then the range (-4 to 10) where KOWWIN v. 1.66 estimates a have been shown to be valid. It is reasonable to conclude that this prediction is indicative that the log Kow for this chemical is high (> 4).

Table 1b. Environmental Fate Properties of the Diester Category[1]

Chemical	CAS No.	Photo-degradation Half-life	Hydrolyis Half-life	Biodegradation	Bio-concentration[2]	K_{oc}[2]	Fugacity (Level III Model)	Persistence[3]	Bioaccumulation[3]
Maleic acid, dibutyl ester (C12) (Supporting Chemical)	105-76-0	0.33 days (estimated)	**2,870 hours (pH 7, 25°C) 50 hours (pH 9, 25°C)**	**95% in 19 days Readily biodegradable**	BCF = 80 (estimated)	126 (estimated)	Soil = 55.9% Air = 2.7% Water = 39.3% Sediment = 2.2%	P1 (low)	B1 (low)
Maleic acid, bis(1,3-dimethylbutyl) ester (C16)	105-52-2	0.23 days (estimated)	12.2 years at pH 7 1.2 years at pH 8 (estimated)	95% in 19 days Readily biodegradable (RA)	BCF = 6,156 (estimated)[4]	791 (estimated)	Soil = 37.3% Air = 0.9% Water = 16.4% Sediment = 45.3%	P1 (low)	B1 (low)
Maleic acid, bis(2-ethylhexyl) ester (C20)	142-16-5	0.19 days (estimated)	190 days at pH 7 19 days at pH 8 (estimated)	95% in 19 days Readily biodegradable (RA)	BCF = 105 (estimated)	14,300 (estimated)	Soil = 29.6% Air = 1.1% Water = 11.2% Sediment = 58.1%	P1 (low)	B1 (low)
Adipic acid, diisopropyl ester (C12)	6938-94-9	1.03 days (estimated)	2.3 years at pH 7 85 days at pH 8 (estimated)	95% in 19 days Readily biodegradable (RA)	BCF = 59 (estimated)	89 (estimated)	Soil = 58.8% Air = 2.7% Water = 38% Sediment = 0.6%	P1 (low)	B1 (low)
Adipic acid, dibutyl ester (C14) (Supporting Chemical)	105-99-7	0.84 days (estimated)	2.1 years at pH 7 75.4 days at pH 8 (estimated)	**90% in 14 days Readily biodegradable[5]**	BCF =43 (estimated)	429 (estimated)	Soil = 68.3% Air = 2.94% Water = 24.6% Sediment = 4.08%	P1 (low)	B1 (low)
Adipic acid, di-C_7-C_9 branched and linear alkyl ester (C20) (Supporting Chemical)	68515-75-3	0.45 days (estimated) **Direct Photolysis = 0% in 14 days (measured)**	2.5 years at pH 7 92 days at pH 8 (estimated)	67–88% in 28 days Inherently biodegradable	BCF =616 (estimated)	12,230 (estimated)	Soil = 27.3% Air = 0.3% Water = 3.6% Sediment = 68.8%	P1 (low)	B1 (low)
Adipic acid, diisooctyl ester (C22)	1330-86-5	0.45 days (estimated)	2.1 years at pH 7 75 days at pH 8 (estimated)	**87% in 28 days Readily biodegradable**	BCF = 61 (estimated)	40,370 (estimated)	Soil = 27.3% Air = 0.3% Water = 3.5% Sediment = 69%	P1 (low)	B1 (low)
Adipic acid, bis(1-methylheptyl) ester (C22)	108-63-4	0.42 days (estimated)	2.3 years at pH 7 85 days at pH 8 (estimated)	87–90% Readily biodegradable (RA)	BCF = 61 (estimated)	44,310 (estimated)	Soil = 29.5% Air = 1.2% Water = 11.1% Sediment = 58.2%	P1 (low)	B1 (low)

Table 1b. Environmental Fate Properties of the Diester Category[1]

Chemical	CAS No.	Photo-degradation Half-life	Hydrolyis Half-life	Biodegradation	Bio-concentration[2]	K_{oc}[2]	Fugacity (Level III Model)	Persistence[3]	Bioaccumulation[3]
Adipic acid, bis(2-ethylhexyl) ester (C22) (Supporting Chemical)	103-23-1	0.4 days (estimated)	3.2 years at pH 7 117 days at pH 8 (estimated)	**83% in 28 days Readily biodegradable[6]**	**BCF = 27 (measured)[6]**	48,630 (estimated)	Soil = 31.4% Air = 1.0% Water = 10.8% Sediment = 56.8%	P1 (low)	B1 (low)
Adipic acid, diisononyl ester (C24)	33703-08-1	0.4 days (estimated)	4.6 years at pH 7 169 days at pH 8 (estimated)	**73% in 28 days Readily biodegradable**	BCF = 3.2 (estimated)	195,500 (estimated)	Soil = 28.8% Air = 0.6% Water = 7.2% Sediment = 63.4%	P1 (low)	B1 (low)
Adipic acid, diisodecyl ester (C26)	27178-16-1	0.36 days (estimated)	2.1 years at pH 7 75 days at pH 8 (estimated)	**76.5% in 28 days Readily biodegradable**	BCF = 3.9 (estimated)	467,200 (estimated)	Soil = 28.5% Air = 0.2% Water = 3.4% Sediment = 67.9%	P1 (low)	B1 (low)
Adipic acid, ditridecyl ester (C32)	16958-92-2	0.28 days (estimated)	4.6 years at pH 7 169 days at pH 8 (estimated)	**57–60% in 28 days Not readily biodegradable**	BCF = 3.2 (estimated)	26,180,000 (estimated)	Soil = 31% Air = 0.4% Water = 7% Sediment = 61.7%	P1 (low)	B1 (low)
Azelaic acid, bis(2-ethylhexyl) ester (C25)	103-24-2	0.36 days (estimated)	4.6 years at pH 7 169 days at pH 8 (estimated)	**81% in 28 days 95% in 28 days[5] Readily biodegradable**	BCF = 3.2 (estimated)	305,100 (estimated)	Soil = 28.4% Air = 0.6% Water = 7.2% Sediment = 63.8%	P1 (low)	B1 (low)
Azelaic acid, diisodecyl ester (C29)	28472-97-1	0.32 days (estimated)	2.1 years at pH 7 75.4 days at pH 8 (estimated)	81–95% Readily biodegradable (RA) 69% in 7 days (primary biodegradation)	BCF = 3.2 (estimated)	2,931,000 (estimated)	Soil = 29.8% Air = 0.2% Water = 7.2% Sediment = 63.8%	P1 (low)	B1 (low)
Sebacic acid, dimethyl ester (C12)	106-79-6	1.1 days (estimated)	3.6 years at pH 7 133 days at pH 8 (estimated)	65% in 28 days Not readily biodegradable (RA)	BCF = 76 (estimated)	126.2 (estimated)	Soil = 60.1% Air = 2.5% Water = 36.7% Sediment = 0.7%	P1 (low)	B1 (low)
Sebacic acid, bis (2-ethylhexyl) ester (C26)	122-62-3	0.35 days (estimated)	7.1 years at pH 7 258 days at pH 8 (estimated)	65% in 28 days Not readily biodegradable	BCF = 4 (estimated)	562,800 (estimated)	Soil = 28.7% Air = 0.5% Water = 7.2% Sediment = 63.6%	P1 (low)	B1 (low)

[1]American Chemistry Council Aliphatic Esters Panel. 2003. Robust Summary for the Aliphatic Esters Category. http://www.epa.gov/chemrtk/pubs/summaries/alipestr/c13466tc.htm.

Table 1b. Environmental Fate Properties of the Diester Category[1]

Chemical	CAS No.	Photo-degradation Half-life	Hydrolyis Half-life	Biodegradation	Bio-concentration[2]	K_{oc}[2]	Fugacity (Level III Model)	Persistence[3]	Bioaccumulation[3]

[2]US EPA. 2008. Estimation Programs Interface Suite™ for Microsoft® Windows, v3.20. United States Environmental Protection Agency, Washington, DC, USA. http://www.epa.gov/opptintr/exposure/pubs/episuite.htm.

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

[4]Although a high BCF (6,156) was estimated for maleic acid, bis(1,3-dimethylbutyl) ester CAS No. 105-52-2, it's potential for bioconcentration is expected to be low (B1) due to metabolism by biota.

[5]NITE 2006. Chemical Risk Information Platform (CHRIP). Biodegradation and Bioconcentration (version 2006.01.30). National Institute of Technology and Evaluation. http://www.safe.nite.go.jp/english/kizon/KIZON_start_hazkizon.html.

[6]From OECD SIDS Dossier for adipic acid, bis(2-ethylhexyl) ester. http://www.chem.unep.ch/irptc/sids/OECDSIDS/103231.pdf.

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.

Acute Toxicity to Fish

In comments on the revised test plan (May 2006), EPA stated that the submitter needed to provide measured acute aquatic toxicity data for the lower molecular weight adipate diesters (e.g., C12). In-depth review of the category chemicals and the supporting chemicals revealed that the use of maleic acid, dibutyl ester (C12; CAS No. 105-76-0) as supporting for the two maleic acid category members is appropriate because they are all predicted by ECOSAR to be toxic via acrylate-type toxicity. The use of adipic acid, dibutyl ester (C14; CAS No. 105-99-7) is a reasonable analog to support the other C12 category members (adipic acid, diisopropyl ester, CAS No. 6938-94-9 and sebacic acid, dimethyl ester, CAS No. 106-79-6) because they are all predicted by ECOSAR to be toxic via ester-type toxicity and the analog is expected to be the most toxic of the three.

Maleic acid, dibutyl ester (CAS No. 105-76-0; supporting chemical) (C12)
Rainbow trout (*Oncorhynchus mykiss*) were exposed to maleic acid, dibutyl ester at 0, 1.0, 1.7, 3.0, 5.2, and 9.0 mg/L for 96 hours. At 48 hours, the concentration of the test substance had decreased to 33% of nominal concentration; therefore, the concentrations were readjusted to 100%. By 96 hours, the concentrations had again decreased to 35% of nominal. Incoordination of swimming movements and darker color were seen at the two highest concentrations five hours after exposure and later at all concentrations. Mortality was seen at all concentrations at 96 hours. The robust summary reports an LC_{50} of 0.6 mg/L, based on the geometric mean of the nominal and measured concentrations. However, LC_{50} based on nominal concentration has previously been accepted by the OECD HPV Chemicals Programme and is therefore used in this hazard characterization.
96-h LC_{50} = 1.2 mg/L

Adipic acid, dibutyl ester (CAS No. 105-99-7; supporting chemical) (C14)
Medaka (*Oryzias latipes*) were exposed to dibutyl adipate at five nominal concentrations from 1.0 – 10 mg/L under semi-static conditions for 96 hours. DMSO:HC 40 (9:1) (dimethylsulfoxide:hydrogenated castor oil 40) was used as a vehicle. No additional information was provided.
96-h LC_{50} = 3.7 mg/L

Adipic acid, diisononyl ester (CAS No. 33703-08-1) (C24)
Rainbow trout (*Oncorhynchus mykiss*) were exposed to adipic acid, diisononyl ester as a water accommodated fraction (WAF) at a loading rate of 100 mg/L (measured concentration of 2.6 mg/L) under semi-static conditions for 96 hours. No effects were noted at the WAF loading rate. 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) which for adipic acid, diisononyl ester, the no effect concentration would be approximately 2.2×10^{-4} mg/L.
No effects at saturation

Sebacic acid, bis(2-ethylhexyl)ester (CAS No. 122-62-3)(C26)
Golden orfe (*Leuciscus idus*) were exposed to sebacic acid, bis(2-ethylhexyl)ester as a WAF at a loading rate of 1,000 mg/L under semi-static conditions for 96 hours. No analytical measurements were made on the WAFs. No mortality was seen. 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), which for sebacic acid, bis(2-ethylhexyl)ester, the no effect concentration would be approximately 1.5×10^{-7} mg/L.
No effects at saturation

Adipic acid, ditridecyl ester (CAS No. 16958-92-2) (C32)
Sheepshead minnow (*Cyprinodon variegates*, 20/concentration*)* were exposed to adipic acid, ditridecyl ester at nominal concentrations of 0, 500, 1000, 2500 and 5000 mg/L under static conditions for 96 hours. No analytical measurements were made. Five fish died at 2500 mg/L and 20 fish died at 5000 mg/L (possibly due to physical toxicity). The results of this test are difficult to interpret because the substance was tested considerably above its water solubility limit (3.4×10^{-9} mg/L).
LC_{50} at or below water solubility limit

Acute Toxicity to Aquatic Invertebrates

Maleic acid, dibutyl ester (CAS No. 105-76-0; supporting chemical) (C12)
Daphnia magna (20/concentration) were exposed to maleic acid, dibutyl ester at 0, 10, 18, 32, 56 and 100 mg/L under static conditions for 48 hours. Measured concentrations were 95% and 91% of the initial concentrations at 24 and 48 hours, respectively.
48-h EC_{50} = 21 mg/L

Adipic acid, dibutyl ester (CAS No. 105-99-7; supporting chemical) (C14)
Daphnia magna were exposed to dibutyl adipate at five nominal concentrations from 5.6 – 56 mg/L for 24 hours. DMSO:HC 40 (9:1) was used as a vehicle. No additional information was provided.
24-h EC_{50} = 17 mg/L

Sebacic acid, bis(2-ethylhexyl)ester (CAS No. 122-62-3)(C26)
Daphnia magna were exposed to sebacic acid, bis(2-ethylhexyl)ester as a WAF using a loading rate of 1000 mg/L under static conditions for 48 hours. No immobilization was observed. No analytical measurements were made on the WAFs. 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) which for sebacic acid, bis(2-ethylhexyl)ester, the no effect concentration would be approximately 1.5×10^{-7} mg/L.
No effects at saturation

Toxicity to Aquatic Plants

Maleic acid, dibutyl ester (CAS No. 105-76-0; supporting chemical) (C12)
Green algae (*Scenedesmus subspicatus*) were exposed to maleic acid, dibutyl ester at nominal concentrations ranging from 0.4 – 12.8 mg/L under static condition for 72 hours. At the end of the test, measured concentrations decreased to 43.4% at lower concentrations. Because of the poor recovery at low concentrations, the only nominal concentrations were reported. Although 43% recovery of the test substance at lower concentrations recommends against use of nominal concentrations, this study was accepted in the OECD HPV Chemicals Programme and published on the UNEP website.
72-h EC_{50} = 6.2 mg/L

Adipic acid, dibutyl ester (CAS No. 105-99-7; supporting chemical) (C14)
Green algae (*Pseudokirchneriella supcapitata*) were exposed to dibutyl adipate at 5 nominal concentrations from 1 – 5 mg/L for 72 hours. No additional information was provided.
72-h EC_{50} (biomass) = 2.8 mg/L

Sebacic acid, bis(2-ethylhexyl)ester (CAS No. 122-62-3) (C26)
Green algae (*Scenedesmus subspicatus*) were exposed to sebacic acid, bis(2-ethylhexyl)ester as WAF a loading rate of 1000 mg/L for 72 hours. Although percent inhibition (according to biomass/AUC) was 1%, the sponsor concluded that there was no inhibition of algae growth. No analytical measurements were made on the WAFs. 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) which for sebacic acid, bis(2-ethylhexyl)ester, the no effect concentration would be approximately 1.5×10^{-7} mg/L.
No effects at saturation

Chronic Toxicity to Aquatic Organisms

In test plan comments, EPA indicated that chronic toxicity of maleic acid, bis(1,3-dimethyl butyl) ester be tested to clarify the trend from acute to chronic toxicities. This data was not provided and remains a data gap under the HPV Challenge Program.

EPA used chronic toxicity to aquatic invertebrates data for the supporting chemical, adipic acid, bis(2-ethylhexyl) ester, which has water solubility (0.0032 mg/L) and log K_{ow} (est. 8.12), to assess potential chronic toxicity of higher molecular weight (C20 and above) diesters. The study was briefly described in the Robust Summaries for the Diesters Category and additional details provided to EPA by the Aliphatic Esters Panel allowed determination of the adequacy of the test.

Adipic acid, bis(2-ethylhexyl) ester (CAS No. 103-23-1; supporting chemical)

Water flea (*Daphnia magna*) were exposed to the supporting chemical, adipic acid, bis(2-ethylhexyl) ester, at measured concentration of 0.00436 mg/L. No effects were observed on survival, growth or reproduction. (http://www.epa.gov/chemrtk/pubs/summaries/alipestr/c13466tc.htm).

No effects at saturation

Conclusion: The aquatic toxicity data for category members with low solubility were generated using Water Accommodated Fractions or dispersion by propeller techniques. The evaluation of available toxicity data indicates that the potential acute hazard to fish is moderate for the maleic acid esters and the C12 adipic acid and sebacic acid esters (based on C14 supporting chemical data) and low for esters above C20 (due to low water solubility). The potential acute hazard of the diester category members to aquatic invertebrates is low and to aquatic plants is moderate in the C12 to C20 range and low above C20. The potential chronic toxicity hazard of the diester category members above the C20 range is low, based on supporting chemical data.

Table 2. Summary of Environmental Effects – Aquatic Toxicity Data[1]

Endpoints	Maleic acid, bis(1,3-di methyl butyl) ester (C16) (105-52-2)	Maleic acid, bis(2-ethylhexyl) ester (C20) (142-16-5)	Adipic acid, diisopropyl ester (C12) (6938-94-9)	Sebacic acid, dimethyl ester (C12) (106-79-6)	Adipic acid, bis (1-methyl heptyl) ester (C22) (108-63-4)	Adipic acid, diisooctyl ester (C22) (1330-86-5)	Adipic acid, diisononyl ester (C24) (33703-08-1)	Azelaic acid, bis(2-ethylhexyl) ester (C25) (103-24-2)	Adipic acid, diisodecyl ester (C26) (27178-16-1)	Sebacic acid, bis(2-ethylhexyl) ester (C26) (122-62-3)	Azelaic acid, diisodecyl ester (C29) (28472-97-1)	Adipic acid, ditridecyl ester (C32) (16958-92-2)
Fish 96-h LC_{50} (mg/L)	No data 1.2 (RA)[2]	No data 1.2 (RA)[2]	No data 3.7 (RA)[3]	No data 3.7 (RA)[3]	No data NES (RA)	No data NES (RA)	**NES**	No data NES (RA)	No data NES (RA)	**NES**	No data NES (RA)	**NES (~3.4 x 10^{9})**
Aquatic Invertebrates 48-h EC_{50} (mg/L)	No data 21 (RA)[2]	No data 21 (RA)[2]	No data 17 (RA)[3]	No data 17 (RA)[3]	No data NES (RA)	No data NES (RA)	No data NES (RA)	No data NES (RA)	No data NES (RA)	**NES**	No data NES (RA)	No data NES (RA)
Aquatic Plants 72-h EC_{50} (mg/L)	No data 6.2 (RA)[2]	No data 6.2 (RA)[2]	No data 2.8 (RA)[3]	No data 2.8 (RA)[3]	No data NES (RA)	No data NES (RA)	No data NES (RA)	No data NES (RA)	No data NES (RA)	**NES**	No data NES (RA)	No data NES (RA)
Chronic Toxicity to Aquatic Invertebrates 21-d NOEC (mg/L)	No Data	No Data	No Data	No Data	No data NES (RA)[4]	No data NES (RA)[4]	No Data NES (RA)[4]	No Data NES (RA)[4]	No Data NES (RA)[4]	No Data NES (RA)[4]	No Data NES (RA)[4]	No Data NES (RA)

Measured data (bold); (RA) = Read Across
NES = No effects at saturation (water solubility limit)
[1]Compounds arranged according to carbon.
[2]Data for supporting chemical: maleic acid, dibutyl ester (CAS No. 105-76-0; C12).
[3]Data for supporting chemical: adipic acid, dibuty ester (CAS No. 105-99-7; C14).
[4]Data for supporting chemical: adipic acid, bis(2ethylhexyl) ester (CAS No. 103-23-1; C22).

3. 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.

Acute Oral Toxicity

For the category members, the LD_{50} values range from > 2000 (azelaic acid, diisodecyl ester, CAS No. 28472-97-1) to > 64,000 mg/kg-bw (adipic acid, bis(1-methylheptyl) ester, CAS No. 108-63-4). Individual LD_{50} values are provided in Table 3.

Acute Dermal Toxicity

Adipic acid, diisononyl ester (CAS No. 33703-08-1) (C24)
Rabbits (4/dose, strain not stated) were administered undiluted adipic acid, diisononyl ester dermally at 50, 200, 794 and 3,160 mg/kg-bw to clipped, abraded abdominal skin for 24 hours and observed for 14 days. No mortality was seen. Slight irritation (slight edema and slight to moderate erythema) was seen at the application site.
LD_{50} > 3160 mg/kg-bw

Adipic acid, ditridecyl ester (CAS No. 16958-92-2) (C32)
New Zealand white rabbits (10 animals, sex not stated) were administered undiluted adipic acid, ditridecyl ester dermally at 5000 mg/kg-bw to abraded skin under semi-occlusive conditions for 24 hours and observed for 14 days. No mortality was seen. Clinical signs consisted of edema, erythema, bloated abdomen, diarrhea, emaciation and lethargy.
LD_{50} > 5000 mg/kg-bw

Repeated-Dose Toxicity

Maleic acid, dibutyl ester (CAS No. 105-76-0; supporting chemical) (C12)
In a combined repeated-dose/reproductive/developmental toxicity screening study, Wistar rats (12/sex/dose) were administered maleic acid, dibutyl ester in arachis oil via gavage at 0, 30, 95 and 300 mg/kg-bw/day during the premating (2 weeks) and mating periods (10 days). Females were then allowed to litter normally and sacrificed with the offspring on day 4 of lactation. Dosing of both sexes continued until the end of the study. Parental toxicity was determined by evaluation of body weight and food consumption changes, necropsy and organ weight analyses, and histopathology of selected tissues. Males were also evaluated for changes in hematology and clinical chemistry. At 300 mg/kg-bw/day, the rats of both sexes had unspecific signs of 'reduced well-being' and increased absolute and/or relative liver and kidney weights. Also at 300 mg/kg-bw/day, males showed a higher incidence of dermal hyperemia, lower body weights, higher albumin, higher total protein, higher bilirubin and decreased mean corpuscular hemoglobin and renal tubular lesions (dilation, epithelial basophila, and epithelial proliferation and karyomegaly). One high-dose female had heart, kidney and liver lesions and lost its litter due to lack of nursing.
LOAEL (systemic toxicity) = 300 mg/kg-bw/day (based on multiple effects in adult animals, with the kidney and liver as the main target organs)
NOAEL (systemic toxicity) = 95 mg/kg-bw/day

Adipic acid, di-C7-9 branched and linear alkyl ester (CAS No. 68515-75-3; supporting chemical)(C20)
In a repeated-dose toxicity study, Sprague-Dawley rats (number unspecified) were administered adipic acid, di-C7-9 branched and linear alkyl ester at 2.5% in the diet (approximately 1,500 mg/kg-bw/day in male rats; 1,950 mg/kg-bw/day in female rats) for 13 weeks (90 days). No other details were provided. No systemic toxicity was reported and no adverse effects to male or female reproductive organs were observed. No other effects were indicated.
NOAEL (systemic toxicity) = 2.5% in the diet (approximately 1,500 mg/kg-bw/day for males; 1950 mg/kg-bw/day in females)

Adipic acid, diisononyl ester (CAS No. 33703-08-1) (C24)
(1) In a repeated-dose toxicity study, rats (10/sex/dose, strain not indicated) were administered adipic acid, diisononyl ester in the diet at 0, 50, 150 or 500 mg/kg-bw/day for 13 weeks. Clinical observations, body weights

and food consumption were recorded weekly. Hematology, blood chemistry and urinalysis were evaluated at weeks 4 and 13. A complete necropsy was performed after 13 weeks. Tissues were examined microscopically. A statistically significant (p-level not provided) increase in the kidney weight relative to body weight was seen at 500 mg/kg-bw/day; however, there was no increase in the absolute kidney weights and no histopathological or blood chemistry changes were observed, therefore, this effect was not considered to be treatment-related. No other effects were reported.
NOAEL (systemic toxicity) = 500 mg/kg-bw/day

(2) In a repeated-dose toxicity study, Beagle dogs (4/sex/dose) were administered adipic acid, diisononyl ester in the diet at 0, 0.3, 1.0 and 3.0 percent (approximately 82.2, 274 and 822 mg/kg-bw/day) for 13 weeks. The high dose was adjusted to 6.0 percent (1644 mg/kg-bw/day) during weeks 9–13. Animals were observed daily and body weights and food consumption determined weekly. Hematology, blood chemistry and urinalysis were performed at the start of the study and at weeks 4 and 13, with a complete necropsy after 13 weeks. Organ weights were taken and tissues/organs were examined microscopically. Decreased food consumption and body weight, increased liver weight and enzyme activities, discoloration of liver and kidney and histopathological changes in the liver and kidneys were seen at the high dose.
LOAEL (systemic toxicity) = ~ 822/1644 mg/kg-bw/day (based on decreased body weights and food consumption, increased liver weight, and enzyme levels and histopathological changes in the liver and kidneys)
NOAEL (systemic toxicity) = ~ 274 mg/kg-bw/day

Sebacic acid, bis(2-ethylhexyl) ester (CAS No. 122-62-3) (C26)
In a repeated-dose toxicity study, Fischer 344 rats (males; 4 treated and 13 control) were administered sebacic acid, bis(2-ethylhexyl) ester in the diet at 2% (~1000 mg/kg-bw/day) for 3 weeks. The study focused on measuring peroxisome proliferation. Liver size and weight were measured and sections of liver were examined for peroxisome proliferation. Cholesterol and triglycerides levels and carnitine acetyltransferase and catalase activities in serum were measured. Results showed that hepatic peroxisome proliferation had occurred and liver weight and hepatic peroxisomal enzymes were increased. Decreases in triglycerides were also seen.
LOAEL (systemic toxicity) = 1,000 mg/kg-bw/day (based on peroxisome proliferation and related effects)
NOAEL(systemic toxicity) = Not established

Adipic acid, ditridecyl ester (CAS No. 16958-92-2) (C32)
In a repeated-dose toxicity study similar to OECD 411, Sprague-Dawley rats (10/sex/dose) were administered undiluted adipic acid, ditridecyl ester dermally at 0, 800 or 2000 mg/kg-bw for 5 days/week for 13 weeks. Mortality, clinical observations, body weights, hematology, serum chemistry, necropsy and gross and microscopic evaluations were conducted. Sperm morphology was evaluated. Dermal absorption was determined to be 10% as measured using ^{14}C-radiolabeled compound in a separate group of rats. No treatment-related effects were seen on sperm morphology, uterus or epididymides weights, urinalysis or macroscopic evaluation. Increased liver and kidney weights were seen in the absence of histopathology or serum chemistry changes and therefore, were not considered to be treatment-related. Slight erythema and flaking of the skin were observed in both dose groups at the application sites. No other effects were reported.
NOAEL (systemic toxicity) = 2,000 mg/kg-bw/day

Reproductive Toxicity

Maleic acid, dibutyl ester (CAS No. 105-76-0; supporting chemical) (C12)
In the combined repeated-dose/reproductive/developmental toxicity screening study in Wistar rats described previously, fertility parameters, gestation parameters and reproductive organ toxicity were evaluated. A single female exhibited heart, kidney and liver lesions at the high dose and lost its entire litter due to lack of nursing behavior; excluding this loss, one additional pup died at the highest dose. The number of dead pups was statistically significantly higher (p level not given) in the mid- and high-dose groups. No other information was provided. No other effects were reported and no effects on reproductive organs or on reproductive performance were observed.
NOAEL (reproductive toxicity) = 300 mg/kg-bw/day

Adipic acid, di-C7-9 branched and linear alkyl ester (CAS No. 68515-75-3; supporting chemical) (C20)
In the 13 week (90 days) repeated-dose toxicity study in Sprague-Dawley rats described previously, gonad weights, examination of testes, seminal vesicles, ovary, prostate, and uterus was conducted at the high dose and

histopathological examination of the testes and ovaries was conducted at all dose levels. No adverse effects on reproductive organs were observed at doses up to 1950 mg/kg-bw/day.

Adipic acid, bis (2-ethylhexyl) ester (103-23-1; supporting chemical)(C22)
(1) In a repeated-dose toxicity study in which male reproductive toxicity was assessed under conditions of renal disease, Fisher 344 rats (males only) were administered adipic acid, bis (2-ethylhexyl) ester in the diet at doses of 0, 6,000, or 25,000 ppm (approximately 0, 600, 2500 mg/kg-bw/day) for 4 weeks following five consecutive weekly subcutaneous injections of folic acid (for induction of chronic renal dysfunction) (Nabae et al., 2006). Control animals received adipic acid, bis (2-ethylhexyl) ester in the diet but without folic acid pretreatment. Endpoints included body weight, and organ and histopathological examination of the kidneys, testes, epididymides, prostate and seminal vesicles. Spermatogenesis was also evaluated. No effects were observed on any parameters measured in any dose groups.
NOAEL (male reproductive toxicity) = 25,000 ppm (or 2500 mg/kg-bw/day)

(2) In a repeated-dose toxicity study, Sprague-Dawley rats were administered by gavage 0, 40, 200, and 1000 mg/kg-bw/day adipic acid, bis (2-ethylhexyl) ester for 28 days from 8 weeks of age (Miyata et al., 2006). General signs and clinical observations were recorded daily. Body weight and food consumption were also recorded. Clinical chemistry, hematology, hormone analysis, spermatology, estrous cycling, and necroscopic and histopathological examination of organs were conducted. Effects observed included disturbance of the estrous cycle and increased ovarian follicle atresia at 1000 mg/kg-bw/day. Increased liver weight, without histopathology, was also observed in male and female rats at 1000 mg/kg-bw/day. In male rats only, increased kidney weight and histopathological changes (increased eosinophilic bodies and hyaline droplets) were observed at 1000 mg/kg-bw/day. Male rat kidney weight was also increased at 200 mg/kg-bw/day, but in the absence of any histopathology. Therefore, this is not considered to be treatment-related. Additionally, since it cannot be determined from the study whether the observed kidney effects are male rat specific, it is not clear whether or not these effects are relevant to humans, therefore, they are not being considered here. Also, it was not specified in the study if the liver/kidney weight changes were relative or absolute. No other effects were reported.
LOAEL (female reproductive toxicity) = 1,000 mg/kg-bw/day (based on disturbance of the estrous cycle and increased ovarian follicle atresia)
NOAEL (female reproductive toxicity) = 200 mg/kg-bw/day
NOAEL (male reproductive toxicity) = 1000 mg/kg-bw/day

(3) In a one-generation reproductive toxicity study, male and female Sprague-Dawley rats were administered 0, 300, 1,800, and 12,000 ppm (approximately 0, 23, 1,200, and 2,400 mg/kg-bw/day) adipic acid, bis (2-ethylhexyl) ester in the diet for 10 weeks prior to mating and continuing in the females for an additional 8-9 weeks until the production of one generation of offspring. No other details were provided. No effects were seen on male or female fertility parameters. Signs of maternal toxicity consisted of decreases in body weight at 2,400 mg/kg-bw/day. Signs of developmental toxicity consisted of decreases in offspring body weight, total litter weight, and litter size at 2,400 mg/kg-bw/day. No other effects were observed.
NOAEL (adult/reproductive toxicity) = 2,400 mg/kg-bw/day
LOAEL (maternal/developmental toxicity) = 2,400 mg/kg-bw/day (based on decreases in body weight in dams; and decreases in body weight, total litter weight and litter size in offspring)
NOAEL (maternal/developmental toxicity) = 1,200 mg/kg-bw/day

(4) In a study similar in design to an OECD Test Guideline 426 Developmental Neurotoxicity Study, pregnant Wistar rats were administered 0, 200, 400, or 800 mg/kg-bw/day adipic acid, bis (2-ethylhexyl) ester from gestation day 7 to pup age day 17 (Dalgaard et al., 2003). Pregnancy data, prenatal and postnatal growth and development, and endpoints of relevance for antiandrogenic effects were also included. From gestation day 21, the animals were inspected twice daily until delivery. Following delivery, body weights of dams and individual pup weights were recorded. Pups were counted, sexed, and checked for anomalies; any found dead were examined macroscopically. The day of delivery was designated postnatal day (PND) 0 (or gestation day 21). One male and one female from each litter were kept after weaning for investigation of sexual maturation, hormone and sperm analysis, and histopathology at adulthood. The pups were randomly selected and housed in pairs of the same sex and same exposure status. Assessment of postnatal development of the pups was conducted by examining the following parameters: body weights (PND 3 and 13), anogenital distance (PND 3), presence of nipples (PND13 and 14), and evidence of sexual maturation (vaginal opening in females, balano-preputial cleavage in males). At PND 21, the

remaining pups and dams were euthanized and examined macroscopically, organs were weighed and examined microscopically (in males only), and the numbers of uterine implantations sites were counted in the dams. Effects observed included a prolonged gestation period at 800 mg/kg-bw/day, a dose-related increase in postnatal deaths at 400 and 800 mg/kg-bw/day (with statistical significance at 800 mg/kg-bw/day), and a permanent decrease in offspring body weight at 800 mg/kg-bw/day (in both sexes during the lactation period as well as in adult males). No antiandrogenic endpoints were affected, that is, no effects on endocrine related endpoints such as anogenital distance, nipple retention, sexual maturation, hormone levels, sperm parameters, organ weights/histopathology of the reproductive system were observed. No other effects were reported.
LOAEL (reproductive toxicity) = 800 mg/kg-bw/day (based on prolonged gestation)
NOAEL (reproductive toxicity) = 400 mg/kg-bw/day

Adipic acid, ditridecyl ester (CAS No. 16958-92-2)(C32)
In the 13-week repeated-dose dermal toxicity study in Sprague-Dawley rats described previously, approximately 10% of the compound was absorbed through the skin. No treatment-related effects were seen in sperm morphology, uterus or epididymides weights or histopathology at doses up to 2,000 mg/kg-bw/day.

Developmental Toxicity

Maleic acid, dibutyl ester (CAS No. 105-76-0; supporting chemical) (C12)
In the combined repeated-dose and reproductive/developmental toxicity screening study in Wistar rats described previously, measurements in the offspring included clinical signs, litter weight, number, sex, viability and necropsy. At 300 mg/kg-bw/day, in the parental generation, rats of both sexes had unspecific signs of 'reduced well-being' and increased absolute and/or relative liver and kidney weights. A single female also exhibited heart, kidney and liver lesions at this dose and lost its entire litter due to lack of nursing behavior; excluding this loss, one additional pup died at the highest dose (300 mg/kg-bw/day). The number of dead pups was statistically significantly higher (p-level not provided) in the mid and high doses. No other information was provided and no other effects were reported. It should be noted that the summary of this study in the SIDS document was limited and provided few details regarding the pup deaths, especially at the mid-dose group. Pup deaths observed at the high-dosed group of 300 mg/kg-bw/day were attributable to lack of nursing behavior in a single dam and therefore not considered to be treatment-related. However, no explanation was provided in the SIDS summary of this study to explain the pup deaths reported at the mid-dose group. In light of the lack of information for this observed effect from the summary of this study provided in the SIDS document, and the fact that the original study cannot be obtained, the pup deaths reported at the mid-dose group of 95 mg/kg-bw/day were not considered in characterizing the developmental toxicity of maleic acid, dibutyl ester at this time.
LOAEL (maternal toxicity) = 300 mg/kg-bw/day (based on increased kidney and liver weights and general decreased health status)
NOAEL (maternal toxicity) = 95 mg/kg-bw/day
NOAEL (developmental toxicity) = 300 mg/kg-bw/day

Adipic acid, di-C7-9 branched and linear alkyl ester (CAS No. 68515-75-3; supporting chemical)(C20)
In a prenatal developmental toxicity study, pregnant Sprague-Dawley rats were administered adipic acid, di-C7-9 branched and linear alkyl ester at 0, 1000, 4000 and 7000 mg/kg-bw/day during gestation days (GD) 6–19. Clinical signs and body weights were recorded on GD 0, 6, 15 and 20. On GD 20, the dams were sacrificed and uteri were removed and weighed. Fetuses were weighed and examined for external, skeletal and soft tissue defects. Sex ratios of fetuses were determined and numbers of implantations, live fetuses, resorptions and corpora lutea were evaluated. The maternal body weights were significantly decreased ($p < 0.01$) at 7000 mg/kg-bw/day. Although fetal body weights were slightly lower than the control at 7000 mg/kg-bw/day, the difference was not statistically significant. The incidence of rudimentary structures (unilateral/bilateral and adjacent to the last thoracic or first lumbar vertebral transverse process) was higher in the high-dose fetuses compared with other doses. There was no indication as to whether this effect was statistically significant.
LOAEL (maternal toxicity) = 7,000 mg/kg-bw/day (based on decreased maternal weight)
NOAEL (maternal toxicity) = 4,000 mg/kg-bw/day
LOAEL (developmental toxicity) = 7,000 mg/kg-bw/day (based on skeletal anomalies and decreased fetal weight)
NOAEL (developmental toxicity) = 4,000 mg/kg-bw/day

Adipic acid, bis (2-ethylhexyl) ester (103-23-1; supporting chemical)(C22)

(1) In a study similar in design to an OECD Test Guideline 426 Developmental Neurotoxicity Study described previously, pregnant Wistar rats were administered 0, 200, 400, or 800 mg/kg-bw/day adipic acid, bis (2-ethylhexyl) ester from gestation day 7 to pup age day 17 (Dalgaard et al., 2003). Effects observed included a prolonged gestation period at 800 mg/kg-bw/day, a dose-related increase in postnatal deaths at 400 and 800 mg/kg-bw/day (with statistical significance at 800 mg/kg-bw/day), and a permanent decrease in offspring body weight at 800 mg/kg-bw/day (in both sexes during the lactation period as well as in adult males). No antiandrogenic endpoints were affected, that is, no effects on endocrine related endpoints such as anogenital distance, nipple retention, sexual maturation, hormone levels, sperm parameters, organ weights/histopathology of the reproductive system were observed. No other effects were reported.
LOAEL (maternal toxicity) = 800 mg/kg-bw/day (based on prolonged gestation)
NOAEL (maternal toxicity) = 400 mg/kg-bw/day
LOAEL (developmental toxicity) = 400 mg/kg-bw/day (based on increased postnatal deaths)
NOAEL (developmental toxicity) = 200 mg/kg-bw/day

(2) In a prenatal developmental toxicity study, pregnant Sprague-Dawley rats were administered 0, 300, 1,800, and 12,000 ppm (approximately 0, 28, 170, and 1,080 mg/kg-bw/day) adipic acid, bis (2-ethylhexyl) ester in the diet on gestation days 1-22. No other details were provided. Signs of maternal toxicity consisted of decreases in body weight and food consumption and increases in implantation losses at the highest dose group of 1,080 mg/kg-bw/day. Signs of developmental toxicity consisted of ureteral malformations and skeletal abnormalities at doses of 170 mg/kg-bw/day and higher. No other details were provided and no other effects were reported. This study was available in summary form only and limited details on study parameters and results were provided. The results of this study were not observed in the previously described developmental toxicity on adipic acid, bis (2-ethylhexyl) ester, which appeared to be a more robust study and which also used a dose range close to the 170 mg/kg-bw/day. Therefore, the adequacy of this study is questionable and was not considered in evaluating the developmental toxicity in the hazard characterization.

Adipic acid, ditridecyl ester (16958-92-2)(C32)

(1) In a prenatal developmental toxicity screen, pregnant Sprague-Dawley rats (15/dose) were administered undiluted adipic acid, ditridecyl ester dermally at 0, 800 or 2,000 mg/kg-bw/day from gestation day 0–19. Dams were examined daily for mortality and clinical signs of toxicity. Body weights and food consumption were measured throughout gestation and all females were sacrificed and examined macroscopically on day 20. Uteri were weighed, examined for number of corpora lutea, number of implantation sites, and number/location of fetuses and resorptions. Number, sex, weight, length, and defects (external, visceral, and skeletal) were recorded. Blood chemistry was evaluated at gestation day 20. No other study details were available. No adverse effects were reported in the dams. In fetuses, visceral anomalies (increased incidence of levocardia) were seen at 2,000 mg/kg-bw/day. However, subsequent studies with a larger number of pregnant animals (n=25) did not show visceral anomalies or levocardia; and no developmental toxicity was observed in the following study (below) at 2,000 mg/kg-bw/day.
NOAEL (maternal toxicity) = 2,000 mg/kg-bw/day (based on no effects at the highest dose tested)
LOAEL (developmental toxicity) = 2,000 mg/kg-bw/day (based on increased incidence of levocardia)
NOAEL (developmental toxicity) = 800 mg/kg-bw/day

(2) In a prenatal developmental toxicity study, pregnant Sprague-Dawley rats (25/dose) were administered 0 or 2,000 mg/kg-bw of undiluted adipic acid, ditridecyl ester dermally from day 0–19 of gestation. Dams were examined daily for mortality and clinical signs of toxicity. Body weights and food consumption were measured throughout gestation and all females were sacrificed and examined macroscopically on day 20. Uteri were weighed, examined for number of corpora lutea, number of implantation sites, and number/location of fetuses and resorptions. Number, sex, weight, and defects (external, visceral, and skeletal) were recorded. No maternal or developmental effects were observed.
NOAEL (maternal/developmental toxicity) = 2,000 mg/kg-bw/day (based on no effects at the only dose tested)

Genetic Toxicity – Gene Mutations

In vitro

Maleic acid, dibutyl ester (CAS No. 105-76-0; supporting chemical) (C12)

Salmonella typhimurium strains TA97a, TA98, TA100 and TA1535A were exposed to maleic acid, dibutyl ester at concentrations up to 500 µg/plate with and without metabolic activation. Positive and negative controls were used and yielded the expected results. Toxicity was observed at 500 µg/plate. The test compound did not show increased mutations in any strain or at any concentration.

Maleic acid, dibutyl ester was not mutagenic in this assay.

Adipic acid, di-C7-9 branched and linear alkyl ester (CAS No. 68515-75-3; supporting chemical) (C22)

(1) *Salmonella typhimurium* strains TA98, TA100, TA1535 and TA1537 were exposed to adipic acid, di-C7-9 branched and linear alkyl ester up to 10 µl/plate (with 25 µL/plate as a spot test) with and without metabolic activation. Positive controls were used, with ethanol as the solvent control. No mutagenicity was observed up to 25 µL/plate. Decreased solubility was observed at 3 and 10 µL in the plate incorporation method.

Adipic acid, di-C7-9 branched and linear alkyl ester was not mutagenic in this assay.

(2) Mouse lymphoma L5178Y TK+/- cells were exposed to adipic acid, di-C7-9 branched and linear alkyl ester up to 3000 µg/mL without metabolic activation and up to 4000 µg/mL with metabolic activation. Cytotoxicity occurred at 500 µg/mL and higher without activation and at 4000 µg/mL with activation. None of the concentrations yielded higher mutation frequencies than the solvent controls.

Adipic acid, di-C7-9 branched and linear alkyl ester was not mutagenic in this assay.

Adipic acid, diisononyl ester (CAS No. 33703-08-1) (C24)

(1) *Salmonella typhimurium* strains TA98, TA100, TA1535, TA1537 and TA1538 were exposed to adipic acid, diisononyl ester at concentrations up to 1,000 µg/plate with and without metabolic activation. Revertant colonies were scored at 72 hours. The positive and negative controls gave expected responses. There was no increase in revertant colonies with or without metabolic activation.

Adipic acid, diisononyl ester was not mutagenic in this assay.

(2) Mouse lymphoma L5178Y cells were exposed to adipic acid, diisononyl ester at 5.6 - 100 µL/mL with metabolic activation and 7.5 - 100 µL/mL without metabolic activation. Mutant colonies per total colony counts were determined using triplicate plates. The positive and negative controls gave expected responses. The compound was negative for mutagenicity both with and without metabolic activation.

Adipic acid, diisononyl ester was not mutagenic in this assay.

Sebacic acid, bis(2-ethylhexyl)ester (CAS No. 122-62-3)(C26)

Salmonella typhimurium strains TA98, TA100, TA1535, TA1537 and TA1538 were exposed to sebacic acid, bis(2-ethylhexyl) ester at concentrations up to 10,000 µg/plate, with and without metabolic activation. The positive and negative controls gave expected responses. Precipitate was observed at 3,333 and 10,000 µg/plate with TA1535, but no toxicity was observed. The compound was negative for mutagenicity both with and without metabolic activation.

Sebacic acid, bis(2-ethylhexyl) ester was not mutagenic in this assay.

Adipic acid, ditridecyl ester (CAS No. 16958-92-2)(C32)

Salmonella typhimurium strains TA98, TA100, TA1535, TA1537 and TA1538 were exposed to adipic acid, ditridecyl ester at concentrations up to 10 µL/plate with and without metabolic activation. The positive and negative controls gave expected responses. The compound was negative for mutagenicity both with and without metabolic activation.

Adipic acid, ditridecyl ester was not mutagenic in this assay.

Adipic acid, bis (2-ethylhexyl) ester (CAS No. 103-23-1)(C22)

(1) Adipic acid, bis (2-ethylhexyl) ester was part of an assessment of a large database of chemicals comparing rodent carcinogenicity data with results from a battery of in vitro genotoxicity tests that included an Ames mouse lymphoma assay, an in vitro micronucleus assay, and a chromosomal aberrations test (Kirkland et al., 2005). Adipic acid, bis (2-ethylhexyl) ester was negative in the Ames and micronucleus assays, with an equivocal result in the chromosomal aberrations test.

(2) Adipic acid, bis (2-ethylhexyl) ester is reported to be negative for mutagenic potential with or without metabolic activation for the following: a reverse mutation tests with *Salmonella typhimurium* or *Escherichia coli* strains; an Ames test using urine from Sprague-Dawley rats given adipic acid, bis (2-ethylhexyl) ester by oral gavage at 2,000 mg/kg-bw/day for 15 days; a DNA repair test with primary rat hepatocyte cultures; a reverse mutation test using mouse lymphoma cells; and in the BALB 3T3 cell transformation assay.
Adipic acid, bis (2-ethylhexyl) ester was not mutagenic in these assays.

Genetic Toxicity – Chromosomal Aberrations

In vivo
Maleic acid, dibutyl ester (CAS No. 105-76-0; supporting chemical) (C12)
Three groups of NMRI mice (5/sex) were administered maleic acid, dibutyl ester via gavage at 2,000 mg/kg-bw/day and were sacrificed at 24, 48 and 72 hours and micronucleated erythrocytes were evaluated in the bone marrow. The ratio of polychromatic erythrocytes (PCEs) to total erythrocytes was not changed by the treatment. Slight increases in micronucleated erythrocytes were observed but were not statistically significant; results at 24 and 48 hours were slightly higher than historical controls. Based on these results, the authors indicated the results as negative, but also stated that a slight clastogenic effect could not be excluded.
Maleic acid, dibutyl ester did not induce chromosomal aberrations in this assay.

Adipic acid, bis (2-ethylhexyl) ester (CAS No. 103-23-1)(C22)
Adipic acid, bis (2-ethylhexyl) ester is reported to be negative in either sex in a micronucleus test in bone marrow cells from B6C3F1 mice given singly or by two repeated administrations and in a sex-linked recessive lethal assay in Drosophilia melanogaster. In a dominant lethal test in male ICR mice treated intraperitoneally, adipic acid, bis (2-ethylhexyl) ester affected spermatogenesis, decreased pregnancy rate, and increased early embryonic death at 9,200 mg/kg-bw/day.

Adipic acid, ditridecyl ester (CAS No. 16958-92-2) (C32)
Male and female Sprague-Dawley rats were administered undiluted adipic acid, ditridecyl ester dermally at 0, 800 and 2000 mg/kg-bw to clipped dorsal skin for 5 days/week for 13 weeks. Normochromatic and polychromatic erythrocytes (NCEs and PCEs) were evaluated for cytotoxicity and micronuclei formation using bone marrow and peripheral blood cells. The ratio of PCE to NCE and numbers of micronucleated PCEs per 1000 PCEs and micronucleated NCEs per 1000 NCEs were determined. No positive controls were used. No animals died and no cytotoxicity of peripheral red blood cells was observed. No increases in micronucleated NCEs/PCEs and no other effects were observed.
Adipic acid, ditridecyl ester did not induce chromosomal aberrations in this assay.

Additional Information

Skin Sensitization

Maleic acid, dibutyl ester (CAS No. 105-76-0; supporting chemical) (C12)
Albino guinea pigs were administered maleic acid, dibutyl ester in a Magnusson-Kligman guinea pig maximization test. Six injections were given to 10 control (corn oil) and 20 test animals (10% test substance in corn oil and Freund's adjuvant) at different locations. After one and two weeks intervals, 100% of the test substance was administered topically for 24 hours. Eighty percent of the test animals showed erythema at 24 hours after the 2-week challenge versus no response in control animals. The study authors concluded that the test substance exhibited a strong sensitizing effect.
Maleic acid, dibutyl ester was a strong sensitizer in this assay.

Carcinogenicity

Adipic Acid, bis (2-ethylhexyl) ester (CAS No. 103-23-1)(C22)
In a 103-week carcinogenicity study, adipic acid, bis (2-ethylhexyl) ester was administered in the diet to male and female B6C3F1 mice (6 weeks of age) and Fisher 344 rats (5 weeks of age) at dietary concentrations of 0, 12,000, and 25,000 ppm (approximately 0, 1,080, and 3,750 mg/kg-bw/day in mice; 0, 600, and 1,250 mg/kg-bw/day in

rats). An increased incidence of hepatocellular carcinoma and adenoma was observed in female mice in the 1,080 mg/kg-bw/day groups and higher; and in male mice in the 3,750 mg/kg-bw/day. Hepatocellular tumor incidence did not increase in the rats. IARC has classified adipic acid, bis (2-ethylhexyl) ester into Group 3 (substances not classifiable as to its carcinogenicity to humans), since proliferation of peroxisome seen in rodents has not been observed in primates and no relevant human epidemiological data are available.

Conclusion: The acute toxicity of the category members is low for the oral and dermal routes. Systemic toxicity in the oral and dermal repeated-dose toxicity studies for category members and for the C12 and C20 supporting chemicals in rats and dogs is low. Oral prenatal developmental toxicity studies for the category members and for the C20 supporting chemical in rats showed low developmental and maternal toxicity. A prenatal developmental toxicity study on the C22 supporting chemical, that included an assessment of postnatal growth and development, also showed low developmental and maternal toxicity, as well as low reproductive toxicity. Likewise, a combined repeated-dose/reproductive/developmental toxicity screening study in rats on the C12 supporting chemical showed low maternal toxicity, and no developmental or reproductive toxicity. A one-generation reproductive toxicity study on the C22 supporting chemical showed no reproductive toxicity. Likewise, numerous repeated-dose toxicity studies in rats on the category members as well as several supporting chemicals with examination of various reproductive organs and endpoints all showed no evidence of reproductive toxicity, with the exception of one study, which showed low reproductive toxicity. The tested category members or supporting chemicals did not induce gene mutation or chromosomal aberrations. Data indicate that maleic acid, dibutyl ester is a strong sensitizer. IARC has classified adipic acid, bis (2-ethylhexyl) ester into Group 3 (substances not classifiable as to its carcinogenicity to humans).

Table 3. Summary of Human Health Data

Endpoints	Maleic acid, bis(1,3di-methylbutyl) ester (C16) (105-52-2)	Maleic acid, bis(2ethyl-hexyl) ester (C20) (142-16-5)	Adipic acid, diisopropyl ester (C12) (6938-94-9)	Sebacic acid, dimethyl ester (C12) (106-79-6)	Adipic acid, diisooctyl ester (C22) (1330-86-5)	Adipic acid, bis(1-methyl heptyl)ester (C22) (108-63-4)	Adipic acid, diisononyl ester (C24) (33703-08-1)	Azelaic acid, bis(2-ethylhexyl) Ester (C25) (103-24-2)	Adipic acid, diisodecyl ester (C26) (27178-16-1)	Sebacic acid, bis(2-ethylhexyl) ester (C26) (122-62-3)	Azelaic acid, diisodecyl ester (C29) (28472-97-1)	Adipic acid, ditridecyl ester (C32) (16958-92-2)
Acute Oral Toxicity LD_{50} (mg/kg-bw)	**7460**	**> 9440**	**> 3110**	No data > 3110 (RA)	**> 4,650 (ml/kg-bw)**	**> 64,000**	**> 10,000**	**7980**	**20,500**	**> 12,800**	**> 2000**	**> 16,000**
Acute Dermal Toxicity LD_{50} (mg/kg-bw)	—*	—*	—*	—*	—*	—*	**> 3160**	—*	—*	—*	—*	**5000**
Repeated-dose Toxicity (mg/kg-bw/day)	No data	No data	No data	No data	No data	No data		No data	No data		No data	
NOAEL	95	95	1500/1950 (males/females) (hdt)	1500/1950 (males/females) (hdt)	(Rat) 150	(Rat) 150	**(Rat) 150**	(Rat) 150	(Rat) 150	**NE**	NE	**NE 2000**
LOAEL	300 (RA)[2]	300 (RA)[2]	(RA)[3]	(RA)[3]	500 (RA)	500 (RA)	**500 (Dog) 274 822/1,644**	500 (RA)	500 (RA)	**1000**	1000 (RA)	
Developmental Toxicity (mg/kg-bw/day)	No data	No data	No data	No data	No data	No data	No data	No data	No data	No data	No data	
Maternal												
NOAEL	95	95	4000	4000	400	400	400	400	400	2000 (hdt)	2000 (hdt)	**2000 (hdt)**
LOAEL	300	300	7000	7000	800	800	800	800	800			
Developmental												
NOAEL	300 (RA)[2]	300 (RA)[2]	4000 7000 (RA)[3]	4000 7000 (RA)[3]	200 400 (RA)[4]	200 400 (RA)[4]	200 400 (RA)[4]	200 400 (RA)[4]	200 400 (RA)[4]	800 2000 (RA)	800 2000 (RA)	**800 2000**
Reproductive Toxicity (mg/kg-bw/day)	No data	No data	No data	No data	No data	No data	No data	No data	No data			
NOAEL	300 (hdt)	300 (hdt)	1950 (hdt)	1950 (hdt)	400	400	400	400	400	2000	2000	**2000 (hdt)**
LOAEL	(RA)[2]	(RA)[2]	(RA)[3]	(RA)[3]	800 (RA)[4]	800 (RA)[4]	800 (RA)[4]	800 (RA)[4]	800 (RA)[4]	(RA)	(RA)	
Genetic Toxicity – Gene Mutations *In vitro*	No data Negative (RA)[2]	No data Negative (RA)[2]	No data Negative (RA)[2]	No data Negative (RA)[2]	No data Negative (RA)[4]	No data Negative (RA)[4]	**Negative**	No data Negative (RA)	No data Negative (RA)	**Negative**	No data Negative (RA)	**Negative**
Genetic Toxicity – Chromosomal Aberrations *In vivo*	No data Negative (RA)[2]	No data Negative (RA)[2]	No data Negative (RA)[2]	No data Negative (RA)[2]	No data Negative (RA)[4]	No data Negative (RA)[4]	No data Negative (RA)[4]	No data Negative (RA)[4]	No data Negative (RA)[4]	No data Negative (RA)	No data Negative (RA)	**Negative**
Additional Info – Sensitization	Positive (RA)[2]	Positive (RA)[2]	—*	—*	—*	—*	—*	—*	—*	—*	—*	—*

Measured data (bold); (RA) = Read Across; NE = not established; — indicates endpoint was not addressed for this chemical; * indicates endpoint not necessary for this chemical; hdt = highest dose tested;
[2]Supporting chemical: maleic acid, dibutyl ester (CAS No. 105-76-0; C12); [3] Supporting chemical: adipic acid, di-C7-9 branched and linear alkyl ester (CAS No. 68515-75-3; C20-24); [4]Supporting chemical: adipic acid, bis (2-ethylhexyl) ester (CAS No. 103-23-1; C22).

4. References

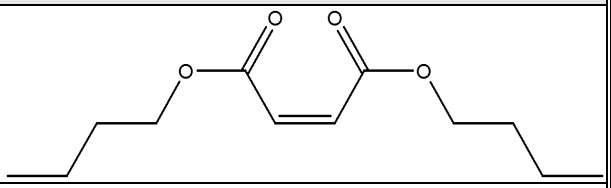
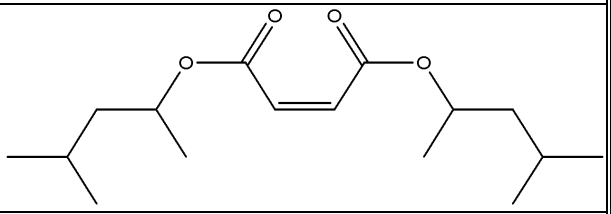
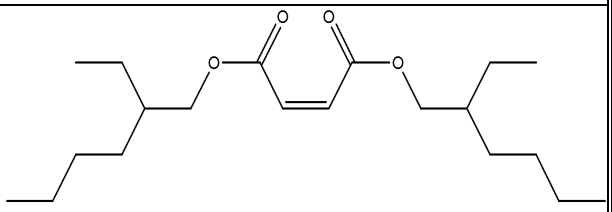
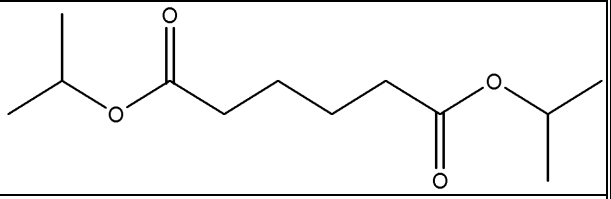
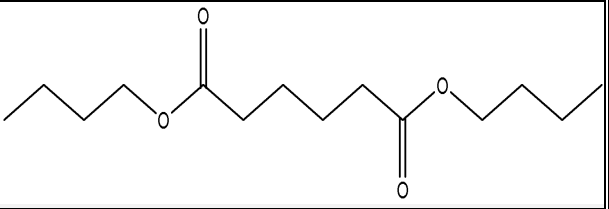
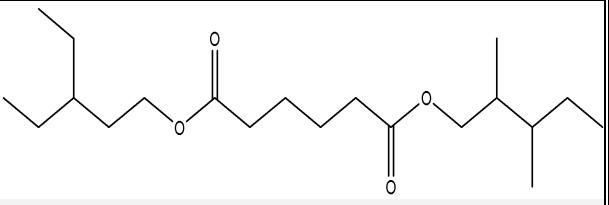
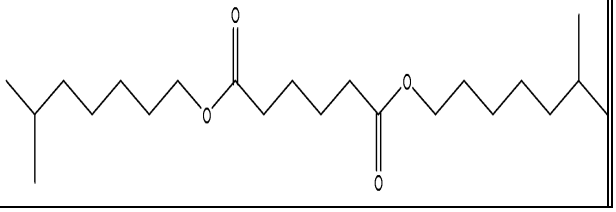
Dalgaard, M., Hass, U., Vinggaard, A.M., Jarfelt, K., Lam, H.R., Sorensen, I.K., Sommer, H.M., and Ladefoged, O. 2003. Di(2-ethylhexyl) adipate (DEHA) induced developmental toxicity but not antiadrogenic effects in pre- and postnatally exposed Wistar rats. Reprod. Toxicol. 17:163-170.

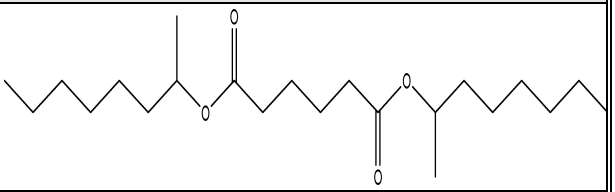
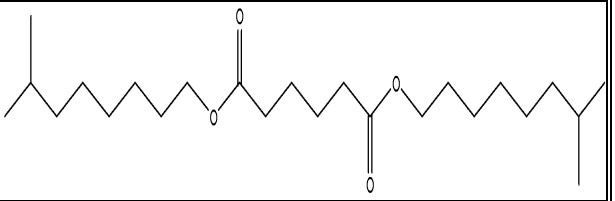
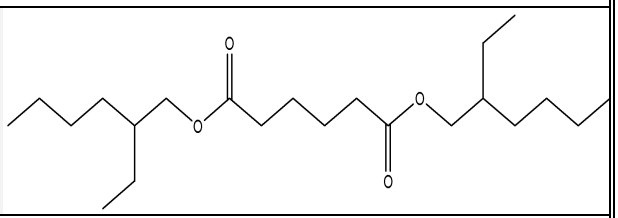
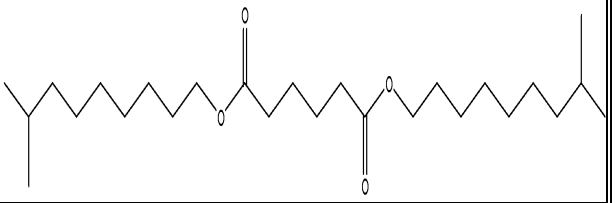
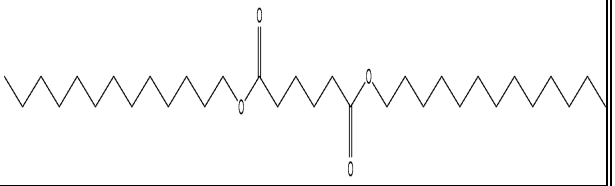
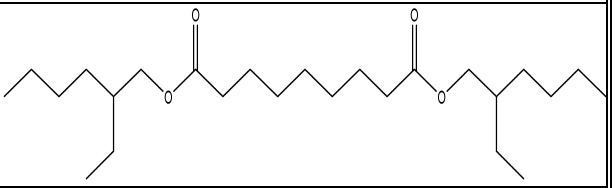
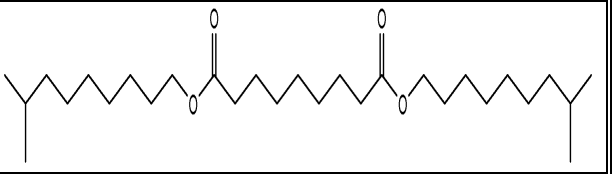
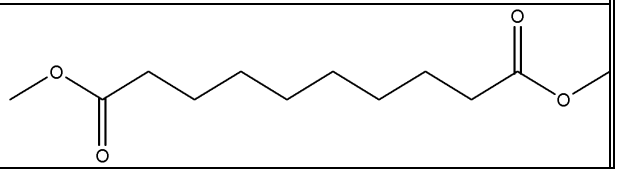
Kirkland, D., Aardema, M., Henderson, L., Muller, L. 2005. Evaluation of the ability of a battery of three in vitro genotoxicity tests to discriminate rodent carcinogens and non-carcinogens I. Sensitivity, specificity, and relative predictivity. 2005. Muta. Res. 584:1-256.

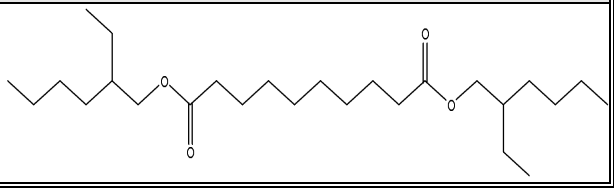
Miyata, K., Shiraishi, K., Houshuyama, S., Imatanaka, N., Umano, T., Minobe, Y., and Yamasaki, K. 2006. Subacute oral toxicity of di(2-ethylhexyl)adipate based on the draft protocol for the "Enhanced OECD Test Guideline no. 407". Arch. Toxicol. 80:181-186.

Nabae, K., Doi, Y., Takahashi, S., Ichihara, T., Toda, C., Ueda, K., Okamato, Y., Kojima, N., Tamano, S., and Shirai, T. 2006. Toxicity of di(2-ethylhexyl) phthalate (DEHP) and di(2-ethylhexyl)adipate (DEHA) under conditions of renal dysfunction induced with folic acid in rats: Enhancement of male reproductive toxicity of DEHP is associated with an increase of the mono-derivative. Reprod. Toxicol. 22:411-417.

APPENDIX

Chemical Name	CAS No.	Structure
Maleic acid, dibutyl ester (C12) (Supporting Chemical)	105-76-0	
Maleic acid, bis(1,3-dimethylbutyl) ester (C16)	105-52-2	
Maleic acid, bis(2-ethylhexyl) ester (C20)	142-16-5	
Adipic acid, diisopropyl ester (C12)	6938-94-9	
Adipic acid, dibutyl ester (C14) (Supporting Chemical)	105-99-7	
Adipic acid, di-C_7-C_9 branched and linear alkyl ester (C20) (Supporting Chemical)	68515-75-3	 (representative structure)
Adipic acid, diisooctyl ester (C22)	1330-86-5	

Chemical Name	CAS No.	Structure
Adipic acid, bis(1-methylheptyl) ester (C22)	108-63-4	
Adipic acid, diisononyl ester (C24)	33703-08-1	
Adipic acid, bis(2-ethylhexyl) ester (C22) (Supporting Chemical)	103-23-1	
Adipic acid, diisodecyl ester (C26)	27178-16-1	
Adipic acid, ditridecyl ester (C32)	16958-92-2	
Azelaic acid, bis(2-ethylhexyl) ester (C25)	103-24-2	
Azelaic acid, diisodecyl ester (C29)	28472-97-1	
Sebacic acid, dimethyl ester (C12)	106-79-6	

Chemical Name	CAS No.	Structure
Sebacic acid, bis(2-ethylhexyl) ester (C26)	122-62-3	

Screening Level Exposure Characterization for HPV Challenge Chemical

Diesters Category

SPONSORED CHEMICALS
CAS #(s): 105-52-2; 142-16-5; 6938-94-9; 1330-86-5; 108-63-4; 33703-08-1; 27178-16-1; 16958-92-2; 103-24-2; 28472-97-1; 106-79-6; 122-62-3;

September 2008

Prepared by

Exposure Assessment Branch
Chemical Engineering Branch
Economics, Exposure and Technology Division
Office of Pollution Prevention and Toxics
Environmental Protection Agency
1200 Pennsylvania Avenue, NW
Washington, DC 20460-0001

Screening Level Exposure Characterization
Diesters Category

Non-CBI Executive Summary

Eleven of the diesters category chemicals have aggregated production and/or import volumes in the range of 26.5 million to 162 million pounds. The aggregated volumes exclude one of the eleven chemicals, adipic acid, bis(1-methylheptyl) ester (CAS# 108-63-4), which does not have Inventory Update Reporting (IUR) submissions.

Non-confidential information in the IUR indicates that these chemicals were manufactured and/or imported at the following companies and sites:

105-52-2:

- Cytec Industries Inc. / Willow Island, WV
- Lynx Chemical Group, LLC / Columbus, GA

142-16-5:

- Celanese Ltd. / Dallas, TX
- Cytec Industries Inc. / Willow Island, WV
- Finetex Inc. / Salisbury, NC
- Lynx Chemical Group, LLC / Columbus, GA
- MFG Chemical, Inc. / Dalton, GA
- Piedmont Chemical Industries Inc / High Point, NC
- Sunoco, Inc. / Pittsburgh, PA
- Velsicol Chemical Corporation / Chestertown, MD

6938-94-9:

- RTD*HallStar / Hacketstown, NJ
- S C Johnson & Son, Inc. / Sturtevant, WI

1330-86-5:

- Teknor Apex / Brownsville, TN

33703-08-1:

- BASF Corporation / Florham Park, NJ
- PolyOne Corporation / Avon Lake, OH
- Sunoco, Inc. / Pittsburgh, PA
- Teknor Apex / Brownsville, TN

27178-16-1:

- Cognis Corporation / Cincinnati, OH
- Croda Inc. / Chicago, ID
- Croda Inc. / New Castle, DE
- Ester Solutions / Bedford Park, IL
- PolyOne Corporation / Avon Lake, OH
- Teknor Apex / Brownsville, TN

16958-92-2:

- BP America Inc. / HOUSTON, TX
- Cognis Corporation / Cincinnati, OH
- Croda Inc. / New Castle, DE
- Ester Solutions / Bedford Park, IL
- Teknor Apex / Brownsville, TN

103-24-2:

- Cognis Corporation / Cincinnati, OH
- Ester Solutions / Bedford Park, IL
- PolyOne Corporation / Avon Lake, OH

28472-97-1:

- BP America Inc. / Wayne, NJ
- Cognis Corporation / Cincinnati, OH
- Croda Inc. / Chicago, ID

106-79-6:

- Ciba Specialty Chemicals Corp. / High Point, NC
- ICC Chemical Corporation / New York, NY

122-62-3:

- Cognis Corporation / Cincinnati, OH
- Ester Solutions / Bedford Park, IL
- PolyOne Corporation / Avon Lake, OH
- The Goodyear Tire & Rubber Company / Marysville, OH
- The Seydel Companies / Greensboro, NC

There may be other companies and sites that are claimed confidential. Non-confidential IUR information indicates that many of the chemicals in the diesters category are used as lubricants in the manufacturing of other basic organic chemicals and all other chemical products and preparations, and as intermediates or functional fluids in various manufacturing processes. Twelve of the sixteen chemicals in this category have IUR submissions that indicate uses in commercial settings or consumer uses.

Information submitted as part of the HPV Challenge Program indicates that diesters chemicals have widespread applications as lubricants, solvents and plasticizers[12].

Potential Exposures to the General Population and the Environment: Based on the information considered, including information found from non-confidential public sources, EPA identifies, for the purposes of risk-based prioritization, a high potential that the general population and the environment might be exposed. The Hazardous Substances Data Bank (HSDB) information for some of these chemicals states that there might be potential releases to the environment from various waste streams. Diester chemicals are not on the Toxics Release Inventory[13].

Persistence and bioaccumulation ratings for these chemicals are P1 and B1. These ratings indicate that these chemicals are not persistent in the environment; and are not bioaccumulative.

Potential Exposures to Workers: Based on the information considered including IUR data, HPV Test Plan and SIDS information, and in combination with Agency's professional judgment, EPA identifies, for the purposes of risk-based prioritization, a medium relative ranking for potential worker exposure. The medium relative ranking is based on the vapor pressure and physical forms of these chemicals, potential dermal exposure during industrial processing and use activities and commercial uses, the number of workers potentially exposed, and the relatively high aggregated production volumes for all chemicals in this category.

Potential Exposures to Consumers: EPA identifies, for the purposes of risk-based prioritization, a high potential that consumers might be exposed based on the use of products containing these chemicals. Ten of the eleven chemicals with IUR submissions are indicated to have uses in commercial settings or consumer uses. The non-confidential consumer uses for many of these chemicals are: rubber and plastic products, and electrical and electronic products.

Potential Exposures to Children: EPA identifies, for the purposes of risk-based prioritization, a high potential that children might be exposed based on the use of products containing these chemicals. Information on two of these chemicals, including maleic acid, bis(2-ethylhexyl) ester (CAS# 142-16-5), adipic acid, diisononyl ester (CAS# 33703-08-1), indicates uses in products intended to be used by children. Reports for three chemicals, including adipic acid, diisodecyl ester (CAS# 27178-16-1), azelaic acid, bis(2-ethylhexyl) ester (CAS# 103-24-2), sebacic acid, bis(2-ethylhexyl) ester (CAS# 122-62-3), indicate that such information was Not Readily Obtainable.

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[12] ACCAEP, 2003. High Production Volume Challenge Program Test Plan for the Diesters Category of the Alpihatic Esters Chemicals. American Chemistry Council's Aliphatic Esters Panel. November 2003. Accessed 6/12/2008 at http://www.epa.gov/chemrtk/pubs/summaries/alipestr/c13466rt.pdf.

[13] USEPA, 2006. Toxics Release Inventory. Accessed, 6/12/08. http://www.epa.gov/tri/.

Below are summaries of non-confidential information in the IUR for each of the individual chemicals in this category.

This exposure characterization was completed using both public, non-confidential sources, and one or more IUR submissions that were available as of this writing.

Non Confidential IUR Data Summary: Maleic acid, bis(1,3-dimethylbutyl) ester (105-52-2)

Manufacturing/Import Information

Production and import volume:	1 million to 10 million pounds
List of non-CBI companies/ sites*:	Cytec Industries Inc. / Willow Island, WV Lynx Chemical Group, LLC / Columbus, GA
Maximum number of potentially exposed workers**:	less than 100 (including those of manufacturing, industrial processing and use)
Highest non-CBI maximum concentration:	up to 100% by weight
Non-CBI physical forms*:	liquid

* There may be other companies/ sites and physical forms that are claimed confidential.
** There may be additional potentially exposed industrial workers that are not included in this estimate since not all submitters were required to report on industrial processing and use and/or there may be at least one use that contains a "Not Readily Obtainable" (NRO) response among the submissions.

Table 1
Industrial Processing and Use Information
Reported in 2006 IUR

Processing Activity	Industrial Sector	Function in Industrial Sector
Processing as a reactant	Other Basic Organic Chemical Manufacturing	Intermediates
Additional line item(s) may be claimed as CBI		

Table 2
Commercial/ Consumer Uses
Reported in 2006 IUR

Commercial/ Consumer Product Category Description	Highest Maximum Concentration Range	Use in Children's Products
Other	Greater than 90%	No
Additional line item(s) may be claimed as CBI		

Non Confidential IUR Data Summary: Maleic acid, bis(2-ethylhexyl) ester (142-16-5)

Manufacturing/Import Information

Production and import volume:	10 million to 50 million pounds
List of non-CBI companies/ sites*:	Celanese Ltd. / Dallas, TX Cytec Industries Inc. / Willow Island, WV Finetex Inc. / Salisbury, NC Lynx Chemical Group, LLC / Columbus, GA MFG Chemical, Inc. / Dalton, GA Piedmont Chemical Industries Inc / High Point, NC Sunoco, Inc. / Pittsburgh, PA Velsicol Chemical Corporation / Chestertown, MD
Maximum number of potentially exposed workers**:	1,000 or greater (including those of manufacturing, industrial processing and use)
Highest non-CBI maximum concentration:	up to 100% by weight
Non-CBI physical forms*:	gas or vapor; liquid

* There may be other companies/ sites and physical forms that are claimed confidential.
** There may be additional potentially exposed industrial workers that are not included in this estimate since not all submitters were required to report on industrial processing and use and/or there may be at least one use that contains a "Not Readily Obtainable" (NRO) response among the submissions.

Table 1
Industrial Processing and Use Information
Reported in 2006 IUR

Processing Activity	**Industrial Sector**	**Function in Industrial Sector**
Processing--incorporation into article	All Other Textile Product Mills	Processing aid, not otherwise listed
Processing--incorporation into article	Other Plastics Product Manufacturing	Processing aid, not otherwise listed
Processing as a reactant	All Other Chemical Product and Preparation Manufacturing	Functional fluids
Processing as a reactant	Soap and Cleaning Compound Manufacturing	Intermediates
Use--nonincorporative activities	Other Basic Organic Chemical Manufacturing	Other
Additional line item(s) may be claimed as CBI		

Table 2 Commercial/ Consumer Uses Reported in 2006 IUR		
Commercial/ Consumer Product Category Description	**Highest Maximum Concentration Range**	**Use in Children's Products**
Fabric, textile and apparel	1% - 30%	Yes
Rubber and plastic products	1% - 30%	NRO
Other	Less than 1%	No
Additional line item(s) may be claimed as CBI		

Non Confidential IUR Data Summary: Adipic acid, diisopropyl ester (6938-94-9)

Manufacturing/Import Information

Production and import volume:	<500,000 pounds
List of non-CBI companies/ sites*:	RTD*HallStar / Hacketstown, NJ S C Johnson & Son, Inc. / Sturtevant, WI
Maximum number of potentially exposed workers**:	less than 100 (including those of manufacturing, industrial processing and use)
Highest non-CBI maximum concentration:	confidential
Non-CBI physical forms*:	liquid

* There may be other companies/ sites and physical forms that are claimed confidential.
** There may be additional potentially exposed industrial workers that are not included in this estimate since not all submitters were required to report on industrial processing and use and/or there may be at least one use that contains a "Not Readily Obtainable" (NRO) response among the submissions.

Table 1
Industrial Processing and Use Information
Reported in 2006 IUR

Processing Activity	Industrial Sector	Function in Industrial Sector
None reported		

Table 2
Commercial/ Consumer Uses
Reported in 2006 IUR

Commercial/ Consumer Product Category Description	Highest Maximum Concentration Range	Use in Children's Products
None reported		

Non Confidential IUR Data Summary: Adipic acid, diisooctyl ester (1330-86-5)

Manufacturing/Import Information

Production and import volume:	1 million to 10 million pounds
List of non-CBI companies/ sites*:	Teknor Apex / Brownsville, TN
Maximum number of potentially exposed workers**:	less than 100 (including those of manufacturing, industrial processing and use)
Highest non-CBI maximum concentration:	up to 100% by weight
Non-CBI physical forms*:	liquid

* There may be other companies/ sites and physical forms that are claimed confidential.
** There may be additional potentially exposed industrial workers that are not included in this estimate since not all submitters were required to report on industrial processing and use and/or there may be at least one use that contains a "Not Readily Obtainable" (NRO) response among the submissions.

Table 1
Industrial Processing and Use Information
Reported in 2006 IUR

Processing Activity	Industrial Sector	Function in Industrial Sector
Processing--incorporation into formulation, mixture, or reaction product	All Other Chemical Product and Preparation Manufacturing	Lubricants
Processing--incorporation into formulation, mixture, or reaction product	All Other Chemical Product and Preparation Manufacturing	Other
Processing--repackaging	Other Basic Organic Chemical Manufacturing	Lubricants
Processing--repackaging	Other Basic Organic Chemical Manufacturing	Other
Additional line item(s) may be claimed as CBI		

Table 2
Commercial/ Consumer Uses
Reported in 2006 IUR

Commercial/ Consumer Product Category Description	Highest Maximum Concentration Range	Use in Children's Products
Rubber and plastics products	NRO	No
Not readily obtainable	NRO	No
Additional line item(s) may be claimed as CBI		

Non Confidential IUR Data Summary: Adipic acid, diisononyl ester (33703-08-1)

Manufacturing/Import Information

Production and import volume:	1 million to 10 million pounds
List of non-CBI companies/ sites*:	BASF Corporation / Florham Park, NJ PolyOne Corporation / Avon Lake, OH Sunoco, Inc. / Pittsburgh, PA Teknor Apex / Brownsville, TN
Maximum number of potentially exposed workers**:	between 100 and 999 (including those of manufacturing, industrial processing and use)
Highest non-CBI maximum concentration:	up to 100% by weight
Non-CBI physical forms*:	pellets or large crystals; gas or vapor; liquid

* There may be other companies/ sites and physical forms that are claimed confidential.
** There may be additional potentially exposed industrial workers that are not included in this estimate since not all submitters were required to report on industrial processing and use and/or there may be at least one use that contains a "Not Readily Obtainable" (NRO) response among the submissions.

Table 1
Industrial Processing and Use Information
Reported in 2006 IUR

Processing Activity	Industrial Sector	Function in Industrial Sector
Processing--incorporation into formulation, mixture, or reaction product	All Other Chemical Product and Preparation Manufacturing	Other
Processing--incorporation into formulation, mixture, or reaction product	Other Plastics Product Manufacturing	Other
Processing--repackaging	Other Basic Organic Chemical Manufacturing	Other
Additional line item(s) may be claimed as CBI		

Table 2
Commercial/ Consumer Uses
Reported in 2006 IUR

Commercial/ Consumer Product Category Description	Highest Maximum Concentration Range	Use in Children's Products
Electrical and electronic products	1% - 30%	NRO
Rubber and plastic products	31% - 60%	Yes
Additional line item(s) may be claimed as CBI		

Non Confidential IUR Data Summary: Adipic acid, diisodecyl ester (27178-16-1)

Manufacturing/Import Information

Production and import volume:	10 million to 50 million pounds
List of non-CBI companies/ sites:	Cognis Corporation / Cincinnati, OH Croda Inc. / Chicago, ID Croda Inc. / New Castle, DE Ester Solutions / Bedford Park, IL PolyOne Corporation / Avon Lake, OH Teknor Apex / Brownsville, TN
Maximum number of potentially exposed workers**:	between 100 and 999 (including those of manufacturing, industrial processing and use)
Highest non-CBI maximum concentration:	up to 100% by weight
Non-CBI physical forms*:	pellets or large crystals

* There may be other companies/ sites and physical forms that are claimed confidential.
** There may be additional potentially exposed industrial workers that are not included in this estimate since not all submitters were required to report on industrial processing and use and/or there may be at least one use that contains a "Not Readily Obtainable" (NRO) response among the submissions.

Table 1
Industrial Processing and Use Information
Reported in 2006 IUR

Processing Activity	Industrial Sector	Function in Industrial Sector
Processing--incorporation into article	Other Basic Organic Chemical Manufacturing	Other
Processing--incorporation into formulation, mixture, or reaction product	Other Plastics Product Manufacturing	Other
Processing--repackaging	Other Basic Organic Chemical Manufacturing	Lubricants
Additional line item(s) may be claimed as CBI		

Table 2
Commercial/ Consumer Uses
Reported in 2006 IUR

Commercial/ Consumer Product Category Description	Highest Maximum Concentration Range	Use in Children's Products
Electrical and electronic products	1% - 30%	NRO
Rubber and plastic products	1% - 30%	NRO
Not readily obtainable	NRO	No
Additional line item(s) may be claimed as CBI		

Non Confidential IUR Data Summary: Adipic acid, ditridecyl ester (16958-92-2)

Manufacturing/Import Information

Production and import volume:	1 million to 10 million pounds
List of non-CBI companies/ sites*:	BP America Inc. / Houston, TX Cognis Corporation / Cincinnati, OH Croda Inc. / New Castle, DE Ester Solutions / Bedford Park, IL Teknor Apex / Brownsville, TN
Maximum number of potentially exposed workers**:	between 100 and 999 (including those of manufacturing, industrial processing and use)
Highest non-CBI maximum concentration:	up to 100% by weight
Non-CBI physical forms*:	liquid

* There may be other companies/ sites and physical forms that are claimed confidential.
** There may be additional potentially exposed industrial workers that are not included in this estimate since not all submitters were required to report on industrial processing and use and/or there may be at least one use that contains a "Not Readily Obtainable" (NRO) response among the submissions.

Table 1
Industrial Processing and Use Information
Reported in 2006 IUR

Processing Activity	**Industrial Sector**	**Function in Industrial Sector**
Processing--incorporation into formulation, mixture, or reaction product	All Other Chemical Product and Preparation Manufacturing	Lubricants
Additional line item(s) may be claimed as CBI		

Table 2
Commercial/ Consumer Uses
Reported in 2006 IUR

Commercial/ Consumer Product Category Description	**Highest Maximum Concentration Range**	**Use in Children's Products**
Not readily obtainable	NRO	No
Additional line item(s) may be claimed as CBI		

Non Confidential IUR Data Summary: Azelaic acid, bis(2-ethylhexyl) ester (103-24-2)

Manufacturing/Import Information

Production and import volume:	1 million to 10 million pounds
List of non-CBI companies/ sites*:	Cognis Corporation / Cincinnati, OH Ester Solutions / Bedford Park, IL PolyOne Corporation / Avon Lake, OH
Maximum number of potentially exposed workers**:	1,000 or greater (including those of manufacturing, industrial processing and use)
Highest non-CBI maximum concentration:	up to 100% by weight
Non-CBI physical forms**:	pellets or large crystals; liquid

* There may be other companies/ sites and physical forms that are claimed confidential.
** There may be additional potentially exposed industrial workers that are not included in this estimate since not all submitters were required to report on industrial processing and use and/or there may be at least one use that contains a "Not Readily Obtainable" (NRO) response among the submissions.

Table 1
Industrial Processing and Use Information
Reported in 2006 IUR

Processing Activity	**Industrial Sector**	**Function in Industrial Sector**
Not readily obtainable	Not readily obtainable	Not readily obtainable
Additional line item(s) may be claimed as CBI		

Table 2
Commercial/ Consumer Uses
Reported in 2006 IUR

Commercial/ Consumer Product Category Description	**Highest Maximum Concentration Range**	**Use in Children's Products**
Not readily obtainable	NRO	NRO
Additional line item(s) may be claimed as CBI		

Non Confidential IUR Data Summary: Azelaic acid, diisodecyl ester (28472-97-1)

Manufacturing/Import Information

Production and import volume:	>500,000 to 1 million pounds
List of non-CBI companies/ sites*:	BP America Inc. / Wayne, NJ Cognis Corporation / Cincinnati, OH Croda Inc. / Chicago, ID
Maximum number of potentially exposed workers**:	between 100 and 999 (including those of manufacturing, industrial processing and use)
Highest non-CBI maximum concentration:	confidential
Non-CBI physical forms*:	liquid

* There may be other companies/ sites and physical forms that are claimed confidential.
** There may be additional potentially exposed industrial workers that are not included in this estimate since not all submitters were required to report on industrial processing and use and/or there may be at least one use that contains a "Not Readily Obtainable" (NRO) response among the submissions.

Table 1
Industrial Processing and Use Information
Reported in 2006 IUR

Processing Activity	Industrial Sector	Function in Industrial Sector
Claimed as CBI		

Table 2
Commercial/ Consumer Uses
Reported in 2006 IUR

Commercial/ Consumer Product Category Description	Highest Maximum Concentration Range	Use in Children's Products
Claimed as CBI		

Non Confidential IUR Data Summary: Sebacic acid, dimethyl ester (106-79-6)

Manufacturing/Import Information

Production and import volume:	<500,000 pounds
List of non-CBI companies/ sites*:	Ciba Specialty Chemicals Corp. / High Point, NC ICC Chemical Corporation / New York, NY
Maximum number of potentially exposed workers**:	less than 100 (including those of manufacturing, industrial processing and use)
Highest non-CBI maximum concentration:	up to 100% by weight
Non-CBI physical forms*:	liquid

* There may be other companies/ sites and physical forms that are claimed confidential.
** There may be additional potentially exposed industrial workers that are not included in this estimate since not all submitters were required to report on industrial processing and use and/or there may be at least one use that contains a "Not Readily Obtainable" (NRO) response among the submissions.

Table 1
Industrial Processing and Use Information
Reported in 2006 IUR

Processing Activity	Industrial Sector	Function in Industrial Sector
Claimed as CBI		

Table 2
Commercial/ Consumer Uses
Reported in 2006 IUR

Commercial/ Consumer Product Category Description	Highest Maximum Concentration Range	Use in Children's Products
Claimed as CBI		

Non Confidential IUR Data Summary: Sebacic acid, bis(2-ethylhexyl) ester (122-62-3)

Manufacturing/Import Information

Production and import volume:	1 million to 10 million pounds
List of non-CBI companies/ sites*:	Cognis Corporation / Cincinnati, OH Ester Solutions / Bedford Park, IL PolyOne Corporation / Avon Lake, OH The Goodyear Tire & Rubber Company / Marysville, OH The Seydel Companies / Greensboro, NC
Maximum number of potentially exposed workers**:	1,000 or greater (including those of manufacturing, industrial processing and use)
Highest non-CBI maximum concentration:	up to 100% by weight
Non-CBI physical forms*:	pellets or large crystals; solid

* There may be other companies/ sites and physical forms that are claimed confidential.
** There may be additional potentially exposed industrial workers that are not included in this estimate since not all submitters were required to report on industrial processing and use and/or there may be at least one use that contains a "Not Readily Obtainable" (NRO) response among the submissions.

Table 1
Industrial Processing and Use Information
Reported in 2006 IUR

Processing Activity	**Industrial Sector**	**Function in Industrial Sector**
Processing--incorporation into formulation, mixture, or reaction product	Other Plastics Product Manufacturing	Other
Processing--repackaging	Other Plastics Product Manufacturing	Other
Additional line item(s) may be claimed as CBI		

Table 2
Commercial/ Consumer Uses
Reported in 2006 IUR

Commercial/ Consumer Product Category Description	**Highest Maximum Concentration Range**	**Use in Children's Products**
Electrical and electronic products	1% - 30%	NRO
Rubber and plastic products	1% - 30%	NRO
Additional line item(s) may be claimed as CBI		