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

**Chemical/Category:** **Dicarboxylic Acids Category**

**CAS No. 110-15-6 Succinic Acid (Butanedioic acid)**
**CAS No. 110-94-1 Glutaric Acid (Pentanedioic acid)**
**CAS No. 124-04-9 Adipic Acid (Hexanedioic acid)**

**Contents:**

**QUALITATIVE SCREENING-LEVEL RISK CHARACTERIZATION FOR**
**Dicarboxylic Acids Category**

| | |
|---|---|
| **Succinic Acid (Butanedioic acid)** | **CAS No. 110-15-6** |
| **Glutaric Acid (Pentanedioic acid)** | **CAS No. 110-94-1** |
| **Adipic Acid (Hexanedioic acid)** | **CAS No. 124-04-9** |

## 1. Background

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

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

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

For these qualitative screening-level risk characterization documents, EPA has reviewed the IUR data to evaluate exposure potential. In addition, exposure information submitted to the Agency as described above for the hazard characterization was also considered, as appropriate. The resulting exposure information has been combined with the screening-level hazard characterizations to develop this qualitative screening-level risk characterization[6,7].

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[1] U.S. EPA. High Production Volume (HPV) Challenge Program; http://www.epa.gov/chemrtk/index.htm.
[2] U.S. EPA. HPV Challenge Program – Information Sources; http://www.epa.gov/chemrtk/pubs/general/guidocs.htm.
[3] U.S. EPA. Risk Assessment Guidelines; http://cfpub.epa.gov/ncea/raf/rafguid.cfm.
[4] OECD. Guidance Document on the Development and Use of Chemical Categories; http://www.oecd.org/document/7/0,2340,en_2649_34379_1947463_1_1_1_1,00.html.
[5] U.S. EPA – Basic IUR Information: http://www.epa.gov/opptintr/iur/pubs/guidance/basic-information.htm
[6] U.S. EPA Guidelines for Exposure Assessment; http://cfpub.epa.gov/ncea/raf/recordisplay.cfm?deid=15263

These screening-level risk characterizations are technical documents intended to support subsequent decisions and actions by OPPT. Accordingly, the document is not written with the goal of informing the general public. The purpose of the qualitative screening level risk characterizations is two-fold: to support initial risk-based decisions to prioritize chemicals and inform risk management options and to identify data needs for individual chemicals or chemical categories.

## 2. Category Justification

The dicarboxylic acids category includes three chemicals: succinic acid, glutaric acid, and adipic acid – also known as butanedioic acid, pentanedioic acid, and hexanedioic acid, respectively. The three discrete substances are short, straight-chain dicarboxylic acids differing by one carbon atom, from four to six carbons. The basis for the category is similarity in structure, physical-chemical properties and toxicity and it is considered acceptable and reasonable for the purposes of the HPV Challenge Program. In addition, this category is related to another, similar category called the dibasic esters category (which consists of butanedioic acid, dimethyl ester [dimethyl succinate, or DMS], pentanedioic acid, dimethyl ester [dimethyl glutarate or DMG], hexanedioic acid, dimethyl ester [dimethyl adipate or DMA] and the dibasic ester mixture [containing DMS, DMG, and DMA]).

## 3. Physical-Chemical Properties and Environmental Fate

This report was prepared using the best available data from a number of sources, but draws no conclusions regarding whether additional relevant data may exist. The members of the dicarboxylic acids category are solids at room temperature. They have negligible vapor pressure, high water solubility, and minimal volatility. They are highly mobile in soil and water systems. They are not persistent or bioaccumulative. They are stable to hydrolysis and photolysis but are expected to degrade at rapid rates by biodegradation. Because the chemicals in this category are readily biodegradable and do not bioaccumulate they are classified as not persistent (P1) and not bioaccumulative (B1).

## 4. Hazard Characterization

*Aquatic Organism Toxicity.* Evaluation of the toxicity data for fish, aquatic invertebrates and aquatic plants indicates the potential acute hazard of category members to aquatic organisms is low.

*Human Health Toxicity.* The acute oral, dermal, and inhalation toxicity of category members is low. The category members are slightly irritating to skin but cause moderate to severe eye irritation. Available data do not suggest that members of the dicarboxylic acid category cause skin sensitization. Repeated exposures via oral route affected body weight and body weight gains at higher doses. There is no indication from animal studies that the category members have an adverse effect on reproduction or development. The category members are not mutagenic or induce chromosomal aberrations. Data from a carcinogenicity study with monosodium succinate indicate that the category members are not potential carcinogens. The potential health hazard of the dicarboxylic acids category members is low based on the available animal data reviewed.

## 5. Exposure Characterization

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

[7] U.S. EPA. Risk Characterization Program; http://www.epa.gov/osa/spc/2riskchr.htm.

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

*Production Volume Information for Each Member*

*Succinic acid* was manufactured in the United States with a production volume in the range of >10 million – 50 million pounds in 2005.

*Glutaric acid* was manufactured in the United States with a production volume in the range of >50 million – 100 million pounds in 2005.

*Adipic acid* has an aggregated production and/or importation volume of greater than one billion pounds in 2005.

*Information Applicable to All Category Members*
IUR information for 2005 was submitted for all category members. Some use and exposure information was provided in the HPV Challenge Submission. An OECD SIDS dossier prepared by Germany is available for adipic acid (http://cs3-hq.oecd.org/scripts/hpv/).

Two category members (glutaric and succinic acids) are by-products produced from the manufacturing of the third category member, adipic acid. In general, over 90% of dibasic acid production generates adipic acid with the remainder (<10%) being the by-products. Adipic acid is an industrial intermediate used for the production of Nylon 6, 6 for use in fibers, engineering resins, films, and monofilaments.

Additional uses identified in public data sources for the category members (see Exposure Characterizations for references):

*Succinic acid* is reported to be used in the manufacture of lacquers, dyes, esters for perfumes, in photography, in foods as a sequestrant (it is listed in FDA's Everything Added to Food in the United States database [EAFUS]), and as a buffer and neutralizing agent.

*Glutaric acid* is used in organic synthesis of chemical intermediates for polymers, e.g., polyamides and polyesters, for its esters and anhydride, and for human and veterinary medication

*Adipic acid:* Other applications for adipic acid include flue gas desulphurization, adhesives, and food additives (it is recognized as a Generally Recognized as Safe, or GRAS, substance by the U.S. Food and Drug Administration).

*Exposures to Workers*
Data suggest the potential for a high number of exposed workers and use sites (including industrial and commercial sites). The National Occupational Exposure Survey (NOES), conducted between 1981 and 1983, estimated a total of 31,198; 1,827; and 140,635 workers potentially exposed to succinic, glutaric, and adipic acids, respectively. The more recently submitted IUR data indicate that the maximum total number of workers likely to be exposed to the category members during manufacturing, industrial processing, and use are: 10,000 or greater (succinic acid); between 10,000 and 25,000 (glutaric acid); and greater than 10,000 (adipic acid). There may be additional potentially exposed workers not included in these estimates, since not all of the production volume is accounted for in the IUR submissions and there is at least one use that contains a "Not Readily Obtainable" (NRO) response for each of the category members. The vapor pressure value for each member of the category (see attached Hazard Characterization supporting document) are below the level of 0.001 torr (the level above which OPPT estimates worker exposures to vapors for chemical assessments). However, based on IUR data, other types of worker exposures are possible for the category members. None of the category members have an OSHA Permissible Exposure Limit.

Based on IUR data, specifically the number of potentially exposed workers and the use codes, the ranking for worker exposure is high for all three category members.

*Exposures to the General Population and the Environment*
None of the dicarboxylic acids are on the Toxics Release Inventory. Based on the known uses for each category member as described above, it is likely that there would be some releases to water during manufacturing, processing, and use. Therefore, EPA assumes for the purpose of this risk prioritization that there is potential for exposures to the general population and the environment.

The IUR-based ranking for the general population and the environment is high due to the assumption that there will be exposure to all members of the dicarboxylic acids category

*Exposures to Commercial Workers and Consumers*
The IUR information has some commercial/consumer products listed for all three dicarboxylic acid category members. Depending on the product, consumers may have potential dermal and inhalation exposure to the chemical. Since this chemical is present in dry powder or other solid form, inhalation exposure to particulates may occur.

The IUR-based ranking for commercial workers/consumers is high due to the assumption that all the category members are used in consumer/commercial products.

*Exposures to Children*
*Succinic and Glutaric acids*: The IUR information suggests that either: (1) succinic and glutaric acids will not be used in children's consumer products; or (2) that this type of information is not readily available for both category members. Therefore, because of this uncertainty, the IUR-based ranking for children is moderate due to the assumption that succinic and glutaric acids may be present in products intended to be used by children.

*Adipic acid:* The IUR information states that adipic acid will be used in products intended for use by children. Depending on the product, children may have potential dermal and inhalation exposure to the chemical. Therefore, the IUR-based ranking for children is high due to the assumption that adipic acid is used in products intended to be used by children.

In characterizing the exposure information for the dicarboxylic acids for this initial risk-based prioritization process, there are two issues that are important to consider regarding potential exposure to the general public, consumers, and children. First, that the TSCA-regulated uses of both succinic and glutaric acids are assumed to be primarily as chemical intermediates. Second, that the potential exposure to the general public, consumers, and children to adipic acid may be considered low because the most likely scenarios would be exposure to Nylon as a finished product, in which adipic acid is bound and thus not likely to be released.

## 6. Risk Characterization

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

### 6.1 Risk Statement and Rationale

*Potential Risk to Aquatic Organisms from Environmental Releases (LOW CONCERN).* EPA assumes there is potential for exposure to aquatic organisms from environmental releases. The low acute aquatic hazard and the overall environmental fate characteristics (not persistent or bioaccumulative) of all members of the dicarboxylic acids category, suggest a low concern for potential risk to aquatic organisms from environmental releases.

*Potential Risk to the General Population from Environmental Releases (LOW CONCERN).* EPA assumes there is potential for exposure to the general population from environmental releases. The low human health hazard due to the lack of specific toxicity to animals following exposure to high doses and the overall environmental fate characteristics of the category members (as described above) suggest a low concern for potential risk to the general population from environmental releases.

*Potential Risk to Workers (LOW CONCERN).* Worker exposures, from particulate matter, to all three category members are likely. The available hazard data suggest a low hazard due to the lack of any specific toxicity to animals following exposures to high doses. There is potential for eye irritation for two category members (severe irritation for succinic acid and moderate irritation for adipic acid). Although there is no OSHA PEL for any category member, acute irritation effects are considered reversible and self-limiting in that professionals would notice them quickly and either protect themselves with appropriate protective equipment or remove themselves from the exposure. Also, hazard communication and standard industrial hygiene practices, if properly followed, may be sufficient to address this concern. Thus, the information suggests a low concern for potential risk to workers.

*Potential Risk to Commercial Workers and Consumers from Known Uses (LOW CONCERN).* All three category members are reported to be in products used by commercial workers and consumers, although the information suggests higher exposures to adipic acid are likely (via the use of Nylon; although the adipic acid is bound in the product and not released). However, the available hazard data show that all category members have low and non-specific toxicity. Thus, the information suggests a low concern for potential risk to commercial workers/consumers.

*Potential Risk to Children (LOW CONCERN).* Two of the category members (succinic and glutaric acid) are not likely to be found in commercially available products available to children. One (adipic acid) of the three category members has a different use profile and is used in products intended for use by children. However, the hazard profile shows that all category members have low and non-specific toxicity and there is no indication of adverse effects on reproduction or development following exposure to high doses in available animal studies. Thus, the information suggests a low concern for potential risk to children.

### 6.2 Uncertainties

The dicarboxylic acids category may have minor uses that were not reported in IUR.

### 6.3 Data Needs

No data needs have been identified at this time.

# SCREENING-LEVEL HAZARD CHARACTERIZATION OF HIGH PRODUCTION VOLUME CHEMICALS

## CHEMICAL CATEGORY NAME:
## Dicarboxylic Acids

## SPONSORED CHEMICALS

| | |
|---|---|
| **Succinic Acid (Butanedioic acid)** | **CAS No. 110-15-6** |
| **Glutaric Acid (Pentanedioic acid)** | **CAS No. 110-94-1** |
| **Adipic Acid (Hexanedioic acid)** | **CAS No. 124-04-9** |

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# SCREENING-LEVEL HAZARD CHARACTERIZATION OF HIGH PRODUCTION VOLUME CHEMICALS

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

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

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

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

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

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

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

# SCREENING-LEVEL HAZARD CHARACTERIZATION
## Dicarboxylic Acids Category

**Introduction**

The sponsor, E.I. du Pont de Nemours & Co., Inc., submitted a Test Plan and Robust Summaries to EPA for the Dicarboxylic Acids Category on July 11, 2001. EPA posted the submission on the ChemRTK HPV Challenge website on September 13, 2001 (http://www.epa.gov/chemrtk/pubs/summaries/dicarbx/c13108tc.htm). EPA comments on the original submission were posted to the website on February 11, 2002. Public comments were also received and posted to the website. The sponsor provided EPA with revised documents on August 12, 2002, which were posted to the ChemRTK website on September 5, 2002. The dicarboxylic acids category consists of the following chemicals:

| | |
|---|---|
| Succinic Acid (Butanedioic acid) | CAS No. 110-15-6 |
| Glutaric Acid (Pentanedioic acid) | CAS No. 110-94-1 |
| Adipic Acid (Hexanedioic acid) | CAS No. 124-04-9 |

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

**Category Justification**

The basis for the category is similarity in structure, physical-chemical properties and toxicity responses among the category members. The three discrete compounds are short, straight-chain dicarboxylic acids differing by one carbon atom, from four to six carbons. The measured physical-chemical properties for the three substances are generally similar or display a trend with molecular weight. The three category members produce similar levels of acute and repeated-dose toxicity in experimental animals, such that information on one category member is expected to represent the toxicity of the category as a whole.

In response to EPA's comments, the sponsor provided additional information (ECOSAR estimates) to support the ecotoxicity endpoints for the purposes of the HPV Challenge Program. The sponsor submitted supporting ecotoxicity data on a mixture of the three acids. EPA did not consider ecotoxicity data on the submitted mixture data to be adequate because the concentrations of the acids in the mixture were too low to allow extrapolation of the mixture data to the individual components (3.9% adipic acid, 16.43% glutaric acid, and 4.77% succinic acid). No data were available on reproductive toxicity for these chemicals and the submitter proposed to conduct such studies. In accordance with HPV Challenge Program guidance, EPA concluded that histological evaluation of reproductive organs from the available 90-day repeated-dose toxicity studies and the availability of developmental toxicity studies would address the reproductive toxicity endpoints. The sponsor's category analysis is available in the revised submission posted at the above web address.

**Summary-Conclusion**

The members of the dicarboxylic acids category are solids at room temperature. They have negligible vapor pressure, high water solubility and minimal volatility. They are highly mobile in soil and water systems. They are not persistent or bioaccumulative. They are stable to hydrolysis and photolysis but are expected to degrade at rapid rates by biodegradation. Because the chemicals in this category are readily biodegradable and do not bioaccumulate, they are classified as not persistent (P1) and not bioaccumulative (B1) and are not Persistent Organic Pollutants (POPs).

Evaluation of the toxicity data for fish, aquatic invertebrates and aquatic plants indicates the potential acute hazard of category members to aquatic organisms is low.

The acute toxicity of category members is low. The category members are slightly irritating to skin but cause moderate to severe eye irritation. They do not have a sensitizing potential. Repeated exposures via oral route affected body weight and body weight gains at higher doses. Reproductive toxicity data are not available for the category members. However, in repeated-dose toxicity studies, no effects on reproductive organs were seen. In developmental toxicity studies, the category members did not show any effects on fetal survival, fetal weight, litter size or implantations, or any skeletal or visceral abnormalities. All category members were not mutagenic in tested strains of *Salmonella typhimurium* as well as in mammalian cells and did not induce statistically significant increase in the mean number of micronucleated polychromatic erythrocytes in the bone marrow of CD-1 mice. In a 2–year carcinogenicity study of monosodium succinate, tumors were found in many organs or tissues in all groups including the controls. None of the treated groups showed a significant increase in the incidence of any tumors over that in the corresponding controls.

The potential health hazard of the dicarboxylic acids category is low. Monosodium succinate did not increase the incidence of any tumors over that in the corresponding controls in a 2-year drinking water study.

No data gaps were identified under the HPV Challenge Program.

## 1. Physical-Chemical Properties and Environmental Fate

This report was prepared using the best available data from a number of sources, including information within the HPV Challenge submission (E.I. du Pont de Nemours, or DuPont, 2007), with some additional information added from EPI Suite (USEPA, 2007) as well as the Hazardous Substance Database (HSDB, 2007). Basic physical-chemical and environmental fate properties of these compounds are listed in Tables 1a and 1b, respectively.

### *Physical-Chemical Properties Characterization*

The dicarboxylic acids in this category are high melting solids with low vapor pressure and high water solubility.

### *Environmental Fate Characterization*

Succinic acid, glutaric acid and adipic acid are highly mobile in the environment. They are expected to partition into both the vapor and particulate phases. In the atmosphere they are expected to degrade by reaction with photochemically-produced hydroxyl radicals with estimated half-lives of 139, 61 and 69.6 hours, respectively. They are not expected to undergo direct photolysis. They are highly mobile in soil, and are not expected to volatilize from dry or wet soil surfaces or water. If released into water these chemicals will exist primarily as anions under environmental conditions (pH 5-9), are not expected to adsorb to soils or suspended solids and sediment in the water column. They are not expected to hydrolyze under environmental conditions. The potential for bioconcentration of all three dicarboxylic acids in aquatic organisms is low (B1) and they are not persistent (P1) with ultimate biodegradation occurring over a period of days to weeks.

| **Table 1a. Physical-Chemical Properties of Dicarboxylic Acids** | | | |
|---|---|---|---|
| | **Butanedioic acid (Succinic acid) CAS No. 110-15-6** | **Pentanedioic acid (Glutaric acid) CAS No. 110-94-1** | **Hexanedioic acid (Adipic acid) CAS No. 124-04-9** |
| **Property** | **Value/Descriptor** | **Value/Descriptor** | **Value/Descriptor** |
| Melting Point (ºC) | **188°C (m)** | **97.8°C (m)** | **152°C (m)** |
| Boiling Point Range (ºC) | **235 °C at 760 torr (m)** | **303°C at 760 torr (m)** | **375.5°C at 760 torr (m)** |
| Vapor Pressure (mm Hg at 25 (ºC) | 1.91X10-7 (e) | 2.88X10-6 (e) | 3.18X10-7 (e) |
| Log $K_{ow}$ | **-0.59 (m)** | **-0.29 (m)** | **0.08 (m)** |
| Water Solubility (mg/L) | **83200 at 25°C (m)** | **540000 at 25°C (m)** | **24300 at 25°C (m)** |
| pKa | **4.21(m)** | **4.34(m)** | **4.44(m)** |

**(m) = measured data** (HSDB, 2007 or EPI Property Database)
(e) = extrapolated data

| **Table 1b. Environmental Fate Characteristics of Dicarboxylic Acids** | | | |
|---|---|---|---|
| **Property** | **Butanedioic acid (Succinic acid) CAS No. 110-15-6** | **Pentanedioic acid (Glutaric acid) CAS No. 110-94-1** | **Hexanedioic acid (Adipic acid) CAS No. 124-04-9** |
| **Property** | **Value/Descriptor** | **Value/Descriptor** | **Value/Descriptor** |
| Direct Photodegradation | Not expected to undergo direct photolysis because chemicals do not contain functional groups that absorb light at greater than 290 nm. | | |
| Indirect ($OH^-$) Photodegradation $t_{1/2}$ (hr) | $t_{1/2}$ =139 (e) | $t_{1/2}$ = 92 (e) | $t_{1/2}$ = 69 (e) |
| Hydrolysis | Hydrolysis is not expected since compounds lack functional groups that hydrolyze under environmental conditions. | | |
| Henry's Law (atm $m^3$/ mol) | $3.6x10^{-13}$ (e) | $9.2x10^{-13}$ (e) | $2.5x10^{-12}$ (e) |
| $K_{oc}$ | 11 (e) | 11 (e) | 26 (e) |
| Distribution (Level III fugacity model) | About <0.001 % air, 40 %water, 60 % soil | About <0.001 % air, 50 %water, 50 % soil | About <0.001 % air, 50 %water, 50 % soil |
| Biodegradation | **Readily biodegradable (m)** | **Readily biodegradable (m)** | **Readily biodegradable (m)** |
| Bioconcentration Factor | 3.162 (e) | 3.162 (e) | 3.162 (e) |
| Bioaccumulation rating | B1 | B1 | B1 |
| Persistance Rating | P1 | P1 | P1 |

**(m) = measured data** (USEPA, 2007a)
(e) = estimated data, (USEPA, 2007b);

**2. Environmental Effects – Aquatic Toxicity**

A summary of aquatic toxicity data submitted for SIDS endpoints is provided in Table 2. The table also indicates where data for tested category members are read-across (RA) to untested members of the category. All data presented below are from the submission by the sponsor (E.I. DuPont de Nemours and Company, 2007) unless otherwise noted

***Acute Toxicity to Fish***

***Succinic acid (Butanedioic acid; CAS No. 110-15-6)***
Chinook salmon (*Oncorhynchus ishawytscha*), Coho salmon (*Oncorhynchus kisutch*) and Northern squawfish (*Ptychocheilus oregonensis*) were exposed to 10 and 15 ppm of succinic acid for 24 hours. No loss of equilibrium or death occurred at these concentrations at the end of exposure period. The 24-hour exposure period is less than the 96-hour duration recommended in test guidelines. Therefore, the sponsor supported these data with toxicity values estimated by ECOSAR. A large difference was observed between the reported ECOSAR estimate ($LC_{50}$ = 238,000 mg/L) and the experimental value obtained in the 24-hour test with succinic acid and the 96-hour test with adipic acid (96-h $LC_{50}$ = 97 mg/L). This discrepancy is attributed to the fact that ECOSAR performs estimates for these chemicals based on pH 7, whereas the test appears to have been conducted with the free acid. Hence, the model estimated data did not support the 24-hour test data. Therefore, a read-across approach was used to estimate acute toxicity of succinic acid to fish.
**24-h $LC_{50}$ = 238,000 mg/L** (estimated)
**96-h $LC_{50}$ = 97 mg/L** (read across from adipic acid)

***Glutaric acid (Pentanedioic acid; CAS No. 110-94-1)***
Bluegill sunfish (*Lepomis macrochirus*) were exposed to glutaric acid for 24 hours. The reported $LC_{50}$ was 330 mg/L. There was no information on concentrations used or mortality. The 24-hour exposure period is less than the 96-hour duration recommended in test guidelines. Therefore, the sponsor supported these data with toxicity values estimated by ECOSAR. A large difference was observed between the reported ECOSAR estimate ($LC_{50}$ = 139,000 mg/L) and the experimental value obtained in the 24-hour test with glutaric acid and the 96-hour test with adipic acid (96-hour $LC_{50}$ = 97 mg/L). This discrepancy is attributed to the fact that ECOSAR performs estimates for these chemicals based on pH 7, whereas the test appears to have been conducted with the free acid. Hence, the model estimated data did not support the 24-hour test data. Therefore, a read-across approach was used to estimate acute toxicity of glutaric acid to fish.
**24-h $LC_{50}$ = 139,000 mg/L** (estimated)
**96-h $LC_{50}$ = 97 mg/L** (read across from adipic acid)

***Adipic acid (Hexanedioic acid; CAS No. 124-04-9)***
Fathead minnow (*Pimephales promelas*) were exposed to adipic acid at nominal concentrations of 97, 114, 172 and 300 mg/L for 96 hours under static conditions. The pH was ≤ 5.9 during the test.
**96-h $LC_{50}$ = 97 mg/L**

***Acute Toxicity to Aquatic Invertebrates***

***Succinic acid (Butanedioic acid; CAS No. 110-15-6)***
*Daphnia magna* were exposed to succinic acid for 48 hours under static conditions (all concentrations were not provided in the robust summary). The pH was 7.7 at the beginning of the test.
**48-h $EC_{50}$ = 374.2 mg/L**

***Glutaric acid (Pentanedioic acid; CAS No. 110-94-1)***
The only data submitted for acute toxicity of glutaric to invertebrates was a model (ECOSAR) estimate for *Daphnia*. A large difference was observed between the reported ECOSAR estimate ($LC_{50}$ = 127,000 mg/L) and the experimental value obtained in the 48-hour tests for succinic acid (48-hour $LC_{50}$ = 374.2 mg/L) and adipic acid (48-hour $LC_{50}$ = 85.7 mg/L). This discrepancy is attributed to the fact that ECOSAR performs estimates for these chemicals based on pH 7, whereas the test appears to have been conducted with the free acid. Hence, the model

estimated data did not support the 24-hour test data. Therefore, a read-across approach was used to estimate acute toxicity of glutaric acid to aquatic invertebrates.
**$LC_{50}$ = 127,000 mg/L** (estimated)
**48-h $EC_{50}$ = 85.7 mg/L** (read across from adipic acid)

***Adipic acid (Hexanedioic acid; CAS No. 124-04-9)***
*D. magna* were exposed to nominal concentrations of 0, 15.6, 31.2, 62.5, 125, 250 and 500 mg/L of adipic acid for 48 hours. The pH was 4 – 8 during the test.
**48-h $EC_{50}$ = 85.7 mg/L**

***Toxicity to Aquatic Plants***

***Succinic acid (Butanedioic acid; CAS No. 110-15-6)***
Blue-green algae (*Spirulina labyrinthiformis*) were exposed to succinic acid in a static test (duration not specified in robust summary). The reported $EC_{50}$ is 120 mg/L. Therefore, the sponsor supported these data with toxicity values estimated by ECOSAR. A large difference was observed between the reported ECOSAR estimate (96-hour $EC_{50}$ = 115,000 mg/L) and the experimental value obtained in the 96-hour test for adipic acid (96-hour $EC_{50}$ = 26.6 mg/L). This discrepancy is attributed to the fact that ECOSAR performs estimates for these chemicals based on pH 7, whereas the test appears to have been conducted with the free acid. Hence, the model estimated data did not support the test data. Therefore, a read-across approach was used to estimate toxicity of succinic acid to aquatic plants.
**$EC_{50}$ = 120 mg/L**
**96-hour $EC_{50}$ = 115,000 mg/L** (estimated)
**96-h $EC_{50}$ = 26.6 mg/L** (read across from adipic acid)

***Glutaric acid (Pentanedioic acid; CAS No. 110-94-1)***
Marine algae (*Nitzschia closterium*) were exposed to glutaric acid for 72 hours. The reported $EC_{50}$ is 264 mg/L. Limited information is available on this test and the exposure period is less than the 96-hour duration recommended in test guidelines. Therefore, the sponsor supported these data with a toxicity value estimated by ECOSAR. Again, a large difference was observed between the reported ECOSAR estimate ($EC_{50}$ > 69,000 mg/L) and the experimental value obtained in the 96-hour test for adipic acid (96-hour $LC_{50}$ = 26.6 mg/L) due to the pH issue described above. Hence, the model estimated data did not support the test data. Therefore, a read-across approach was used to estimate toxicity of succinic acid to aquatic plants.
**72-h $EC_{50}$ = 264 mg/L**
**96-h $EC_{50}$ > 69,000 mg/L** (estimated)
**96-h $EC_{50}$ = 26.6 mg/L** (read across from adipic acid)

***Adipic acid (Hexanedioic acid; CAS No. 124-04-9)***
Green algae (*Scenedesmus subspicatus*) were exposed to nominal concentrations of 0, 1.95, 3.91, 7.81, 15.6, 31.3, 62.5, 125, 250 and 500 mg/L of adipic acid for 96 hours. The pH values ranged from 3.8 to 8.1 at 0 hours (without algae) and 3.9 – 10.2 at 96 hours (with algae). The robust summary states that the low pH values at higher concentrations might have affected the toxicity in the test.
**96-h $EC_{50}$ = 26.6 mg/L**

**Conclusion:** Evaluation of the toxicity data for fish, aquatic invertebrates and aquatic plants indicates the potential acute hazard of category members to aquatic organisms is low.

**Table 2. Summary of Environmental Effects – Aquatic Toxicity Data**

| Endpoints | Succinic acid (Butanedioic acid) (110-15-6) | Glutaric acid (Pentanedioic acid) (110-94-1) | Adipic acid (Hexanedioic acid) (124-04-9) |
|---|---|---|---|
| **Fish** **96-h $LC_{50}$ (mg/L)** | **> 15 (m, 24-h)** 97 (RA)[1] | **330 (m, 24-h)** 97 (RA)[1] | **97 (m)** |
| **Aquatic Invertebrates** **48-h $EC_{50}$ (mg/L)** | **374.2 (m)** | No Data 85.7 (RA) | **85.7 (m)** |
| **Aquatic Plants** **72-h $EC_{50}$ (mg/L)** | **120 (m)** 26.6 (RA)[1] | **264 (m)** 26.6 (RA)[1] | **26.6 (m)** |

**(m) = measured data (i.e. derived from testing);** (e) = estimated data (i.e. derived from modeling); (RA) = read across; [1]Read across because available data are inadequate

## 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. All data presented below are from the submission by the sponsor (E.I. DuPont de Nemours and Company, 2007) unless otherwise noted

### *Acute Oral Toxicity*

***Succinic Acid (Butanedioic acid; CAS No. 110-15-6)***

(1) Rats (3 or 5/dose) were administered succinic acid via gavage at doses of 400, 800, 1600 or 3200 mg/kg-bw and observed for 14 days.
**$LD_{50}$ = 2260 mg/kg-bw**

(2) Male and female Fischer 344 rats (4/sex/dose) were administered monosodium succinic acid at doses of 500, 1000, 2000, 4000 or 8000 mg/kg-bw and observed for 10 days. No clear toxicological effects were observed in rats that died or were killed; except hemorrhage of the lungs observed in some high-dose rats.
**$LD_{50}$ > 8000 mg/kg-bw**

***Glutaric acid (Pentanedioic acid; CAS No. 110-94-1)***

Male and female Sprague-Dawley rats (5/dose) were administered glutaric acid at doses of 2000, 2510, 3160 and 3980 mg/kg-bw. The survival time was several hours to 2 days. Mortality ratios were 0/5, 3/5, 3/5, and 5/5 for the 2000, 2510, 3160 and 3980 mg/kg groups, respectively. Clinical signs included tremors, followed by salivation, diarrhea and increased weakness. Necropsy revealed inflammation of gastric mucosa and liver hyperemia.
**$LD_{50}$ = 2750 mg/kg-bw**

***Adipic acid (Hexanedioic acid; CAS No. 124-04-9)***

(1) In rats, using 20% solution in corn oil, the $LD_{50}$ was 5050 mg/kg-bw.
**$LD_{50}$ = 5050 mg/kg-bw**

(2) Male mice (13/dose) were administered adipic acid as a 6% suspension in methylcellulose (0.5%) at doses of 1500, 2000, and 2500 mg/kg-bw. Mice that died at high doses showed marked distention of the stomach and small intestine with spastic contraction of the cecum. There was an evidence of irritation and hemorrhage of the intestine.
**$LD_{50}$ = 1900 mg/kg-bw**

***Acute Dermal Toxicity***

***Glutaric acid (Pentanedioic acid; CAS No. 110-94-1)***
Male and female New Zealand White rabbits (1/sex/concentration) were exposed to a 50% solution of glutaric acid at concentrations of 1000, 1580, 2510, 3980, 6310 and 10,000 mg/kg-bw. No deaths occurred. No appreciable signs of toxicity were observed.
**$LD_{50}$ > 10,000 mg/kg-bw**

***Adipic acid (Hexanedioic acid; CAS No. 124-04-9)***
Male and female New Zealand White rabbits were exposed dermally to 40% adipic acid (in corn oil) at doses of 5010 and 7940 mg/kg-bw for 24 hours under occluded conditions and observed for 14 days. No deaths occurred at either dose.
**$LD_{50}$ > 7940 mg/kg-bw**

***Acute Inhalation Toxicity***

***Adipic acid (Hexanedioic acid; CAS No. 124-04-9)***
Male and female Sprague-Dawley rats (10/sex/dose) were exposed via inhalation (nose-only dust-aerosol) to adipic acid at nominal concentrations of 5.41 and 7.67 mg/L (measured) for 4 hours and observed for 14 days. No mortalities occurred at either dose.
**$LC_{50}$ > 7.7 mg/L**

***Repeated-Dose Toxicity***

***Succinic acid (Butanedioic acid; CAS No. 110-15-6)***
In a 13-week study, groups of male and female F344 rats were administered monosodium succinate at 0, 0.3, 0.6, 1.25, 2.5, 5 and 10% (approximately 0, 300, 600, 1250, 2500 and 10,000 mg/kg-bw/day) in their drinking water. All animals in the 10% group showed severely decreased body weight gain (severely emaciated) and died within the first 4 weeks of the study. The decreased body weight gain was also seen at and above 2.5%. No effects were seen on hematological or biochemical parameters. No treatment-related histological lesions were seen in any organ, although atrophy of organs was noted.
**LOAEL = 2.5% (~2500 mg/kg-bw/day;** based on severely decreased body weight gain**)**
**NOAEL = 1.25% (~1250 mg/kg-bw/day)**

***Glutaric acid (Pentanedioic acid; CAS No. 110-94-1)***
(1) Groups of male and female Sprague-Dawley rats were fed glutaric acid at 0, 0.5, 1.0 and 2.0% (approximately 250, 500 and 1000 mg/kg-bw/day) for 90 days. No treatment-related mortality was noted. Body weight gain was markedly decreased in the 2% group in both sexes. No effects were seen on food consumption, hematology, clinical chemistry, urinalysis, absolute or relative organ weights or histopathology. No difference between control and treatment groups was observed in absolute or relative testes and ovary weights. Histopathological examination of testes, seminal vesicles, ovaries and uterus did not reveal any treatment-related effects.
**LOAEL = 2% (approximately 1000 mg/kg-bw/day**; based on decreased body weight gain**)**
**NOAEL = 1% (approximately 500 mg/kg-bw/day)**

(2) In a 90-day study, groups of male and female Beagle dogs were fed diets containing 0, 1, 3 and 5% glutaric acid for days 1 – 10 and 0.5, 1, 2 and 2% glutaric acid for days 11 – 90. Body weight loss was seen in male and females in the 5% group and in females of the 3% group after 10 days. The dogs in the high-dose group did not gain weight during the study whereas the body weight gain for animals from the low- and mid-dose groups was comparable to the control group. No changes to other parameters, including histology of testes or ovaries, were noted.
**LOAEL = 2% (approximately 500 mg/kg-bw/day**; based on decreased body weight gain**)**
**NOAEL = 1% (approximately 250 mg/kg-bw/day)**

***Adipic acid (Hexanedioic acid; CAS No. 124-04-9)***
(1) In a 2-year chronic feeding study, male and female Carworth Farms rats were fed diets containing 0, 0.1, 1.0, 3.0 and 5.0% (males) or 0 and 1% (females) adipic acid—corresponding to approximately 2.7, 280, 809 and 1302 mg-kg-bw/day, respectively. In males, body weight gain was suppressed in the 3 and 5% dose groups. There was a

slight but consistent reduction in food consumption in the 5% exposure group. The following clinical signs were noted in all groups, including control animals, throughout the study: wheezing, bloody crust about eyes and nose and body sores. There was a lower incidence of signs indicative of respiratory infection and body sores in animals from the 5% exposure group. Soft edematous testes were noted in control and treated animals. No marked differences between control and treated groups were noted in organ weights or microscopic examination. In females, body weight gain and food consumption were not affected by treatment. Clinical signs noted in control and treated groups were bloody crust about eyes and noses, lack of vigorous growth, and body sores. There were no marked differences between control and treated animal's organ weights or gross or microscopic pathology.
**LOAEL = 3% (approximately 809 mg/kg-bw/day,** based on decreased body weight gains and food consumption in males**)**
**NOAEL = 1% (approximately 280 mg/kg-bw/day)**

(2) Male and female rats were administered adipic acid (powdered solid) via inhalation at 126 µg/L for 6 hours/day for a total of 15 exposures. Adipic acid did not produce clinical signs of toxicity or treatment-related effects on blood parameters. Gross examination of organs did not reveal any effects. There was no indication that microscopic examination of tissues/organs was conducted.
**LOAEL > 126** m**g/L** (based on no effects seen at the only dose tested)
**NOAEL = 126** m**g/L**

***Reproductive Toxicity***

Reproductive toxicity tests were not submitted to address the reproductive toxicity endpoint for this category. Evaluation of reproductive organs in repeated-dose toxicity was used to address the reproductive endpoints for the purposes of the HPV Challenge Program. Therefore, NOAEL/LOAELs for fertility and/or reproductive toxicity cannot be determined for this endpoint.

***Succinic acid (Butanedioic acid; CAS No. 110-15-6)***
In the 13-week drinking water study described previously, all animals in the 10% group showed severely suppressed body weight gain (severely emaciated) and died within the first 4 weeks of the study. The decreased body weight gain was also seen at and above 2.5% succinic acid treatment. No treatment-related histological lesions were seen in any organ, although atrophy of organs was seen.

***Glutaric acid (Pentanedioic acid; CAS No. 110-94-1)***
(1) In the 90-day repeated-dose study with rats described previously, no treatment-related mortality was noted. Body weight gain was suppressed in animals of both sexes in the 2% treatment group. No effects were seen on absolute or relative organ weights, including testes and ovaries. No treatment related histological findings were seen in any organ, including testes, seminal vesicles, ovaries and uterus.

(2) In the 90-day dietary study described previously, body weight loss was seen in male and female dogs in the 5% (~1250 mg/kg-bw/day) group and in females of the 3% (~750 mg/kg-bw/day) group after 10 days. The dogs in the high-dose group showed no body weight gain during the study. Histopathological examination of the testes or ovaries revealed no treatment-related changes.

***Adipic acid (Hexanedioic acid; CAS No. 124-04-9)***
In the 2-year chronic feeding study described previously, body weight gain was depressed in males in the 3 and 5% (~750 and 1250 mg/kg-bw/day) treatment groups. Soft edematous testes were noted in control and treated animals. No treatment-related effects were seen on organ weights or gross or microscopic examination.

***Developmental Toxicity***

***Glutaric acid (Pentanedioic acid; CAS No. 110-94-1)***
(1) Groups of pregnant female CD rats were administered doses of glutaric acid a 0, 125, 400 and 1300 mg/kg-bw/day via gavage on gestation days 6 – 15; animals were sacrificed on gestation day 20 and examined for any gross pathological changes. At 400 mg/kg-bw/day and higher, clinical signs such as salivation, rales and nasal discharge were observed. Mean body weight gain was decreased at 1300 mg/kg-bw/day during the dosing period, but they

were comparable to control animals during post-dosing (GD 15 – 20). At 1300 mg/kg-bw/day, one female died and one was sacrificed on gestation day 13. No changes were seen in reproductive status. There were no effects on the number of corpora lutea, implantation sites, number of live and dead fetuses or fetal body weights. No differences were seen in visceral and skeletal abnormalities between the control and the treatment groups. No adverse effects on pregnancy and no teratogenic effects were observed. A marked increase in the number of resorptions was observed at 1300 mg/kg-bw/day. The incidence was 0.4, 0.9, 0.5 and 1.0 in the 0, 125, 400 and 1300 mg/kg-bw/day groups, respectively.
**LOAEL for maternal toxicity = 400 mg/kg-bw/day** (based on clinical signs)
**NOAEL for maternal toxicity = 125 mg/kg-bw/day**
**LOAEL for developmental toxicity > 1300 mg/kg-bw/day**
**NOAEL for developmental toxicity = 1300 mg/kg-bw/day**

(2) Groups of pregnant female New Zealand White rabbits were administered glutaric acid at 0, 50, 160 and 500 mg/kg-bw/day via gavage on days 6 – 18 of gestation; females were sacrificed on gestation day 29 and examined for gross pathological changes. No changes were seen in reproductive status. There were no effects on the number of corpora lutea, implantations, number of live and dead fetuses, resorptions, fetal body weights or external, visceral and skeletal abnormalities. There were no adverse effects on pregnancy and no embryotoxic or teratogenic effects were observed.
**NOAEL for maternal toxicity > 500 mg/kg-bw/day** (highest dose tested)
**NOAEL for developmental toxicity > 500 mg/kg-bw/day** (highest dose tested)

***Adipic acid (Hexanedioic acid; CAS No. 124-04-9)***
(1) Groups of pregnant female Wistar rats were administered adipic acid via gavage at 0, 2.9, 13, 62 and 288 mg/kg-bw/day during gestation days 6 – 15. Females were sacrificed on gestation day 20 and were examined for any gross pathological changes. There were no effects on the number of corpora lutea, implantations, number of live and dead fetuses, resorptions, fetal body weights, or external, visceral and skeletal abnormalities.
**NOAEL for maternal toxicity = 288 mg/kg-bw/day** (highest dose tested)
**NOAEL for developmental toxicity = 288 mg/kg-bw/day** (highest dose tested)

(2) Groups of pregnant female Dutch-belted rabbits were administered adipic acid at 0, 2.5, 12, 54 and 250 mg/kg-bw/day via gavage on gestation days 6-18; females were sacrificed on gestation day 29 and examined for gross pathological changes. No changes were seen in reproductive status. There were no effects on the number of corpora lutea, implantations, number of live and dead fetuses, resorptions, fetal body weights, and external, visceral and skeletal abnormalities. There were no adverse effects on pregnancy and no embryotoxic or teratogenic effects were observed.
**NOAEL for maternal toxicity > 250 mg/kg-bw/day** (highest dose tested)
**NOAEL for developmental toxicity > 250 mg/kg-bw/day** (highest dose tested)

***Genetic Toxicity – Gene Mutation***

***In vitro***
***Succinic acid (Butanedioic acid; CAS No. 110-15-6)***
In Ames assays, *Salmonella typhimurium* strains TA92, TA94, TA98, TA100, TA1535 and TA1537, were exposed to succinic acid, in the presence and absence of metabolic activation, up to 5000 µg/plate. No marked increases in the number of revertant colonies were detected at the maximum concentration.
**Succinic acid was not mutagenic in these assays.**

***Glutaric acid (Pentanedioic acid; CAS No. 110-94-1)***
(1) Glutaric acid was tested in an *in vitro* Ames assay using *Salmonella typhimurium* strains TA98, TA100, TA1535, and TA1538 with and without metabolic activation and up to 5000 µg/plate of test substance. Cytoxicity was evident at and above 2000 µg/plate without metabolic activation and at 5000 µg/plate with metabolic activation in TA100. Positive, negative and solvent controls showed appropriate responses.
**Glutaric acid was not mutagenic in these assays.**

(2) Glutaric acid tested negative in *in vitro* in mouse lymphoma cells (L5178Y; TK locus) with metabolic activation up to 8295 µg/plate in three tests. The positive and negative controls gave appropriate responses.
**Glutaric acid was not mutagenic in these assays.**

***Adipic acid (Hexanedioic acid; CAS No. 124-04-9)***
Adipic acid did not induce increased revertant counts when tested in an *in vitro* Ames assay using *Salmonella typhimurium* strains TA98, TA100, TA1535, TA1537 and TA1538 and *Escherichia coli* strain WP2, with and without metabolic activation and up to 10 mg/plate. Positive control showed appropriate response.
**Adipic acid was not mutagenic in these assays.**

***Genetic Toxicity – Chromosomal Aberrations***

***In vitro***
***Succinic acid (Butanedioic acid; CAS No. 110-15-6)***
Succinic acid did not induce structural aberrations when tested *in vitro* in Chinese Hamster fibroblasts at 10 mg/mL. Negative controls gave appropriate response.
**Succinic acid did not induce chromosomal aberrations in this assay.**

***Adipic acid (Hexanedioic acid; CAS No. 124-04-9)***
(1) Adipic acid was negative up to 200 µg/mL in an *in vitro* cytogenetic assay using human embryonic lung cell cultures.
**Adipic acid did not induce chromosomal aberrations in this assay.**

(2) Adipic acid was negative in a dominant lethal assay in rats when tested up to 375 mg/kg-bw.
**Adipic acid did not induce chromosomal aberrations in this assay.**

***In vivo***
***Glutaric acid (Pentanedioic acid; CAS No. 110-94-1)***
In an *in vivo* mouse micronucleus assay, glutaric acid, administered to male and female mice via intraperitoneal injection at 800 mg/kg-bw did not produce a statistically significant increase in micronuclei. The positive and negative controls showed appropriate response.
**Glutaric acid was not mutagenic in this assay.**

***Adipic acid (Hexanedioic acid; CAS No. 124-04-9)***
Adipic acid was negative in an *in vivo* rat cytogenetic chromosomal aberration assay at doses up to 5000 mg/kg-bw...
**Adipic acid did not induce chromosomal aberrations in this assay.**

***Additional Information***

***Carcinogenicity***

***Succinic acid (Butanedioic acid; CAS No. 110-15-6)***
In a 2-year carcinogenicity study, male and female F344 rats were administered monosodium succinate in drinking water at 0, 1 and 2% (~1000 or 2000 mg/kg-bw/day). After 104 weeks of treatment, the rats were given distilled water for additional 9 weeks and then sacrificed at week 113. The test substance intake was 196 and 437 mg/rat/day for males and 146, and 309 mg/rat/day for females, at 1 and 2%, respectively. Treatment- and dose-dependent decreases in growth rate were seen. In both sexes, there were no statistically significant differences between the control and treated groups in overall tumor incidences and mean survival times. Tumors were found in many organs or tissues in all groups including the controls. None of the treated groups showed a significant increase in the incidence of any tumors over that in the corresponding controls.
**Monosodium succinate did not increase the incidence of any tumors over that in the corresponding controls in a 2-year drinking water study.**

***Skin Irritation***

***Succinic Acid (Butanedioic acid; CAS No. 110-15-6)***
Succinic acid is slightly irritating to skin.

***Glutaric acid (Pentanedioic acid; CAS No. 110-94-1)***
Glutaric acid was slightly irritating to skin.

***Adipic acid (Hexanedioic acid; CAS No. 124-04-9)***
Adipic acid showed slight to mild skin irritation.

***Eye Irritation***

***Succinic Acid (Butanedioic acid; CAS No. 110-15-6)***
Succinic acid is severely irritating to eyes causing damage to cornea and severe necrosis.

***Glutaric acid (Pentanedioic acid; CAS No. 110-94-1)***
Glutaric acid was irritating to eyes with erythema and edema, and iritic dullness persisting after 7 days.

***Adipic acid (Hexanedioic acid; CAS No. 124-04-9)***
Adipic acid showed moderate eye irritation.

***Sensitization***

***Adipic acid (Hexanedioic acid; CAS No. 124-04-9)***
Adipic acid is not a sensitizer based on a study in guinea pigs.

**Conclusion:** The acute toxicity of category members is low. The category members are slightly irritating to skin but cause moderate to severe eye irritation. They do not have a sensitizing potential. Repeated exposures via oral route affected body weight and body weight gains at higher doses. Reproductive toxicity data are not available for the category members. However, in repeated-dose toxicity studies, no effects on reproductive organs were seen. In developmental toxicity studies, the category members did not show any effects on fetal survival, fetal weight, litter size or implantations, or any skeletal or visceral abnormalities. All category members were not mutagenic in tested strains of *Salmonella typhimurium* as well as in mammalian cells and did not induce statistically significant increase in the mean number of micronucleated polychromatic erythrocytes in the bone marrow of CD-1 mice. In a 2–year carcinogenicity study of monosodium succinate, tumors were found in many organs or tissues in all groups including the controls. None of the treated groups showed a significant increase in the incidence of any tumors over that in the corresponding controls.

The potential health hazard of the dicarboxylic acids category is low. Monosodium succinate did not increase the incidence of any tumors over that in the corresponding controls in a 2-year drinking water study.

**Table 3. Summary of Human Health Data**

| Endpoints | Succinic acid (Butanedioic acid) (110-15-6) | Glutaric acid (Pentanedioic acid) (110-94-1) | Adipic acid (Hexanedioic acid) (124-04-9) |
|---|---|---|---|
| **Acute Oral Toxicity $LD_{50}$ (mg/kg-bw)** | **2260** | **2750** | **5050** |
| **Acute Dermal Toxicity $LD_{50}$ (mg/kg-bw)** | No Data<br>> 7940<br>(RA) | **> 10,000** | **> 7940** |
| **Acute Inhalation Toxicity $LC_{50}$ (mg/L)** | No Data<br>> 7.7<br>(RA) | No Data<br>> 7.7<br>(RA) | **> 7.7** |
| **Repeated-Dose Toxicity NOAEL/LOAEL (mg/kg-bw/day)** | **NOAEL ~ 1250**<br>**LOAEL ~ 2500** | **Rat**<br>**NOAEL ~ 500**<br>**LOAEL = ~1000**<br>**Dog**<br>**NOAEL ~ 250**<br>**LOAEL = 500** | **NOAEL ~ 280**<br>**LOAEL ~ 809** |
| **Reproductive Toxicity** | No Data<br>Evaluation of male reproductive organs from 90-day study —No effects | No Data<br>Evaluation of male reproductive organs from 90-day study —No effects | No Data<br>Evaluation of male reproductive organs from 90-day study —No effects |
| **Developmental Toxicity**<br><br>**(maternal toxicity)**<br><br>**(developmental toxicity)**<br><br><br><br>**(maternal toxicity)**<br><br>**(developmental toxicity)** | No Data<br><br>Rat<br>NOAEL > 288<br>LOAEL = Not established<br>NOAEL > 288<br>LOAEL = Not established<br><br>Rabbit<br>NOAEL > 250<br>LOAEL = Not established<br>NOAEL > 250<br>LOAEL = Not established<br>(RA) | <br><br>**Rat**<br>**NOAEL = 125**<br>**LOAEL= 400**<br>**NOAEL > 1300**<br>**LOAEL = Not established**<br><br>**Rabbit**<br>**NOAEL >500**<br>**LOAEL = Not established**<br>**NOAEL >500**<br>**LOAEL = Not established** | <br><br>**Rat**<br>**NOAEL > 288**<br>**LOAEL = Not established**<br>**NOAEL > 288**<br>**LOAEL = Not established**<br><br>**Rabbit**<br>**NOAEL > 250**<br>**LOAEL = Not established**<br>**NOAEL > 250**<br>**LOAEL = Not established** |
| **Genetic Toxicity – Gene Mutation** ***In vitro*** | **Negative** | **Negative** | **Negative** |
| **Genetic Toxicity – Chromosomal Aberrations** ***In vitro*** | **Negative** | No Data<br>Negative<br>(RA) | **Negative** |
| **Genetic Toxicity – Chromosomal Aberrations** ***In vivo*** | No Data<br>Negative<br>(RA) | **Negative** | **Negative** |
| **Carcinogenicity** | **Monosodium succinate did not increase the incidence of any tumors over that in the corresponding controls in a 2-year drinking water study.** | – | **-** |
| **Skin Irritation** | **Slight skin irritant** | **Slight skin irritant** | **Slight to mild skin irritant** |
| **Eye Irritation** | **Severe irritant** | **Moderate** | **Mild to moderate** |
| **Dermal Sensitization** | – | – | **Not a sensitizer** |

**Measured data in bold text**; (RA) = read across; – = No data

**4. Hazard Identification**

The members of the dicarboxylic acids category are solids at room temperature. They have negligible vapor pressure, high water solubility and minimal volatility. They are highly mobile in soil and water systems. They are not persistent or bioaccumulative. They are stable to hydrolysis and photolysis but are expected to degrade at rapid rates by biodegradation. Because the chemicals in this category are readily biodegradable and do not bioaccumulate, they are classified as not persistent (P1) and not bioaccumulative (B1) and are not Persistent Organic Pollutants (POPs).

Evaluation of the toxicity data for fish, aquatic invertebrates and aquatic plants indicates the potential acute hazard of category members to aquatic organisms is low.

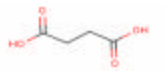
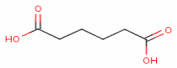
The acute toxicity of category members is low. The category members are slightly irritating to skin but cause moderate to severe eye irritation. They do not have a sensitizing potential. Repeated exposures via oral route affected body weight and body weight gains at higher doses. Reproductive toxicity data are not available for the category members. However, in repeated-dose toxicity studies, no effects on reproductive organs were seen. In developmental toxicity studies, the category members did not show any effects on fetal survival, fetal weight, litter size or implantations, or any skeletal or visceral abnormalities. All category members were not mutagenic in tested strains of *Salmonella typhimurium* as well as in mammalian cells and did not induce statistically significant increase in the mean number of micronucleated polychromatic erythrocytes in the bone marrow of CD-1 mice. In a 2–year carcinogenicity study of monosodium succinate, tumors were found in many organs or tissues in all groups including the controls. None of the treated groups showed a significant increase in the incidence of any tumors over that in the corresponding controls.

The potential health hazard of the dicarboxylic acids category is low. Monosodium succinate did not increase the incidence of any tumors over that in the corresponding controls in a 2-year drinking water study.

**5. Data Gaps**

No data gaps were identified under the HPV Challenge Program.

## Appendix

| Dicarboxylic Acids | | |
|---|---|---|
| **CAS No.** | **Chemical Name** | **Structure** |
| SPONSORED CHEMICALS | | |
| 110-15-6 | **Succinic acid (Butanedioic acid)** |  |
| 110-94-1 | **Glutaric acid (Pentanedioic acid)** |  |
| 124-04-9 | **Adipic acid (Hexanedioic acid)** |  |

## References

E.I. du Pont de Nemours and Company (du Pont) , 2007. Robust Summaries & Test Plans: Dicarboxylic Acids Category HPV Test Plan, http://www.epa.gov/chemrtk/pubs/summaries/dicarbx/c13108tc.htm

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

HSDB, 2007. Hazard Substances Data Base. Accessed August 22, 2007
As cited in HSDB records for:

SUCCINIC ACID.
http://toxnet.nlm.nih.gov/cgi-bin/sis/search/d?./temp/~pMPzmM:0:@sa0+

GLUTARIC ACID
http://toxnet.nlm.nih.gov/cgi-bin/sis/search/d?./temp/~t9xw9D:0:@sa0+

ADIPIC ACID
http://toxnet.nlm.nih.gov/cgi-bin/sis/search/d?./temp/~yurRnz:0:@sa0+

OECD, 2001. OECD Series on Testing and Assessment, Number 33. Harmonized Integrated Classification System For Human Health and Environmental Hazards of Chemical Substances and Mixtures. Joint Meeting of the Chemicals Committee and the Working Party on Chemicals, Pesticides and Biotechnology, August 14, 2001.

USEPA, 2007. EPI Suite™ (version 3.2) PC-Computer software developed by EPA's Office of Pollution Prevention Toxics and Syracuse Research Corporation. http://www.epa.gov/opptintr/exposure/pubs/episuite.htm

# Exposure Characterization for HPV Challenge Chemical

## Butanedioic Acid
**(Succinic Acid)**

**CAS #110-15-6**

**March 14, 2008**

**Prepared by**

Exposure Assessment Branch
Chemical Engineering Branch
Economics Exposure and Technology Division
Office of Pollution Prevention and Toxics
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# Exposure Characterization for HPV Challenge Chemical
**Butanedioic acid (CAS #110-15-6)**

## Non-CBI Executive Summary

Butanedioic acid (Succinic acid) has an annual production volume between 10 million and 50 million pounds in the United States (USEPA, 2006). Butanedioic acid is included in the dicarboxylic acids category which also includes pentanedioic and hexanedioic acids. The chemicals in the dicarboxylic acid category are readily biodegradable and do not bioaccumulate; therefore, they are classified as P1B1. They are not Persistent Organic Pollutants (POPs) (USEPA, 2007b). Public information on toxicity and fate and transport of butanedioic acid was submitted under the HPV Challenge Program. A SIDS dossier has not been prepared for this chemical. The chemical is not on the Toxics Release Inventory (USEPA, 2007a). Butanedioic acid is listed in FDA's Everything Added to Food in the United States database (EAFUS, 2007).

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

*Exposures to Workers*

Based on IUR data, more than 10,000 workers engaged in manufacturing and industrial processing of butanedioic acid are reasonably likely to be exposed to this chemical. The National Occupational Exposure Survey (NOES) conducted by NIOSH between 1981 and 1983 estimated a total of 31,198 workers potentially exposed to this chemical (NIOSH, 2007b).

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

This chemical has a vapor pressure of 1.9 x 10e-7 torr at 25°C (USEPA, 2007b). OPPT has established 0.001 torr as a value above which worker exposures to vapors should be estimated for chemical assessments. Below this value, OPPT assumes exposure to vapor is negligible. However, based on IUR data, other types of worker exposures are possible for this chemical. Some use and exposure information was contained in the HPV submission, including air monitoring data for dicarboxylic acid vapors which measured a maximum TWA of 0.15 mg/m3 and an average of 0.11 mg/m3 in 15 samples. OSHA has not established a permissible exposure limit (PEL) for butanedioic acid (NIOSH, 2007b).

Based on IUR data, specifically the number of potentially exposed workers and use codes, the potential worker exposure is considered high.

*Exposures to the General Population and the Environment*

One non-CBI source indicated that butanedioic acid's production and use in the manufacture of lacquers, dyes, esters for perfumes, in photography, and in foods as a sequestrant, buffer and neutralizing agent may result in its release to the environment through various waste streams. (HSDB, 2007). The potential for exposure to the general population and the environment is likely based on the uses and expected releases. Therefore, based on the totality of the information considered and expert judgment, EPA assumes, for purposes of this risk based prioritization that the potential for general population and/or environmental exposure to this chemical is high.

*Exposures to Commercial Workers and Consumers*

IUR information has some commercial/ consumer products listed. Depending on the product, consumers may have potential dermal and inhalation exposure to the chemical. Since this chemical is present in dry powder or other solid form, inhalation exposure to particulates may occur.

The likelihood that this chemical is used in consumer/commercial products is high based on IUR data.

*Exposures to Children*

Information suggests either that butanedioic acid will not be used in children's consumer products or that this type of information is not readily available.

There is a moderate likelihood that this chemical is used in products intended to be used by children but there is uncertainty in the IUR data.

***References***

EAFUS, 2007. Everything Added to Food in the United States. As cited in EAFUS record for CAS#110-15-6. http://vm.cfsan.fda.gov/~dms/eafus.html

HSDB,2007. Hazard Substances Data Base. As cited in HSDB record for succininc acid, CAS 110-15-6, accessed December 19, 2007. http://toxnet.nlm.nih.gov/cgi-bin/sis/htmlgen?HSDB.

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

NIOSH, 2007b. National Occupational Exposure Survey (NOES). Accessed December 2007. http://www.cdc.gov/noes/noes2/84381occ.html

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

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

USEPA 2007b. Physical/Chemical and Environmental Fate Characterization for High Production Volume Chemicals Chemical Name: Butanedioic Acid, CAS 110-15-6. http://www.epa.gov/chemrtk/hpvis/index.html.

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# Exposure Characterization for HPV Challenge Chemical

## Pentanedioic Acid
**(Glutaric Acid)**

**CAS #110-94-1**

**March 14, 2008**

**Prepared by**

Exposure Assessment Branch
Chemical Engineering Branch
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# Exposure Characterization for HPV Challenge Chemical
**Pentanedioic Acid (CAS #110-94-1)**

## Non-CBI Executive Summary

Pentanedioic acid (Glutaric acid) has an annual production volume in the range between 50 million and 100 million pounds (USEPA, 2006). Pentanedioic acid is a member of the dicarboxylic acid category; other members of this category are butanedioic acid and hexanedioic acids. The chemicals in the dicarboxylic acid category are readily biodegradable and do not bioaccumulate; and, therefore, are classified as P1B1. They are not Persistent Organic Pollutants (POPs) (USEPA, 2007b). Information on the toxicity and fate and transport of pentanedioic acid is available in the public record for the HPV Challenge Program.

One non-CBI source indicated that pentanedioic acid is used in organic synthesis of chemical intermediates for polymers, e.g., polyamides and polyesters, for its esters and anhydride, and for human and veterinary medication (HSDB, 2007). A SIDS dossier has not been prepared for this chemical. Pentanedioic acid is not on the Toxics Release Inventory (USEPA, 2007a).

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

*Exposures to Workers*

Based on IUR data, there are between 10,000 and 25,000 manufacturing and industrial processing workers who reasonably likely to be exposed to this chemical. The National Occupational Exposure Survey (NOES) conducted between 1981 and 1983 estimated a total of 1,827 workers potentially exposed to this chemical (NIOSH, 2007b).

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

This chemical has a vapor pressure of 2.9 x 10e-6 torr at 25°C (USEPA, 2007b). OPPT has established 0.001 torr as a value above which worker exposures to vapors should be estimated for chemical assessments; below this value, OPPT assumes exposure to vapor is negligible. However, based on IUR data, other types of worker exposures are possible for pentanedioic acid. The HPV submission for dicarboxylic acids included exposure monitoring data for dicarboxylic acid vapors. The monitoring data showed maximum TWA of 14 samples of 0.21 mg/m3 and an

average of 0.13 mg/m3. This chemical does not have an OSHA Permissible Exposure Limit (NIOSH, 2007a).

Based on IUR data, specifically the number of potentially exposed workers and use codes, the potential worker exposure is considered high.

*Exposures to the General Population and the Environment*

Information suggests that pentanedioic acid will be used in consumer/commercial products which can be a route of environmental and general population exposure. In addition, these uses may result in direct exposure to consumers and/or indirect exposure to children. Based on the totality of the information considered and expert judgment, EPA assumes, for purposes of this risk based prioritization that the potential for general population and/or environmental exposure to this chemical is high.

*Exposures to Commercial Workers and Consumers*

Information suggests that pentanedioic acid will be used in consumer/commercial products which can be a route of environmental and general population exposure, as well as direct to consumers and/or indirect exposure children. Depending on the product, consumers may have potential dermal and inhalation exposure to the chemical.

The likelihood that this chemical is used in consumer/commercial products is high based on IUR data.

*Exposures to Children*

IUR information indicates that either that pentanedioic acid will not be used in product produced directly marketed for children's use or that this type of information is not readily available.

There is a moderate likelihood that this chemical is used in products intended to be used by children but there is uncertainty in the IUR data.

## References

HSDB, 2007. Hazard Substances Data Base. As cited in HSDB record for pentanedioic acid, CAS 110-94-1, accessed December 2007. http://toxnet.nlm.nih.gov/cgi-bin/sis/htmlgen?HSDB

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

NIOSH, 2007b. National Occupational Exposure Survey (NOES). Accessed December 2007. http://www.cdc.gov/noes/noes2/x4684occ.html

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

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

USEPA 2007b. Physical/Chemical and Environmental Fate Characterization for High Production Volume Chemicals Chemical Name: Petanedioic Acid.

# Exposure Characterization for HPV Challenge Chemical

# Hexanedioic Acid
## (Adipic Acid)

**CAS #124-04-9**

**March 14, 2008**

**Prepared by**

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# Exposure Characterization for HPV Challenge Chemical
## Hexanedioic Acid (CAS #110-94-1)

### Non-CBI Executive Summary

Hexanedioic acid (Adipic acid) has an annual production volume in excess of one billion pounds in the United States (USEPA, 2006). This chemical is a member of the dicarboxylic acids category; other members of the category are butanedioic acid and pentanedioic acid. Chemicals in the dicarboxylic acid category are readily biodegradable and do not bioaccumulate and are classified as P1B1. They are not Persistent Organic Pollutants (POPs) (USEPA, 2007b). Information on the toxicity and fate and transport of hexanedioic acid as well as limited use and exposure information is publicly available through the HPV Challenge Program. A SIDS dossier has been prepared for this chemical by Germany (OECD, 2007).

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

*Exposures to Workers*

The number of workers reasonably likely to be exposed to hexanedioic acid during manufacture and industrial processing of the chemical is estimated to be greater than 10,000 based on IUR data. The National Occupational Exposure Survey (NOES) conducted by NIOSH between 1981 and 1983 estimated a total of 140,635 workers potentially exposed to this chemical (NIOSH, 2007b).

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

This chemical has a vapor pressure of $3.2 \times 10^{-7}$ torr at 25°C (USEPA., 2007b). OPPT has established 0.001 torr as a value above which worker exposures to vapors should be estimated for chemical assessments. Below this value, OPPT assumes exposure to vapor is negligible. However, based on IUR data, other types of worker exposures are possible for this chemical. The SIDS dossier included inhalation monitoring data of personnel handling dicarboxylic acids which showed a maximum TWA of 14 samples was 15 mg/m3, with an average TWA of 2.3 mg/m3. The chemical is not on the Toxics Release Inventory (U.S. EPA, 2007a) and does not have an OSHA Permissible Exposure Limit (NIOSH, 2007).

Based on IUR data, specifically the number of potentially exposed workers and use codes, the potential worker exposure is considered high

### *Exposures to the General Population and the Environment*

Information suggests that hexanedioic acid will be used in consumer/commercial products which can be a route of environmental and general population exposure, as well as direct or indirect exposure to consumers and children. Hexanedioic acid may be released into the environment in various waste streams from its production and use in the manufacture of synthetic fibers, plasticizers, resins plastics, and as a food acidulant (HSDB, 2007). Based on the totality of the information considered and expert judgment, EPA assumes, for purposes of this risk based prioritization that the potential for general population and/or environmental exposure to this chemical is high.

*Exposures to Commercial Workers and Consumers*

IUR information states that hexanedioic acid will be used in consumer/commercial products which can be a route of environmental and general population exposure, as well as direct or indirect exposure to consumers and children. Depending on the product, consumers may have potential dermal and inhalation exposure to the chemical.

The likelihood that this chemical is used in consumer/commercial products is high based on IUR data.

*Exposures to Children*

IUR information states that hexanedioic acid will be used in products intended for use by children. Depending on the product, children may have potential dermal and inhalation exposure to the chemical.

The likelihood that this chemical is used in products intended to be used by children is high based on IUR data.

*References*

EAFUS, 2007. Everything Added to Food in the United States. As cited in EAFUS record for CAS#110-15-6. http://vm.cfsan.fda.gov/~dms/eafus.html

HSDB, 2007. National Institute of Health's (NIH) Household Products Database. Accessed December 2007. http://hpd.nlm.nih.gov/products.htm

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OECD 2007, Organization for Economic Cooperation and Development SIDS Initial Assessments of HPV Chemicals, http://www.chem.unep.ch/irptc/sids/oecdsids/sidspub.html, Accessed August 2, 2007.

USEPA, 2003. Source Ranking Database (SRD), Version 3.0 http://www.epa.gov/opptintr/exposure/pubs/srd.htm

USEPA, 2006. 2006 Partial Updating of TSCA Chemical Inventor

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

USEPA 2007b, Physical/Chemical and Environmental Fate Characterization for High Production Volume Chemicals Chemical Name: Hexanedioic Acid.