SCREENING-LEVEL HAZARD CHARACTERIZATION
Phthalate Esters Category

Sponsored Chemicals
19 Different Chemicals (See Section 1.0 for Details)

The High Production Volume (HPV) Challenge Program[1] was conceived as 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 sponsored chemicals; sponsorship entailed the identification and initial assessment of the adequacy of existing toxicity data/information, conducting new testing if adequate data did 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.

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 by developing hazard characterizations (HCs). These HCs consist of an evaluation of the quality and completeness of the data set provided in the Challenge Program submissions. They are not intended to be definitive statements regarding the possibility of unreasonable risk of injury to health or the environment.

The evaluation is performed according to established EPA guidance[2,3] and is based primarily on hazard data provided by sponsors; however, 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 one year prior to the date of the HPV Challenge submission to the present: (ChemID to locate available data sources including Medline/PubMed, Toxline, HSDB, IRIS, NTP, ATSDR, IARC, EXTOXNET, EPA SRS, etc.), STN/CAS online databases (Registry file for locators, ChemAbs for toxicology data, RTECS, Merck, etc.) and Science Direct. OPPT's focus on these specific sources is based on their being of high quality, highly relevant to hazard characterization, and publicly available.

OPPT does not develop HCs for those HPV chemicals which have already been assessed internationally through the HPV program of the Organization for Economic Cooperation and Development (OECD) and for which Screening Initial Data Set (SIDS) Initial Assessment Reports (SIAR) and SIDS Initial Assessment Profiles (SIAP) are available. These documents are presented in an international forum that involves review and endorsement by governmental authorities around the world. OPPT is an active participant in these meetings and accepts these documents as reliable screening-level hazard assessments.

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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.

These hazard characterizations are technical documents intended to inform 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.

CASRN	**See Section 1.0**
Chemical Abstract Index Name	**See Section 1.0**
Structural Formulae	**See Section 1.0 and Appendix 1**

Summary

The phthalate esters category contains 19 liquid compounds that are split into 3 subcategories: low molecular weight phthalate esters, transitional phthalate esters, and high molecular weight phthalate esters. The low molecular weight phthalate esters have moderate vapor pressure. The transitional phthalate esters have low vapor pressure. The high molecular weight phthalate esters have negligible to low vapor pressure. The water solubility of the low molecular weight phthalate esters is high. The water solubility of the transitional phthalate esters is low. The high molecular weight phthalate esters water solubility is negligible to low. The phthalate esters are expected to have low to moderate mobility in soil. Volatilization of the phthalate esters is expected to be low to moderate. Although members of this category possess hydrolysable functional groups, the rate of hydrolysis is considered negligible for these compounds. The rate of atmospheric photooxidation is considered negligible to slow for the low molecular weight phthalate esters and moderate for the transitional and high molecular weight phthalate esters. The phthalate esters are expected to have low persistence (P1) and low bioaccumulation potential (B1).

Human Health Effects

Subcategory I: Low Molecular Weight Phthalate Esters (CASRNs 131-11-3 and 84-66-2)

The acute oral (rats and mice), dermal (guinea pigs) and inhalation (rats) toxicity of low molecular weight phthalate esters in animal studies is low. Oral repeated-dose and reproductive toxicity data in rats and mice are available for CASRN 84-66-2 and show effects at 750 mg/kg/day (decreases in body weight) and 3250 mg/kg/day (reduced litter size), respectively. The NOAELs for these studies were 150 mg/kg/day and 1625 mg/kg/day, respectively. These data may also reasonably represent CASRN 131-11-3. Prenatal developmental toxicity data in rats are available for both members of this subcategory. Maternal toxicity is seen at oral (dietary) doses of 1910 mg/kg/day (CASRN 84-66-2, decreased body weight) and 3570 mg/kg/day (CASRN 131-11-3, decreased body weight and kidney effects), with the NOAELs of 200 and 840 mg/kg/day, respectively. There are no developmental effects following exposure to CASRN 131-11-3 (highest dose of 3570 mg/kg/day) and skeletal variations are observed at the highest tested dose of CASRN 84-66-2 (3210 mg/kg/day). Both members of the low molecular weight phthalate esters category are not mutagenic when tested *in vitro* in bacteria and do not induce chromosomal aberrations when tested *in vitro.* CASRN 84-66-2 is not a skin or eye irritant in rabbits. Both CASRN 131-11-3 and CASRN 84-66-2 are negative in one-year initiation/promotion cancer studies (dermal route of exposure) in mice. The NTP reported negative results in rats and equivocal results in mice in separate two-year dermal cancer studies with CASRN 84-66-2.

Subcategory II: Transitional Phthalate Esters (CASRN 68515-50-4)

The acute oral and dermal toxicity of CASRN 68515-50-4 in rats and rabbits, respectively, is low. Available repeated-dose toxicity studies with CASRN 68515-50-4 show increased heart weights at 76.6 mg/kg/day (highest tested dose in rats) and changes in body, liver and testes weights at 900 mg/kg/day (highested tested dose in dogs). Reproductive toxicity data exist for the supporting compound CASRN 84-75-3 (decreased pregnancy rates, fetal survival and testicular effects all at the highest tested dose of 430 mg/kg/day). There are no prenatal developmental toxicity data with either CASRN 68515-50-4 or the

supporting chemical CASRN 84-75-3; however available data exist for phthalate esters that fall within the boundaries of this subcategory (i.e., dibutyl phthalate and dipentyl phthalate; CASRNs 84-74-2 and 131-18-0, respectively). Both of these phthalate esters are known to cause male reproductive tract abnormalities following neonatal and early postnatal exposures (known as the phthalate syndrome). CASRN 68515-50-4 is not mutagenic when tested in bacteria *in vitro* and has not induced chromosomal aberrations when tested *in vitro* in mammalian cell lines.

Subcategory III: High Molecular Weight Phthalate Esters (CASRNs 68515-44-6, 71888-89-6, 111381-89-6, 27554-26-3, 117-84-0,111381-90-9, 68515-45-7, 68515-43-5, 84-77-5, 111381-91-0, 16883-83-3, 3648-20-2, 85507-79-5, 68515-40-2, 68648-93-1 and 68515-47-9)

Acute oral toxicity data in rats and mice are available for 4/16 sponsored members and for 5/6 supporting data and all show a low order of toxicity. Dermal acute toxicity data in rabbits are available for 4/16 sponsored members and 4/6 supporting members, again showing low toxicity. There is only one acute inhalation study (with a supporting chemical) in rats which also shows a low order of toxicity.

Repeated-dose toxicity data exist for only one (CASRN 117-84-1) of the 16 members of this subcategory; however, there are four different studies in supporting chemicals which are used to read-across to untested sponsored members of this subcategory. The range in doses and effects across the subcategory are from 29 mg/kg/day (sperm effects, CASRN 117-81-7, a supporting chemical) to 381 mg/kg/day (liver and thyroid effects, CASRN 85-68-7). The range in reported NOAELs for these same studies is 5.8 mg/kg/day (CASRN 117-81-7) to 151 mg/kg/day (CASRN 85-68-7). Reproductive toxicity studies (one-generation, two generation, or combined repeated-dose/reproductive/developmental toxicity protocols) are available for two sponsored subcategory members (CASRN 117-84-0 and CASRN 68515-43-5) and data are also available for five supporting chemicals. The range in doses and effects observed are from 140 mg/kg/day (decreased number of litters, live pups per litter, and live pup weights,CASRN 117-81-7, a supporting chemical) to 750 mg/kg/day (decreased pup body weight in both CASRN 68515-41-3 [a supporting chemical] and CASRN 68515-43-5 studies). The range in reported NOAEL values is 14 mg/kg/day (CASRN 117-81-7, supporting chemical) to the highest tested dose in the CASRN 117-84-0 reproductive study (7500 mg/kg/day).

Five prenatal developmental studies in rats with sponsored Subcategory III members exist and there are additional data for all six supporting chemicals. Overall, maternal toxicity is seen at doses of between 50 mg/kg/day (liver effects, CASRN 119-06-2, a supporting chemical) to 1000 mg/kg/day (multiple effects in studies with CASRNs 68515-44-6, 111381-89-6 111381-90-9, 68515-48-0 [a supporting chemical], and 68515-49-1 [a supporting chemical]). The lowest reported NOAEL for maternal toxicity is 10 mg/kg/day (CASRN 119-06-2, supporting chemical). Two studies show no maternal toxicity at the highest dose tested (CASRN 68515-43-5 and CASRN 68515-41-3 [a supporting chemical], both at 1000 mg/kg/day). In 9/11 studies, developmental toxicity is observed (the two for which no developmental toxicity is seen at the highest tested dose of 1000 mg/kg/day are for the two supporting chemicals CASRNs 68515-49-1 and 119-06-2). A variety of developmental effects (most frequently reported are malformations and skeletal variations) are seen in the other nine studies from doses of 91 mg/kg/day (CASRN 117-81-7, a supporting chemical), to 500 mg/kg/day (CASRN 68515-43-5) and from 750 mg/kg/day to 1000 mg/kg/day (CASRNs 85-68-7 [a supporting chemical], 71888-89-6, 68515-44-6, 111381-89-6, 68515-41-3 [a supporting chemical], 111381-90-9, and 68515-48-0 [a supporting chemical]). The lowest reported NOAEL for developmental toxicity is 44 mg/kg/day (CASRN 117-81-7, supporting chemical). Many sponsored subcategory members (and supporting chemicals) are negative for mutagenicity following testing at both the gene and chromosome level.

Environmental Toxicity Effects
Aquatic Toxicity

Subcategory I: Low Molecular Weight Phthalate Esters

The 96-hr LC_{50} of CASRN 131-11-3 for fish is 56 mg/L. The 48-hr EC_{50} of CASRN 131-11-3 for aquatic invertebrates is 45.9 mg/L. The 6-d EC_{50} of CASRN 131-11-3 for aquatic plants is 142 mg/L (growth). The 60-d NOEC of CASRN 131-11-3 for fish is 11 mg/L. The 21-d LOEC of CASRN 131-11-3 to aquatic invertebrates is 23 mg/L.

The 96-hr LC_{50} of CASRN 84-66-2 for fish is 12 mg/L. The 48-hr EC_{50} of CASRN 84-66-2 for aquatic invertebrates is 86 mg/L. The 8-d EC_{50} of CASRN 84-66-2 for aquatic plants is 16 mg/L (growth). The 21-d LOEC of CASRN 84-66-2 is 59 mg/L.

Subcategory II: Transitional Phthalate Esters

There are no acute toxicity effects of CASRN's 68515-50-4 and 71888-89-6 for fish at the water solubility limit. However, the 96-hr LC_{50} of the supporting chemical, CASRN 85-68-7, for fish is 0.82 mg/L. There are no chronic effects of CASRN 68515-50-4 for fish at the water solubility limit.

The 48-hr LC_{50} of CASRN 68515-50-4 for aquatic invertebrates is $\geq$ 0.18 mg/L. There are no acute toxicity effects of CASRN 85-68-7 for aquatic invertebrates at the water solubility limit. There are no chronic effects of CASRN 7188-89-6 for aquatic invertebrates at the water solubility limit. The LOEC of the supporting chemical CASRN 85-68-7, for aquatic invertebrate is 1.4 mg/L.

The 7-d EC_{50} of CASRN 68515-50-4 for aquatic plants is > 0.33 mg/L (biomass), and the 5-d NOEC or LOEC of the supporting chemical, CASRN 85-68-7, for aquatic plants is 0.21 mg/L (biomass).

Subcategory III: High Molecular Weight Phthalate Esters

There are no acute toxicity effects reported for CASRN's 111381-90-9, 27554-26-3, 68648-93-1, 68515-40-2, 3648-20-2, 68515-47-9, and 16883-83-3 for fish at the water solubility limit. There are no chronic effects of CASRN 111381-90-9 to fish at the water solubility limit.

There are no acute toxicity effects of CASRN's 111381-90-9, 27554-26-3, 68648-93-1, 68515-40-2, 3648-20-2 and 68515-47-9 for aquatic invertebrates at the water solubility limit. However, the acute 48-hr LC_{50} of CASRN 16883-83-3 for aquatic invertebrates is 7.5 mg/L. There are no chronic effects of CASRNs 68515-47-9 and 3648-20-2 to aquatic invertebrates at the water solubility limit.

There are no acute toxicity effects reported for CASRN's 111381-90-9, 27554-26-3, 68648-93-1, 68515-40-2, 3648-20-2, 68515-47-9 and 16883-83-3 for aquatic plants at the water solubility limit.

Data Gaps

There are no data gaps for endpoints in the HPV Challenge Program.

The sponsor, the Phthalate Esters Panel HPV Testing Group[4] of the American Chemistry Council, submitted a Test Plan and Robust Summaries to EPA for the phthalate esters category on December 14, 2001. EPA posted the submission on the ChemRTK HPV Challenge website on February 20, 2002 (http://www.epa.gov/hpv/pubs/summaries/benzene/c13467tc.htm). EPA comments on the original submission were posted to the website on December 13, 2002. Public comments were also received and posted to the website. The sponsor submitted updated/revised documents on December 22, 2005, February 28, 2007 and October 3, 2007, which were posted to the ChemRTK website on February 1, 2006, July 27, 2007 and January 7, 2008, respectively. The phthalate esters category consists of the 19 substances described in Section 1 below.

Category Justification

General

The sponsor proposed a phthalate esters category consisting of 19 phthalate esters. The phthalate esters in this category are all benzenedicarboxylic acids esterified with side groups ranging from C_1 to approximately C_{13}. The structural formula for phthalate esters varies depending upon the composition of the alcohols used in manufacturing them. Alkyl side groups may be linear alkyl isomers (e.g., di-methyl and di-n-hexyl phthalates), branched alkyl isomers (e.g., diisohexyl phthalate) and/or a combination of benzyl and linear or branched isomers (e.g., benzyl butyl phthalate and benzyl C_{7-9} branched and linear phthalate). The sponsor then proposed subdividing the category into three subcategories based on similar physicochemical and toxicological properties: Low Molecular Weight Phthalates (produced from alcohols with straight-chain carbon backbones of C_{1-3}), Transitional Phthalates (produced from alcohols with straight-chain carbon backbones of C_{4-6}) and High Molecular Weight Phthalates (produced from alcohols with straight-chain carbon backbones of $C_{>7}$ or a ring structure). EPA agrees that the rationale for the makeup of the category and each subcategory is reasonable for the purposes of the HPV Challenge Program; however, as stated in our comments in 2002, EPA believes that the subcategory assignments of some of the chemicals require revision based on the definition provided in the submission. The purpose of this redistribution is to ensure a more robust read-across approach that is only permitted between members of a subcategory for both environmental and human health effects endpoints.

Human Health Endpoints

As shown in Table 1 in Section 1.0, EPA agrees with the assignment of sponsored chemicals to the low molecular weight subcategory and most of the assignments for the high molecular weight subcategory. The difference between the original submission subcategory assignment and the ones chosen for this hazard characterization is in the moving of six sponsored chemicals from the transitional subcategory to the high molecular weight category (these are CASRNs 68515-44-6, 71888-89-6, 27554-26-3, 111381-89-6, 111381-90-9 and 16883-83-3). This change is based on the primary carbon chain length of the esterified side groups and molecular weight of these chemicals; both of which are presented in Table 1. Thus, the transitional subcategory is restricted to members with primary carbon chain lengths of C_{4-6}.

Environmental Effect Endpoints

For aquatic toxicity, the phthalate esters are divided into three sub categories; the low molecular weight group, the transitional phthalate group, and the high molecular weight group. The rationale for these sub categories are based on similar toxicity, water solubility, and the octanol water partition coefficient (Log K_{ow}).

[4] The Panel was made up of the following companies: BASF Corp., CONDEA Vista Co., Eastman Chemical Co., ExxonMobil Chemical Co., Ferro Corp., ICI Americas/Uniqema, Sunoco Chemicals, and Teknor Apex Co.

Supporting Chemical Justification

The sponsor did not explicitly provide a justification for the supporting chemicals, stating only that the sponsored phthalate esters were supplemented with published information on other phthalate esters currently being assessed under the OECD SIDS program. EPA acknowledged the use of supporting chemical information in comments provided on December 10, 2002, and stated that the supporting information was adequate to characterize ecological and human health endpoints. The supporting chemicals were assigned to the appropriate subcategories based on their structural attributes:

Supporting Chemicals	CASRN	Endpoint(s) Supporting
For the Transitional Subcategory		
Di-n-hexyl phthalate (DnHP)	84-75-3	Human health effects
For the High Molecular Weight Subcategory		
Butyl benzyl phthalate (BBP)	85-68-7	Aquatic toxicity and health effects
Diethylhexyl phthalate (DEHP)	117-81-7	Human health effects
Di-C_{7-9} branched and linear alkyl phthalates (in79P)	68515-41-3	
Diisononyl phthalate (DINP)	68515-48-0	
Diisodecyl phthalate (DIDP)	68515-49-1	
Ditridecyl phthalate (DTP)	119-06-2	

Other Information

Four sponsored chemicals and six of the seven supporting chemicals have either been assessed or are in progress in the OECD HPV Programme. Available information on each case may be viewed at the following links:

CASRNs 85507-79-5, 68515-43-5, 3648-20-2 and 68515-47-9 [all sponsored chemicals] – assessed as part of a category - http://webnet.oecd.org/hpv/ui/SIDS_Details.aspx?id=cf32b7ba-55bb-494b-857e-23d8c8d11b3c

CASRN 117-81-7 [supporing chemical] – http://webnet.oecd.org/hpv/UI/SIDS_Details.aspx?Key=005bc957-a1ea-498d-9f7c-b637a52e0aeb&idx=0
CASRN 85-68-7 [supporting chemical] – assessment in progress (Sponsor country is Norway – http://webnet.oecd.org/hpv/UI/SIDS_Details.aspx?Key=e442e996-f3e7-422a-a516-8e56111558de&idx=0
CASRN 68515-41-3 [supporting chemical]– a member of a category with CASRN 119-06-2 - http://webnet.oecd.org/hpv/UI/SIDS_Details.aspx?Key=c6e75e06-1cb5-4ab9-b149-e5722cfbd00d&idx=0
CASRN 68515-48-0 [supporting chemical] – http://webnet.oecd.org/hpv/UI/SIDS_Details.aspx?Key=0ca90094-1b46-4561-883f-9cd27e9ab09b&idx=0
CASRN 68515-49-1 [supporting chemical] – http://webnet.oecd.org/hpv/UI/SIDS_Details.aspx?Key=3ca4624a-a7b0-4ecf-8d8a-7637478b9004&idx=0

CASRN 119-06-2 [supporting chemical] — a member of a category with CASRN 68515-41-3- http://webnet.oecd.org/hpv/UI/SIDS_Details.aspx?Key=bc13742a-88aa-4e67-8f9e-84e01fc9a9c6&idx=0

One sponsored chemical (CASRN 117-84-1) and four of the supporting chemicals (CASRN 117-81-7, CASRN 68515-48-0, CASRN 68515-49-1 and CASRN 85-68-7) are part of the recent phthalates Action Plan posted on the EPA website on December 30, 2009 (see http://www.epa.gov/oppt/existingchemicals/pubs/ecactionpln.html).

In addition, many of the phthalate esters that are the subject of this hazard characterization have extensive reviews and analyses done by various countries. In particular, the reader can go to the European Union website at http://ecb.jrc.ec.europa.eu/esis/ and insert the CASRN number of interest in the search field to download individual Risk Assessment Reports (RARs). Australia has also published a number of Chemical Assessment Reports (CARs) on phthalate esters (go to http://www.nicnas.gov.au/Publications/CAR.asp and again enter a CASRN in the search field); including a compendium summary of 24 phthalate esters (http://www.nicnas.gov.au/Publications/CAR/Other/Phthalate%20Hazard%20Compendium.pdf).

1. Chemical Identity

1.1. Identification and Purity

The following description is taken from the revised 2006 Test Plan and Robust Summary:

The Phthalate Esters Category consists of 19 esters that are made from combining 1,2-benzenedicarboxylic acids and alcohols. The alcohols range in carbon numbers from C1-C13 and are the basis of the range of esters formed and the makeup of the three subcategories: (1) low molecular weight phthalate esters (alcohol backbone of C3 or less); (2) transitional phthalate esters (C4 to C6 alcohol backbone); and (3) high molecular weight phthalate esters (alcohol backbone of greater than or equal to C7, or a ring). Many of the high molecular weight phthalate esters are mixtures. Information on purity was not provided for the sponsored category members (was often listed as "no information" in the dossier). Table 1 lists the sponsored and supporting chemicals and their associated abbreviations.

Table 1: Identity of Phthalate Esters Category Members (Arranged According to Human Health Subcategory Chemical Assignment – See Table 4 for Environmental Effects Subcategory Chemical Assignment)

CASRN	Common Name and Abbreviation	Primary Carbon Length Backbone	Molecular Wt.	Chemical Abstracts Service Index Name
SPONSORED CHEMICALS				
Subcategory I: Low Molecular Weight Group (Two Members)				
131-11-3	**Dimethyl phthalate (DMP)**	**C1**	**194**	**1,2-benzenedicarboxylic acid, 1,2-dimethyl ester**
84-66-2	**Diethyl phthalate (DEP)**	**C2**	**222**	**1,2-benzenedicarboxylic acid, 1,2-diethyl ester**
Subcategory II: Transitional Phthalates Group (One Member)				
68515-50-4	**Dihexyl phthalate, mixed isomers (DHP)**	**C6**	**336**	**1,2-benzenedicarboxylic acid, dihexyl ester, branched and linear**
Subcategory III: High Molecular Weight Group (16 Members)				
68515-44-6	**Diheptyl phthalate, branched and linear isomers (DinHP)**	**C7**	**364**	**1,2-benzenedicarboxylic acid, diheptyl ester, branched and linear**
71888-89-6	**C_7 rich di-C_{6-8} –branched alkyl phthalates (DIHP)**	**C7**	**393**	**1,2-benzenedicarboxylic acid, di-C_{6-8} branched alkyl esters, C_7 rich**
111381-89-6	**Di (heptyl, nonyl) phthalate, branched and linear isomers (Din79P)**	**C7, C9**	**391**	**1,2-benzenedicarboxylic acid, heptyl nonyl ester, branched and linear**
27554-26-3	**Diisooctyl phthalate (DIOP)**	**C8**	**391**	**1,2-benzenedicarboxylic acid, 1,2-diisooctyl ester**
117-84-0	**Dioctyl phthalate (DnOP)**	**C8**	**391**	**1,2-benzenedicarboxylic acid, dioctyl ester**
111381-90-9	**Di (heptyl, undecyl) phthalate (branched and linear isomers) (711P)**	**C7, C11**	**419**	**1,2-benzenedicarboxylic acid,1- heptyl 2-undecyl ester, branched and linear**
68515-45-7	**Dinonyl phthalate, branched and linear isomers (DNP)**	**C9**	**421**	**1,2-benzenedicarboxylic acid, dinonyl ester, branched andLinear**
68515-43-5	**Di-C_{9-11} branched and linear alkyl phthalates (911P)**	**C10**	**447**	**1,2-benzenedicarboxylic acid, di-C_{9-11} branched and linear alkyl esters**
84-77-5	**Didecyl phthalate (DDP)**	**C10**	**447**	**1,2-benzenedicarboxylic acid, didecyl este**
111381-91-0	**1,2-benzenedicarboxylic acid, (C_9, C_{11}) ester, branched and linear (Din911P)**	**C9, C11**	**447**	**1,2-benzenedicarboxylic acid, nonyl undecyl ester, branched and linear**
16883-83-3	**1,2-benzenedicarboxylic acid, benzyl 3-hydroxy-1-isopropyl-2,2-dimethylpropyl ester isobutyrate (B84P)**	**C12, ring**	**455**	**1,2-benzenedicarboxylic acid,1-[2,2-dimethyl-1-(1-methylethyl)-3-(2-methyl-1-oxopropoxy) propyl] 2-(phenylmethyl ester)**
3648-20-2	**Diundecyl phthalate (DUP)**	**C11**	**475**	**1,2-benzenedicarboxylic acid, 1,2-diundecyl ester**
85507-79-5	**1,2-benzenedicarboxylic acid, di (C_{11}) ester, branched and linear (DIUP)**	**C11**	**489**	**1,2-Benzenedicarboxylic acid, 1,2-diundecyl ester, branched and linear**
68515-40-2	**Benzyl C_{7-9}-branched and linear alkyl phthalates (B79P)**	**C7, C9, rings**	**550**	**1,2-benzenedicarboxylic acid, benzyl C_{7-9} branched and linear alkyl esters**
68648-93-1	**Mixed hexyl, octyl, decyl phthalates (610P)**	**C6, C8, C10**	**557**	**1,2-benzenedicarboxylic acid, mixed decyl, hexyl, and octyl diesters**
68515-47-9	**Ditridecyl phthalate (mixed isomers) (DTDP)**	**C13**	**561**	**1,2-benzenedicarboxylic acid, di-C_{11-14} branched alkyl esters, C_{13} rich**

Table 1: Identity of Phthalate Esters Category Members (Arranged According to Human Health Subcategory Chemical Assignment – See Table 4 for Environmental Effects Subcategory Chemical Assignment)

CASRN	Common Name and Abbreviation	Primary Carbon Length Backbone	Molecular Wt.	Chemical Abstracts Service Index Name
SUPPORTING CHEMICALS				
Subcategory II: Transitional Subcategory (One chemicals)				
84-75-3	**Di-n-hexyl phthalate (DnHP)**	**C6**	**334**	**1,2-benzenedicarboxylic acid, 1,2-dihexyl ester**
Subcategory III: High Molecular Weight Subcategory (Six chemicals)				
85-68-7	**Butyl benzyl phthalate (BBP)**	**C4, ring**	**312**	**1,2-benzenedicarboxylic acid, 1,2-butyl phenylmethyl ester**
117-81-7	**Diethylhexyl phthalate (DEHP)**	**C8**	**391**	**1,2-benzenedicarboxylic acid, bis(2-ethylhexyl) ester**
68515-41-3	**Di-C_{7-9}-branched and linear alkyl phthalates (in79P)**	**C7, C9**	**405**	**1,2-benzenedicarboxylic acid, di-C_{7-9} branched and linear alkyl esters**
28553-12-0 and 68515-48-0	**Diisononyl phthalate (DINP)** **Diisononyl phthalate**	**C9**	**419**	**1,2-benzenedicarboxylic acid, 1,2-diisononyl ester** **1,2-benzenedicarboxylic acid, di-C_{8-10}-branched alkyl esters, C_9-rich**
26761-40-0 and 68515-49-1	**Diisodecyl phthalate (DIDP)** **Diisodecyl phthalate (mixed isomers)**	**C10**	**447**	**1,2-benzenedicarboxylic acid,1,2- diisodecyl ester** **1,2-benzenedicarboxylic acid, di-C_{9-11}-branched alkyl esters, C_{10}-rich**
119-06-2	**Ditridecyl phthalate (DTP)**	**C13**	**531**	**1,2-benzenedicarboxylic acid, 1,2-ditridecyl ester**

1.2. Physical-Chemical Properties

A summary of the physicochemical properties for the sponsored members of the phthalate ester category is provided in Tables 2a-c. The structures of the compounds are provided in the Appendix.

The phthalate esters category contains liquids with negligible to moderate vapor pressure. The water solubility of the phthalate esters is negligible to high. Both vapor pressure and water solubility decrease with increasing molecular weight.

Table 2a. Physical-Chemical Properties Phthalate Esters – Low Molecular Weight Phthalate Esters Subcategory[1]		
Property	**1,2-Benzenedicarboxylic acid, 1,2-diethyl ester**	**1,2-Benzenedicarboxylic acid, 1,2-dimethyl ester**
CASRN	84-66-2	131-11-3
Molecular Weight	222.30	194.19
Physical State	Liquid	Liquid
Melting Point	-40°C (measured)	5.5°C (measured)
Boiling Point	295°C (measured)[2]	283.7°C (measured)[2]
Vapor Pressure	0.00040–0.0016 mm Hg at 25°C (measured)[3]	0.0016 mm Hg at 25°C (measured)[3]; 0.0031 mm Hg at 25°C (measured)[4]
Water Solubility	680–1,080 mg/L at 25°C (measured)[3]	2,810–4,320 mg/L at 25°C (measured)[3]
Dissociation Constant (pK_a)	Not applicable	Not applicable
Henry's Law Constant	6.1×10^{-7} atm-m^3/mole (estimated)[5]	1.9×10^{-7} atm-m^3/mole (estimated)[5]
Log K_{ow}	2.21–3.27 (measured)[3]	1.46–1.90 (measured)[3]

[1] ExxonMobil Biomedical Sciences, Inc. for the Phthalate Esters Panel, HPV Testing Group of the American Chemistry Council. December 18, 2006. Original and Revised Robust Summary and Test Plan for the Phthalate Esters Category. Available from: http://www.epa.gov/hpv/pubs/summaries/benzene/c13467tc.htm as of December 19, 2009.
[2] Lide DR. 2007. CRC Handbook of Chemistry and Physics. 88th edition 2007–2008. CRC Press, Taylor & Francis: Boca Raton, FL.
[3] Cousins I; Mackay D. 2000. Correlating the physical - chemical properties of phthalate esters using the 'three solubility' approach. Chemosphere 41:1389–1399.
[4] SRC. 2009. The Physical Properties Database (PHYSPROP). SRC: Syracuse, NY. Available from: http://www.srcinc.com/what-we-do/free-demos.aspx as of December 19, 2009.
[5] U.S. EPA. 2009. Estimation Programs Interface Suite™ for Microsoft® Windows, v4.0. U.S. Environmental Protection Agency, Washington, DC. Available from: http://www.epa.gov/opptintr/exposure/pubs/episuite.htm as of December 19, 2009.

Table 2b. Physical-Chemical Properties Phthalate Esters – Transitional and High Molecular Weight Phthalate Esters Subcategories[1]

Property	1,2-Benzene-dicarboxylic acid, dihexyl ester, branched and linear (Only Sponsored Member of Transitional Subcategory)	1,2-Benzene-dicarboxylic acid, diheptyl ester, branched and linear	1,2-Benzene-dicarboxylic acid, di-C_{6-8}-branched alkyl esters, C_7-rich	1,2-Benzene-dicarboxylic acid, 1,2-diisooctyl ester	1,2-Benzene-dicarboxylic acid, heptyl nonyl ester, branched and linear	1,2-Benzenedi-carboxylic acid, 1-heptyl 2-undecyl ester, branched and linear	1,2-Benzenedi-carboxylic acid, 1-[2,2-dimethyl-1-(1-methylethyl)-3-(2-methyl-1-oxoprop-oxy)propyl] 2-(phenylmethyl) ester
CASRN	68515-50-4	68515-44-6	71888-89-6	27554-26-3	111381-89-6	111381-90-9	16883-83-3
Molecular Weight	334.46	362.51	362.51 (typical)	390.57	390.57 (typical)	418.60 (typical)	454.57
Physical State	Liquid	Liquid	Liquid	Liquid	Liquid	Liquid	Liquid
Melting Point	-27.4°C(measured)[7]	-45°C (measured)	-45°C (measured)[8]	-50°C (measured)[2]	-45°C (measured)	<-50°C (measured)	-6.5°C (measured)
Boiling Point	>300°C (estimated)[3]	>300°C (estimated)[3]	>300°C (estimated)[3]	370°C (measured)[6]	>300°C (estimated)[3]	>300°C (estimated)[3]	>300°C (estimated)[3]
Vapor Pressure	1.8×10^{-6} mm Hg at 25°C (measured)[4,5]; 1.4×10^{-5} mm Hg at 25°C (measured)[4,5]	1.2×10^{-5} mm Hg at 25°C (estimated)[3]	1.2×10^{-5} mm Hg at 25°C (estimated)[3] 7×10^{-5} mm Hg at 25°C (measured)[8]	5.5×10^{-6} mm Hg at 25°C (measured)[2,4]	7.0×10^{-6} mm Hg at 25°C (estimated)[3]	4.2×10^{-6} mm Hg at 25°C (estimated)[3]	1.2×10^{-7} mm Hg at 25°C (estimated)[3]
Water Solubility	0.24 mg/L at 25°C (measured)[4,5]; 0.007 mg/L at 25°C (measured)[4,5]; 0.046 mg/L at 25°C (measured)[4,5]	0.01 mg/L at 25°C (estimated)[3]	0.010 mg/L at 25°C (estimated)[3] 1.7×10^{-2} mg/L at 22°C (measured)[8]	0.09 mg/L at 25°C (measured)[2,4]	0.001 mg/L at 25°C (estimated)[3]	1.9×10^{-4} mg/L at 25°C (estimated)[3]	0.016 mg/L at 25°C (estimated)[3]
Dissociation Constant (pK_a)	Not applicable						
Henry's Law Constant	2.1×10^{-6} atm-m^3/mole (estimated)[3]	5.1×10^{-6} atm-m^3/mole (estimated)[3]	5.1×10^{-6} atm-m^3/mole (estimated)[3]	3.1×10^{-5} atm-m^3/mole (estimated)[3]	2.0×10^{-5} atm-m^3/mole (estimated)[3]	5.9×10^{-5} atm-m^3/mole (estimated)[3]	2.3×10^{-11} atm-m^3/mole (estimated)[3]
Log K_{ow}	5.65 (measured)[4,5]; 5.93 (measured)[4,5]; 6.82 (measured)[4,5] 6.30 (measured)[7]	7.4 (estimated)[3] 6.87 (measured)[8]	7.4 (estimated)[3]	8.4 (estimated)[3]	8.3 (estimated)[3]	9.1 (estimated)[3]	7.0 (estimated)

[1] ExxonMobil Biomedical Sciences, Inc. for the Phthalate Esters Panel, HPV Testing Group of the American Chemistry Council. December 18, 2006. Revised Robust Summary and Test Plan for the Phthalate Esters Category. Available from: http://www.epa.gov/hpv/pubs/summaries/benzene/c13467tc.htm as of December 19, 2009.
[2] SRC. 2009. The Physical Properties Database (PHYSPROP). SRC: Syracuse, NY. Available from: http://www.srcinc.com/what-we-do/free-demos.aspx as of December 19, 2009.
[3] U.S. EPA. 2009. Estimation Programs Interface Suite™ for Microsoft® Windows, v4.0. U.S. Environmental Protection Agency, Washington, DC. Available from: http://www.epa.gov/opptintr/exposure/pubs/episuite.htm as of December 19, 2009.
[4] Cousins I; Mackay D. 2000. Correlating the physical - chemical properties of phthalate esters using the 'three solubility' approach. Chemosphere 41:1389–1399.
[5] Data obtained for a mixture of 1,2-benzenedicarboxylic acid, dihexyl ester isomers, both linear and branched.
[6] HSDB (Hazardous Substances Data Bank). 2009. TOXNET Toxicology Data Network. U.S. National Library of Medicine. Available from: http://toxnet.nlm.nih.gov/cgi-bin/sis/htmlgen?HSDB as of December 22, 2009.
[7] This value was obtained for linear hexyl (n-C6 alkyl) - i.e., DnHP (CASRN: 84-75-3) - based on Australian Government (NICNAS) Existing Chemical Hazard Assessment Report for 24 ortho-phthalate chemicals (Phthalates Hazard Compendium). http://www.nicnas.gov.au/Publications/CAR/Other/Phthalates.asp
[8] This value was obtained for DiHepP (CASRN: 71888-89-6) - based on Australian Government (NICNAS) Existing Chemical Hazard Assessment Report for 24 ortho-phthalate chemicals (Phthalates Hazard Compendium). http://www.nicnas.gov.au/Publications/CAR/Other/Phthalates.asp

Table 2c. Physical-Chemical Properties Phthalate Esters – High Molecular Weight Phthalate Esters Subcategory[1]

Property	1,2-Benzene-dicarboxylic acid, mixed decyl and hexyl and octyl diesters	1,2-Benzenedicarboxylic acid, 1,2-dioctyl ester	1,2-Benzene-dicarboxylic acid, benzyl C_{7-9}-branched and linear alkyl esters	1,2-Benzene-dicarboxylic acid, dinonyl ester, branched and linear	1,2-Benzene-dicarboxylic acid, di-C_{9-11}-branched and linear alkyl esters	1,2-Benzene-dicarboxylic acid, 1,2-didecyl ester	1,2-Benzene-dicarboxylic acid, 1,2-diundecyl ester	1,2-Benzene-dicarboxylic acid, 1,2-diundecyl ester, branched and linear	1,2-Benzene-dicarboxylic acid, 1-nonyl 2-undecyl ester, branched and linear	1,2-Benzene-dicarboxylic acid, di-C_{11-14}-branched alkyl esters, C_{13}-rich
CASRN	68648-93-1	117-84-0	68515-40-2	68515-45-7	68515-43-5	84-77-5	3648-20-2	85507-79-5	111381-91-0	68515-47-9
Molecular Weight	390.57 (typical)	390.57	368.47 (typical)	418.62	446.68 (typical)	446.68	474.73	474.73	446.68 (typical)	530.82 (typical)
Physical State	Liquid	Liquid	Liquid	Liquid	Liquid	Liquid	Liquid	Liquid	Liquid	Liquid
Melting Point	-45°C (measured)	-25°C (measured)	-45°C (measured)[2]	-48°C (measured)	-48°C to -9°C (measured)[3]	-46°C (measured)	-9°C (measured)	-9°C (measured)	-48°C to -9°C (measured)	-37°C (measured)[3]
Boiling Point	>300°C (estimated)	386°C (measured)[4]	>300°C (estimated)	>300°C (estimated)	>300°C (estimated)	261°C at 5 mm Hg (measured)[5]	>300°C (estimated)	>300°C (estimated)	>300°C (estimated)	235°C at 6 mm Hg (measured)[6]
Vapor Pressure	4.9×10^{-6} mm Hg at 25°C (measured)[7,8]	1.9×10^{-4} mm Hg at 25°C (measured)[9]	1.8×10^{-6} mm Hg at 25°C (estimated)[10]	7.5×10^{-7} mm Hg at 25°C (estimated)[10]	2.0×10^{-7} mm Hg at 25°C (estimated)[10]	1.0×10^{-7} mm Hg at 25°C (estimated)[10]	1.2×10^{-9} mm Hg at 25°C (estimated)[10]	6.0×10^{-8} mm Hg at 25°C (estimated)[10]	1.5×10^{-7} mm Hg at 25°C (estimated)[10]	6.8×10^{-9} mm Hg at 25°C (estimated)[10]
Water Solubility	0.9 mg/L at 25°C (measured)[7,8]	5×10^{-4}–3.0 mg/L at 25°C (measured)[9]	0.04 mg/L at 25°C (estimated)[10]	9.3×10^{-5} mg/L at 25°C (estimated)[10]	9.2×10^{-6} mg/L at 25°C (estimated)[10]	2.2×10^{-4} mg/L at 25°C (measured)[11]	1.1 mg/L at 20°C (measured)[7,12]	1.1 mg/L at 20°C (measured)[7,12]	8.5×10^{-6} mg/L at 25°C (estimated)[10]	0.34 mg/L at 25°C (measured) [13,14]
Dissociation Constant (pK_a)	Not applicable									
Henry's Law Constant	2.6×10^{-6} atm-m^3/mole (estimated)[10]	2.6×10^{-6} atm-m^3/mole (estimated)[10]	1.0×10^{-8} atm-m^3/mole (estimated)[10]	1.7×10^{-5} atm-m^3/mole (estimated)[10]	3.4×10^{-5} atm-m^3/mole (estimated)[10]	2.8×10^{-5} atm-m^3/mole (estimated)[10]	5.6×10^{-5} atm-m^3/mole (estimated)[10]	8.1×10^{-5} atm-m^3/mole (estimated)[10]	4.7×10^{-5} atm-m^3/mole (estimated)[10]	3.2×10^{-4} atm-m^3/mole (estimated)[10]
Log K_{ow}	7.25 (measured)[7,8]	5.22–8.18 (measured)[9]	6.7 (estimated)[10]	9.4 (estimated)[10]	10.4 (estimated)[10]	8.83–9.27 (measured)[11]	11.5 (estimated)[10]	11.3 (estimated)[10]	10.4 (estimated)[10]	13.2 (estimated)[10]

[1] ExxonMobil Biomedical Sciences, Inc. for the Phthalate Esters Panel, HPV Testing Group of the American Chemistry Council. December 18, 2006. Revised Robust Summary and Test Plan for the Phthalate Esters Category. Available from: http://www.epa.gov/hpv/pubs/summaries/benzene/c13467tc.htm as of December 19, 2009.
[2] Flick E. 1985. Industrial Solvents Handbook. Noyes Data Corporation: Park Ridge, NJ. p.963.
[3] NICNAS. 2008. Phthalates Hazard Assessment Reports from the National Industrial Chemicals Notification and Assessment Scheme, Department of Health and Ageing, Australian Government. Available from: http://www.nicnas.gov.au/Publications/CAR/Other/Phthalates.asp as of December 22, 2006.
[4] Beilstein Database search. Gasanov AG.; Azizov AG.; Alieva LI.; Mamedov EG.; Babaeva RZ.; Rustamov RA.; Ayubov IG. 2008. Ester Plasticizers Derived from 2(3)-Methylcyclohexenedicarboxylic acid. Russian Journal of Applied Chemistry. 81(4): 720 – 722.
[5] Lewis RJ, Sr. 2007. Hawley's Condensed Chemical Dictionary. 15th edition. John Wiley & Sons, Inc.: New York, NY. p. 412.
[6] Sears J; Touchette NN. 1982. Plasticizers. In: Kirk-Othmer Encyclopedia of Chemical Technology, 3rd edition. Wiley-Interscience: New York, NY. 18:111–183.
[7] Howard PH; Banerjee S; Robillard KH. 1985. Measurement of water solubilities, octanol/water partition coefficients and vapor pressures of commercial phthalate esters. Environ. Toxicol. Chem. 4:653–661.
[8] Data obtained for a commercial product (610P) consisting of the following diester composition: 1% (C6 + C6); 14% (C6 + C8); 33% (C8 + C8); 38% (C8 + C10); 14% (C10 + C10).
[9] Cousins I; Mackay D. 2000. Correlating the physical - chemical properties of phthalate esters using the 'three solubility' approach. Chemosphere 41:1389–1399.
[10] U.S. EPA. 2009. Estimation Programs Interface Suite™ for Microsoft® Windows, v4.0. U.S. Environmental Protection Agency, Washington, DC. Available from: http://www.epa.gov/opptintr/exposure/pubs/episuite.htm as of December 19, 2009.
[11] Ellington JJ. 1999. Octanol/water partition coefficients and water solubilities of phthalate esters. J. Chem. Eng. Data 44:1414–1418.

Table 2c. Physical-Chemical Properties Phthalate Esters – High Molecular Weight Phthalate Esters Subcategory[1]										
Property	**1,2-Benzene-dicarboxylic acid, mixed decyl and hexyl and octyl diesters**	**1,2-Benzenedicarboxylic acid, 1,2-dioctyl ester**	**1,2-Benzene-dicarboxylic acid, benzyl C_{7-9}-branched and linear alkyl esters**	**1,2-Benzene-dicarboxylic acid, dinonyl ester, branched and linear**	**1,2-Benzene-dicarboxylic acid, di-C_{9-11}-branched and linear alkyl esters**	**1,2-Benzene-dicarboxylic acid, 1,2-didecyl ester**	**1,2-Benzene-dicarboxylic acid, 1,2-diundecyl ester**	**1,2-Benzene-dicarboxylic acid, 1,2-diundecyl ester, branched and linear**	**1,2-Benzene-dicarboxylic acid, 1-nonyl 2-undecyl ester, branched and linear**	**1,2-Benzene-dicarboxylic acid, di-C_{11-14}-branched alkyl esters, C_{13}-rich**
CASRN	68648-93-1	117-84-0	68515-40-2	68515-45-7	68515-43-5	84-77-5	3648-20-2	85507-79-5	111381-91-0	68515-47-9

[12] Data obtained for a commercial product consisting of the following diester composition: approximately 96% (C11 + C11, various branched and linear combinations); ≤3% (C9 + C11,).
[13] Hollifield HC. 1979. Rapid nephelometric estimate of water solubility of highly insoluble organic chemicals of environmental interest. Bull. Environ. Contam. Toxicol. 23:579–586.
[14] Data obtained for a multi-component di-tridecyl phthalate substance.

2. General Information on Exposure

2.1. Production Volume and Use Pattern

The Phthalate Esters Category chemicals had an aggregated production and/or import volume between 205.5 and 751 million pounds in the United States in calendar year 2005:

- CASRN 131-11-3: 10 to <50 million pounds;
- CASRN 84-66-2: 10 to <50 million pounds;
- CASRN 68515-50-4: 1 to <10 million pounds;
- CASRN 68515-44-6: 10 to <50 million pounds;
- CASRN 71888-89-6: 50 to <100 million pounds;
- CASRN 111381-89-6: 10 to <50 million pounds;
- CASRN 111381-90-9: 50 to <100 million pounds;
- CASRN 27554-26-3: 10 to <50 million pounds;
- CASRN 68648-93-1: 10 to <50 million pounds;
- CASRN 68515-40-2: 1 to <10 million pounds;
- CASRN 68515-45-7: 10 to <50 million pounds;
- CASRN 68515-43-5: 1 to <10 million pounds;
- CASRN 3648-20-2: 10 to <50 million pounds;
- CASRN 85507-79-5: 1 to <10 million pounds;
- CASRN 111381-91-0: 500,000 to <1 million pounds:
- CASRN 68515-47-9: 10 to <50 million pounds;
- CASRN 16883-83-3: 1 to <10 million pounds; and
- CASRN 117-84-0: 10 to <50 million pounds.

CASRN 84-77-5 was not reported under the 2006 IUR. Of the 18 sponsored chemicals listed above, only one was no longer an HPV in 2005 (CASRN 111381-91-0).

No industrial processing and uses were reported in the 2006 IUR submissions for CASRN 68515-40-2. Also, no commercial and consumer uses were reported for this chemical.

Non-confidential industrial processing and use reported in the 2006 IUR submissions for CASRN 117-84-0 were NRO "not readily obtainable". Commercial and consumer uses were claimed confidential.

Industrial processing and uses reported in the 2006 IUR submissions for CASRN 71888-89-6 and 27554-26-3 were claimed confidential. Commercial and consumer uses were also claimed confidential.

Non-confidential industrial processing and uses reported in the 2006 IUR submissions for CASRN 68515-44-6, 111381-89-6 and 111381-90-9 include petrochemical manufacturing. Non-confidential commercial and consumer uses of these chemicals include automotive care products and rubber and plastic products.

Non-confidential industrial processing and uses reported in the 2006 IUR submissions for CASRN 68515-45-7, and 111381-91-0 include petrochemical manufacturing and plastics products and packaging materials manufacturing. Non-confidential commercial and consumer uses of these chemicals include automotive care products and rubber and plastic products.

Non-confidential industrial processing and uses reported in the 2006 IUR submissions for CASRN 16883-83-3 include adhesives and binding agents. Non-confidential commercial and consumer uses of the chemical include adhesives and sealants.

Non-confidential industrial processing and uses reported in the 2006 IUR submissions for CASRN 131-11-3 include chemical manufacturing and paint and coating manufacturing. Non-confidential commercial and consumer uses include paints and coating and rubber and plastic products.

Non-confidential industrial processing and uses reported in the 2006 IUR submissions for CASRN 84-66-2 include chemical product and preparation manufacturing and soap and cleaning compound manufacturing. Non-confidential commercial and consumer uses include adhesives and sealants, rubber and plastic products, soaps and detergents and others.

Non-confidential industrial processing and uses reported in the 2006 IUR submissions for CASRN 68515-50-4 include chemical product and preparation manufacturing and basic organic chemical manufacturing. Non-confidential commercial and consumer uses include rubber and plastic products and others.

Non-confidential industrial processing and uses reported in the 2006 IUR submissions for CASRN 68648-93-1 include chemical product and preparation manufacturing and basic organic chemical manufacturing. Non-confidential commercial and consumer uses include rubber and plastic products.

Non-confidential industrial processing and uses reported in the 2006 IUR submissions for CASRN 68515-43-5 include chemical product and preparation manufacturing, plastics product manufacturing and basic organic chemical manufacturing. Non-confidential commercial and consumer uses include electrical and electronic products, fabrics, textiles and apparel and rubber and plastic products.

Non-confidential industrial processing and uses reported in the 2006 IUR submissions for CASRN 3648-20-2 include plastics product manufacturing, chemical product and preparation manufacturing and other basic organic chemical manufacturing. Non-confidential commercial and consumer uses include electrical and electronic products and rubber and plastic products.

Non-confidential industrial processing and uses reported in the 2006 IUR submissions for CASRN 85507-79-5 include plastic packaging materials and unlamented film and sheet manufacturing, plastics product manufacturing, petrochemical manufacturing and resin and synthetic rubber manufacturing. Non-confidential commercial and consumer uses include automotive care products, electrical and electronic products and rubber and plastic products.

Non-confidential industrial processing and uses reported in the 2006 IUR submissions for CASRN 68515-47-9 include other plastics product manufacturing. Non-confidential commercial and consumer uses include electrical and electronic products and rubber and plastic products.

2.2. Environmental Exposure and Fate

The environmental fate properties of the sponsored members of the phthalate esters category are summarized in Tables 3a-c. The structures of the compounds are provided in the Appendix.

The phthalate esters are expected to have low to moderate mobility in soil. Biodegradation studies on several category members suggest that the phthalate esters are not expected to be highly persistent in the environment. 1,2-Benzenedicarboxylic acid, 1,2-diethyl ester; 1,2-benzenedicarboxylic acid, 1,2-dimethyl ester; 1,2-benzenedicarboxylic acid, dihexyl ester, branched and linear; 1,2-benzenedicarboxylic acid, di-C_{6}-$_{8}$-branched alkyl esters, C_{7}-rich; and 1,2-benzenedicarboxylic acid, 1-heptyl 2-undecyl ester, branched and linear were readily biodegradable using a manometric respirometry test (OECD 301F). Several other category members and mixtures of commercial products showed a high degree of biodegradation using other screening studies. For example, a commercial mixture of phthalate esters (711P) was quickly degraded (half-life approximately 5 days) using a shake-flask CO_2 evolution study that used an organically rich soil mixed with raw domestic influent obtained from a wastewater treatment plant as the inoculum. The half-life of 1,2-benzenedicarboxylic acid, 1,2-diisooctyl ester was approximately 9 days using the same experimental procedure. Estimated Henry's Law constants suggest volatilization is low to moderate for the phthalate esters. Although members of this category possess hydrolysable functional groups, the rate of hydrolysis is considered negligible for these compounds. The overall weight of evidence suggests that the phthalate esters are expected to have low persistence (P1) and low bioaccumulation potential (B1).

Table 3a. Environmental Fate Characteristics of Phthalate Esters – Low Molecular Weight[1]		
Property	**1,2-Benzenedicarboxylic acid, 1,2-diethyl ester**	**1,2-Benzenedicarboxylic acid, 1,2-dimethyl ester**
CASRN	84-66-2	131-11-3
Photodegradation Half-life	3.1 days (estimated)	18.6 days (estimated)
Hydrolysis Half-life	106 days at pH 8 and 2.91 years at pH 7 (estimated)[2]	100 days at pH 8 and 2.75 years at pH 7 (estimated)[2]
Biodegradation	88–97% after 28 days (readily biodegradable); Half-life of 3 days in natural water[3]; Half-lives of 0.39-4.33 days in aerobic aquatic tests[4]; Half-life of 1.83 days in aqueous suspension of aerobic soil[4]	93–98% after 28 days (readily biodegradable); Half-life of 1.9 days in soil/sewage inoculum[3]; Half-life of 1.7 days in aerobic garden soil[4]; 100% biodegradation in 8 to 11 days (river die-away study)[5]; >81% biodegradation in 1 day (SCAS test, primary biodegradation)[6]; Half-life of 21 days in flooded soil (anaerobic conditions)[4]
Bioconcentration	BCF = 117 (measured in bluegill sunfish)[3,7]	BCF = 57 (measured in bluegill sunfish)[3,7]
Bioaccumulation factor	BAF = 6 (estimated)[2]	BAF = 2 (estimated)[2]
Log K_{oc}	2.65 (measured)[8]; 1.83–1.99 (measured)[3]	1.88–1.89 (measured)[3]
Fugacity (Level III Model)[2]		
Air (%)	2.8	2.4
Water (%)	25.4	27.0
Soil (%)	71.7	70.5
Sediment (%)	0.1	0.1
Persistence[9]	P1	P1
Bioaccumulation[9]	B1	B1

[1] ExxonMobil Biomedical Sciences, Inc. for the Phthalate Esters Panel, HPV Testing Group of the American Chemistry Council. December 18, 2006. Revised Robust Summary and Test Plan for the Phthalate Esters Category. Available from: http://www.epa.gov/hpv/pubs/summaries/benzene/c13467tc.htm as of December 19, 2009.

[2] U.S. EPA. 2009. Estimation Programs Interface Suite™ for Microsoft® Windows, v4.0. U.S. Environmental Protection Agency, Washington, DC. Available from: http://www.epa.gov/opptintr/exposure/pubs/episuite.htm as of December 19, 2009.

[3] HSDB (Hazardous Substances Data Bank). 2009. TOXNET Toxicology Data Network. U.S. National Library of Medicine. Available from: http://toxnet.nlm.nih.gov/cgi-bin/sis/htmlgen?HSDB as of December 22, 2009.

[4] Peterson DR; Staples CA. 2003. Degradation of phthalate esters in the environment. Handbook of Environmental Quality 3: 85-124.

[5] Hattori Y; Kuge Y; Nakagawa S. 1975. Microbial decomposition of phthalate esters in environmental water. Pollut. Control Cent. Osaka Prefect. Mizu Shori Gijutsu 16:951–954.

[6] O'Grady DP; Howard PH; Werner AF. 1985. Activated sludge biodegradation of 12 commercial phthalate esters. Appl. Environ. Microbiol. 49:443–445.

[7] Staples C; Peterson DR; Parkerton TF; Adams WJ. 1997. The environmental fate of phthalate esters: A literature review. Chemosphere 35:667–749.

[8] Wolfe N; Steen WC; Burns LA. 1980. Phthalate ester hydrolysis: Linear free energy relationships. Chemosphere 9:403–408. Reported in ATSDR Toxicological Profile on Diethyl Phthalate. Available from: http://www.atsdr.cdc.gov/toxprofiles/tp73-c3.pdf as of December 19, 2009.

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

Table 3b. Environmental Fate Characteristics of the Transitional and High Molecular Weight Phthalate Esters Subcategories [1]							
Property	**1,2-Benzene-dicarboxylic acid, dihexyl ester, branched and linear (Only sponsored member of the Transitional Subcategory**	**1,2-Benzene-dicarboxylic acid, diheptyl ester, branched and linear**	**1,2-Benzene-dicarboxylic acid, di-C_{6-8}-branched alkyl esters, C_7-rich**	**1,2-Benzene-dicarboxylic acid, 1,2-diisooctyl ester**	**1,2-Benzene-dicarboxylic acid, heptyl nonyl ester, branched and linear**	**1,2-Benzenedi-carboxylic acid, 1-heptyl 2-undecyl ester, branched and linear**	**1,2-Benzenedi-carboxylic acid, 1-[2,2-dimethyl-1-(1-methylethyl)-3-(2-methyl-1-oxopro-poxy)propyl] 2-(phenylmethyl) ester**
CASRN	68515-50-4	68515-44-6	71888-89-6	27554-26-3	111381-89-6	111381-90-9	16883-83-3
Photodegradation Half-life	11.4 hours (estimated)	6.9 hours (estimated)	7.2 hours (estimated)	6.2 hours (estimated)	5.9 hours (estimated)	5.1 hours (estimated)	7.4 hours (estimated)
Hydrolysis Half-life	126 days at pH 8 and 3.5 years at pH 7 (estimated)[2]	152 days at pH 8 and 4.2 years at pH 7 (estimated)[2]	125 days at pH 8 and 3.4 years at pH 7 (estimated)[2]	125 days at pH 8 and 3.4 years at pH 7 (estimated)[2]	155 days at pH 8 and 4.2 years at pH 7 (estimated)[2]	243 days at pH 8 and 6.7 years at pH 7 (estimated)[2]	57 days at pH 8 and 1.6 years at pH 7 (estimated)[2]
Biodegradation	79.7% after 28 days (readily biodegradable); 77% biodegradation in 28 days using a shake flask test (half-life = 2.9 days)[3]	98% biodegradation in 28 days using a shake flask test (half-life = 5 days)[3,4]	82.2% after 28 days (readily biodegradable)	57% ultimate biodegradation after 28 days; >99% primary biodegradation after 28 days using a shake flask test (half-life = 8.8 days)[3]	98% biodegradation in 28 days using a shake flask test (half-life = 5 days)[3,4]	98% after 28 days (readily biodegradable); 98% biodegradation in 28 days using a shake flask test (half-life = 5 days)[3,4]; 40–48% ultimate biodegradation in 41 days using water/sediment microcosm study[5]; Half-life of 6–8 days (river die-away study)[5]	No data
Bioconcentration	BCF = 160 (estimated)[2]	BCF = 2,122 (estimated)[2]	BCF = 2,122 (estimated)[2]	BCF = 207 (measured in mosquito fish)[6,7]	BCF = 3,266 (estimated)[2]	BCF = 1273 (estimated)[2]	BCF = 13,300 (estimated)[2]
Bioaccumulation factor	BAF = 98 (estimated)[2]	BAF = 43 (estimated)[2]	BAF = 221 (estimated)[2]	BAF = 23 (estimated)[2]	BAF = 26 (estimated)[2]	BAF = 17 (estimated)[2]	BAF = 5 (estimated)[2]
Log K_{oc}	4.7 (measured)[6]; 3.9 (estimated)[2]	4.6 (estimated)[2]	4.5 (estimated)[2]	5.0 (estimated)[2]	4.9 (estimated)[2]	5.3 (estimated)[2]	6.1 (estimated)[2]
Fugacity (Level III Model)[2]							
Air (%)	1.5	0.4	0.4	0.4	0.4	0.3	<0.1
Water (%)	22.2	14.6	14.8	16.1	15.6	16.3	2.4
Soil (%)	70.9	72.8	73.5	76.3	76.7	79.9	44.3
Sediment (%)	5.4	12.2	11.3	7.1	7.3	3.4	53.3

Table 3b. Environmental Fate Characteristics of the Transitional and High Molecular Weight Phthalate Esters Subcategories [1]

Property	1,2-Benzene-dicarboxylic acid, dihexyl ester, branched and linear (Only sponsored member of the Transitional Subcategory	1,2-Benzene-dicarboxylic acid, diheptyl ester, branched and linear	1,2-Benzene-dicarboxylic acid, di-C_{6-8}-branched alkyl esters, C_7-rich	1,2-Benzene-dicarboxylic acid, 1,2-diisooctyl ester	1,2-Benzene-dicarboxylic acid, heptyl nonyl ester, branched and linear	1,2-Benzenedi-carboxylic acid, 1-heptyl 2-undecyl ester, branched and linear	1,2-Benzenedi-carboxylic acid, 1-[2,2-dimethyl-1-(1-methylethyl)-3-(2-methyl-1-oxopro-poxy)propyl] 2-(phenylmethyl) ester
CASRN	68515-50-4	68515-44-6	71888-89-6	27554-26-3	111381-89-6	111381-90-9	16883-83-3
Persistence[8]	P1	P1	P1	P1	P1	P1	P1
Bioaccumulation[8]	B1	B1	B1	B1	B1	B1	B1

[1] ExxonMobil Biomedical Sciences, Inc. for the Phthalate Esters Panel, HPV Testing Group of the American Chemistry Council. December 18, 2006. Revised Robust Summary and Test Plan for the Phthalate Esters Category. Available from: http://www.epa.gov/hpv/pubs/summaries/benzene/c13467tc.htm as of December 19, 2009.
[2] U.S. EPA. 2009. Estimation Programs Interface Suite™ for Microsoft® Windows, v4.0. U.S. Environmental Protection Agency, Washington, DC. http://www.epa.gov/opptintr/exposure/pubs/episuite.htm as of December 19, 2009.
[3] Sugatt RH; O'Grady DP; Banerjee S; Howard PH; Gledhill WE. 1984. Shake Flask Biodegradation of 14 Commercial Phthalate Esters. Appl. Microbiol. 47(4):601–606.
[4] Data obtained for a commercial test substance (711P) composed of six phthalate esters consisting of C_7, C_9, and C_{11} ester side chains. This test substance is considered by EPA under the following CASRNs: 68515-44-6 (di C_7), 68515-45-7 (di C_9), 3648-20-2 (di C_{11}), 111381-89-6 (C_7, C_9), 111381-90-9 (C_7, C_{11}), and 111381-91-0 (C_9, C_{11}).
[5] Carson DB; Saeger VW; Gledhill WE. 1990. Use of microcosms versus conventional biodegradation testing for estimating chemical persistence. Aquat. Toxicol. Risk Assess. 13th Volume, ASTM STP 1096. pp. 48–59.
[6] Staples C; Peterson DR; Parkerton TF; Adams WJ. 1997. The environmental fate of phthalate esters: A literature review. Chemosphere 35:667–749.
[7] HSDB (Hazardous Substances Data Bank). 2009. TOXNET Toxicology Data Network. U.S. National Library of Medicine. Available from: http://toxnet.nlm.nih.gov/cgi-bin/sis/htmlgen?HSDB as of December 22, 2009.
[8] Federal Register. 1999. Category for Persistent, Bioaccumulative, and Toxic New Chemical Substances. *Federal Register* 64, Number 213 (November 4, 1999) pp. 60194–60204.

Table 3c. Environmental Fate Characteristics of Phthalate Esters – High Molecular Weight Phthalate Esters Subcategory[1]										
Property	**1,2-Benzene-dicarboxylic acid, mixed decyl and hexyl and octyl diesters**	**1,2-Benzenedicarboxylic acid, 1,2-dioctyl ester**	**1,2-Benzene-dicarboxylic acid, benzyl C_{7-9}-branched and linear alkyl esters**	**1,2-Benzene-dicarboxylic acid, dinonyl ester, branched and linear**	**1,2-Benzene-dicarboxylic acid, di-C_{9-11}-branched and linear alkyl esters**	**1,2-Benzene-dicarboxylic acid, 1,2-didecyl ester**	**1,2-Benzene-dicarboxylic acid, 1,2-diun-decyl ester**	**1,2-Benzene-dicarboxylic acid, 1,2-diun-decyl ester, branched and linear**	**1,2-Benzene-dicarboxylic acid, 1-nonyl 2-undecyl ester, branched and linear**	**1,2-Benzene-dicarboxylic acid, di-C_{11-14}-branched alkyl esters, C_{13}-rich**
CASRN	68648-93-1	117-84-0	68515-40-2	68515-45-7	68515-43-5	84-77-5	3648-20-2	85507-79-5	111381-91-0	68515-47-9
Photodegradation Half-life	6.2 hours (estimated)	6.2 hours (estimated)	7.6 hours (estimated)	6.5 hours (estimated)	5.7 hours (estimated)	4.9 hours (estimated)	4.4 hours (estimated)	4.2 hours (estimated)	4.7 hours (estimated)	4.7 hours (estimated)
Hydrolysis Half-life	173 days at pH 8 and 4.7 years at pH 7 (estimated)[2]	281 days at pH 8 and 7.7 years at pH 7 (estimated)[2]	55 days at pH 8 and 1.5 years at pH 7 (estimated)[2]	173 days at pH 8 and 4.7 years at pH 7 (estimated)[2]	173 days at pH 8 and 4.7 years at pH 7 (estimated)[2]	281 days at pH 8 and 7.7 years at pH 7 (estimated)[2]	281 days at pH 8 and 7.7 years at pH 7 (estimated)[2]	230 days at pH 8 and 6.3 years at pH 7 (estimated)[2]	188 days at pH 8 and 5.1 years at pH 7 (estimated)[2]	281 days at pH 8 and 7.7 years at pH 7 (estimated)[2]
Biodegradation	90.3% after 28 days (inherently biodegradable); 59.8% biodegradation in 1 day in SCAS test (inherently biodegradable)[3]	90% after 10 days river die-away test; 67% after 4 weeks (readily biodegradable)[4]	No data	74% after 4 weeks (readily biodegradable – data for diisononyl phthalate CASRN 28553-12-0)[4]; 98% biodegradation in 28 days using a shake flask test (half-life 5 days)[5,6]	No data	1% after 15 days and 10% after 15 days after the inoculum was acclimated[7]; 99% in 28 days[7]	76% in 28 days (inherently biodegradable); 98% biodegradation in 28 days using a shake flask test (half-life = 5 days)[5,6]; Half-life of 2.5 weeks in a river die-away test[8]	No data	98% biodegradation in 28 days using a shake flask test (half-life = 5 days)[5,6]	12.8% in 28 days; 37% after 28 days (ultimate biodegradation); >50% biodegradation in 28 days using a shake flask test (half-life = 27 days)[5]
Bioconcentration	BCF = 2,541 (estimated)[2]	BCF = 974 (estimated)[2]	BCF = 12,900 (estimated)[2]	BCF = 222 (estimated)[2]	BCF = 73 (estimated)[2]	BCF = 333 (estimated)[2]	BCF = 21 (estimated)[2]	BCF = 25 (estimated)[2]	BCF = 70 (estimated)[2]	BCF = 12 (estimated)[2]
Bioaccumulation factor	BAF = 53 (estimated)[2]	BAF = 34 (estimated)[2]	BAF = 27 (estimated)[2]	BAF = 32 (estimated)[2]	BAF = 20 (estimated)[2]	BAF = 19 (estimated)[2]	BAF = 7 (estimated)[2]	BAF = 7 (estimated)[2]	BAF = 12 (estimated)[2]	BAF = 5 (estimated)[2]
Log K_{oc}	5.2 (estimated)[2]	5.1 (estimated)[2]	4.8 (estimated)[2]	5.5 (estimated)[2]	6.0 (estimated)[2]	6.2 (estimated)[2]; 5.45 (measured)[9]	6.7 (estimated)[2]	6.7 (estimated)[2]	6.1 (estimated)[2]	7.4 (estimated)[2]; 6.08 (measured)[9]
Fugacity (Level III Model)[2]										
Air (%)	0.7	0.6	0.2	0.3	0.3	0.8	0.5	0.2	0.6	0.2
Water (%)	14.8	18.2	12.8	15.3	15.1	19.9	21.4	15.4	21.5	11.9
Soil (%)	55.2	71.1	67.9	82.2	83.8	64	77.8	84.0	77.3	87.9
Sediment (%)	29.3	10.1	19.1	2.2	0.7	15.4	0.2	0.4	0.6	<0.1

Table 3c. Environmental Fate Characteristics of Phthalate Esters – High Molecular Weight Phthalate Esters Subcategory[1]

Property	1,2-Benzene-dicarboxylic acid, mixed decyl and hexyl and octyl diesters	1,2-Benzenedicarboxylic acid, 1,2-dioctyl ester	1,2-Benzene-dicarboxylic acid, benzyl C_{7-9}-branched and linear alkyl esters	1,2-Benzene-dicarboxylic acid, dinonyl ester, branched and linear	1,2-Benzene-dicarboxylic acid, di-C_{9-11}-branched and linear alkyl esters	1,2-Benzene-dicarboxylic acid, 1,2-didecyl ester	1,2-Benzene-dicarboxylic acid, 1,2-diundecyl ester	1,2-Benzene-dicarboxylic acid, 1,2-diundecyl ester, branched and linear	1,2-Benzene-dicarboxylic acid, 1-nonyl 2-undecyl ester, branched and linear	1,2-Benzene-dicarboxylic acid, di-C_{11-14}-branched alkyl esters, C_{13}-rich
CASRN	68648-93-1	117-84-0	68515-40-2	68515-45-7	68515-43-5	84-77-5	3648-20-2	85507-79-5	111381-91-0	68515-47-9
Persistence[10]	P1	P1	P1	P1	P1	P1	P1	P1	P1	P1
Bioaccumulation[10]	B1	B1	B1	B1	B1	B1	B1	B1	B1	B1

[1] ExxonMobil Biomedical Sciences, Inc. for the Phthalate Esters Panel, HPV Testing Group of the American Chemistry Council. December 18, 2006. Revised Robust Summary and Test Plan for the Phthalate Esters Category. Available from: http://www.epa.gov/hpv/pubs/summaries/benzene/c13467tc.htm as of December 19, 2009.
[2] U.S. EPA. 2009. Estimation Programs Interface Suite™ for Microsoft® Windows, v4.0. U.S. Environmental Protection Agency, Washington, DC. Available from: http://www.epa.gov/opptintr/exposure/pubs/episuite.htm as of December 19, 2009.
[3] O'Grady DP; Howard PH; Werner AF. 1985. Activated sludge biodegradation of 12 commercial phthalate esters. Appl. Environ. Microbiol. 49:443–445.
[4] National Institute of Technology and Evaluation. 2002. Biodegradation and Bioaccumulation of the Existing Chemical Substances under the Chemical Substances Control Law. Available from: http://www.safe.nite.go.jp/english/kizon/KIZON_start_hazkizon.html as of December 19, 2009.
[5] Sugatt RH; O'Grady DP; Banerjee S; Howard PH; Gledhill WE. 1984. Shake Flask Biodegradation of 14 Commercial Phthalate Esters. Appl. Microbiol. 47(4):601–606.
[6] Data obtained for a commercial test substance (711P) composed of six phthalate esters consisting of C_7, C_9, and C_{11} ester side chains. This test substance is considered by EPA under the following CASRNs: 68515-44-6 (di C_7), 68515-45-7 (di C_9), 3648-20-2 (di C_{11}), 111381-89-6 (C_7, C_9), 111381-90-9 (C_7, C_{11}), and 111381-91-0 (C_9, C_{11}).
[7] HSDB (Hazardous Substances Data Bank). 2009. TOXNET Toxicology Data Network. U.S. National Library of Medicine. Available from: http://toxnet.nlm.nih.gov/cgi-bin/sis/htmlgen?HSDB as of December 22, 2009.
[8] Saeger VW; Tucker ES. 1976. Biodegradation of phthalic acid esters in river water and activated sludge. Appl. Environ. Microbiol. 31:29–34.
[9] Staples C; Peterson DR; Parkerton TF; Adams WJ. 1997. The environmental fate of phthalate esters: A literature review. Chemosphere 35:667–749.
[10] Federal Register. 1999. Category for Persistent, Bioaccumulative, and Toxic New Chemical Substances. *Federal Register* 64, Number 213 (November 4, 1999) pp. 60194–60204.

3. Human Health Effects

A summary of health effects data submitted for SIDS endpoints is provided in Tables 4a-d. The table also indicates where data for tested category members are read-across (RA) to untested members of the category.

Acute Oral Toxicity

Subcategory I: Low Molecular Weight Phthalate Esters

1,2-Benzenedicarboxylic acid, dimethyl ester (DMP, CASRN 131-11-3)
In a 1948 study 40 animals (gender and age not specified) were dosed with undiluted CASRN 131-11-3 (method not specified) and observed for six days. Specific doses used were not provided in the robust summary, but CASRN 131-11-3 was administered in graded doses to achieve a dose-mortality curve. Mortality information (number of deaths/dose) was not provided.
LD_{50} = 6900 mg/kg-bw

1,2-Benzenedicarboxylic acid, diethyl ester (DEP, CASRN 84-66-2)
(1) Although not reported in the HPV submission, according to the EPA Office of Pesticide Program (OPP) inert reassessment for CASRN 84-66-2 (found at http://www.epa.gov/opprd001/inerts/lists.html), reported that LD_{50} values for rat and mouse are 9200-9500 mg/kg and 8600 mg/kg, respectively (as presented in Table 4 of the inerts document).

(2) Albino rats (5/sex/dose) were administered CASRN 84-66-2 via gavage at 0.5, 1.0, 2.0 or 5.0 mL/kg and observed for 14 days following dosing. One mortality occurred at 5 mL/kg. (Go to http://www.srcinc.com/what-we-do/databaseforms.aspx?id=384, key in CASRN 84-66-2, restrict the search to "health effects" and scroll down to to Item #3 [442767 or Fiche # OTS0557297).
LD_{50} > 5900 mg/kg-bw

Subcategory II: Transitional Phthalate Esters

1,2-Benzenedicarboxylic acid, dihexyl ester, branched and linear (DHP, CASRN 68515-50-4)
Sprague-Dawley rats (3 males and 2 females/dose) were administered CASRN 68515-50-4 via gavage at 15,800 mg/kg-bw and observed for 14 days following dosing. No mortalities were observed.
LD_{50} > 15,800 mg/kg-bw

1,2-benzenedicarboxylic acid, dihexyl ester (DnHP, CASRN 84-75-3; supporting chemical)
In a 1973 study in male and female rats (strain, number, and doses not provided in robust summary) LD_{50} values of 29.6 ml/kg-bw and 38.9 ml/kg-bw were reported for males and females, respectively (assuming a density of 1, these would be equivalent to approximately 30 g/kg-bw and 39 g/kg-bw, respectively). There were no details on symptoms or mortalities.
LD_{50} = 30,000 mg/kg-bw

1,2-benzenedicarboxylic acid, di-C_{6-8} branched alkyl ester, C_7 rich (DIHP, CASRN 71888-89-6)

Wistar rats (5 males/dose) were administered CASRN 71888-89-6 via gavage at 1.0, 1.47, 2.15, 3.16, 4.64, 6.81 or 10.0 g/kg-bw and observed for 14 days following dosing. No mortalities were observed.

LD_{50} > 10,000 mg/kg-bw

1,2-benzenedicarboxylic acid, bis(2-ethylhexyl) ester (DEHP, CASRN 117-81-7; supporting chemical)

Seventeen robust summaries are provided in the dossier submitted by industry; most (11/17) only provide an LD_{50} value with no explanation of test conditions or results and the others that provide some text are in German. Values are presented for a variety of test species. The range in values presented is 6860 mg/kg-bw (rat) to 49,000 mg/kg-bw (rat).

1,2-benzenedicarboxylic acid, di-C_{7-9} branched and linear alkyl esters (in79P, CASRN 68515-41-3, supporting chemical)

Four robust summaries are presented showing results in mice and rats. The range in oral (all presumed gavage studies) LD_{50} values reported are >19,300 to >20,000 mg/kg-bw. Males and females were used, matted/wet fur was the only clinical sign noted. No mortalities were noted in any study.

LD_{50} > 19,300 mg/kg-bw

1,2-benzenedicarboxylic acid, dioctyl ester (DnOP, CASRN 117-84-0)

(1) Rats were administered CASRN 117-84-0 via unspecified oral route in a range-finding study. No test details provided.

LD_{50} = 53,700 mg/kg-bw

(2) Mice were administered CASRN 117-84-0 via unspecified oral route in a range-finding study. No test details provided.

LD_{50} = 13,000 mg/kg-bw

(3) Hozman albino rats (5/sex/dose) were administered CASRN 117-84-0 via intubation at 7.71, 15.4 or 30.72 g/kg-bw and observed for 14 days following dosing. No mortalities were observed.
http://www.srcinc.com/what-we-do/databaseforms.aspx?id=384
LD_{50} > 30,720 mg/kg-bw

1,2-benzenedicarboxylic acid, di-C_{8-10}-branched alkyl esters, C_9-rich (DINP, CASRN 68515-48-0, supporting chemical)

Sprague-Dawley rats (30 males/dose) were administered CASRN 68515-48-0 via gastric intubation at 34.6, 120, 417, 1450, 5000 or 10,000 mg/kg-bw and observed for 14 days following dosing. No mortalities were observed.

LD_{50} > 10,000 mg/kg-bw

1,2-benzenedicarboxylic acid, di-C_{11-14} branched alkyl esters, C_{13} rich (DTDP, CASRN 68515-47-9)

Sprague-Dawley rats (35 males/dose) were administered CASRN 68515-47-9 via an unspecified oral route at 1, 1.47, 2.15, 3.15, 4.64, 6.81 or 10.0 g/kg-bw and observed for 14 days following dosing. No mortalities were observed.

LD_{50} > 10,000 mg/kg-bw

1,2-benzenedicarboxylic acid, ditridecyl ester (DTP, CASRN 119-06-2, supporting chemical)
Sprague-Dawley rats (5/sex/dose) were administered CASRN 119-06-2 ester via gavage at 0 or 2000 mg/kg-bw and observed for 14 days following dosing. No mortalities were observed.
LD_{50} > 2000 mg/kg-bw

***1,2-benzenedicarboxylic acid, 2,2-dimethyl-1-(1-methylethyl)-3-(2-methyl-1-oxopropoxy) propyl phenylmethyl ester (B84P,* CASRN 16883-83-3)**
Sprague-Dawley rats (20/sex/dose) were administered CASRN 16883-83-3 via stomach tube at 2000, 31600, 5010, 7940, 12,600 or 15,800 mg/kg-bw and observed for 14 days following dosing. No mortalities were observed.
LD_{50} > 15,800 mg/kg-bw

1,2-benzenedicarboxylic acid, butyl phenylmethyl ester (BBP, CASRN 85-68-7, supporting chemical)
Fischer 344 rats (10/sex/dose) were administered CASRN 85-68-7 via gavage at 0, 80, 160, 320, 630, 1250, 2500, 5000, 10,000 or 20,000 mg/kg-bw and observed for 14 days following dosing. Mortalities were observed at ≥ 2500 mg/kg-bw.
LD_{50} = 2330 mg/kg-bw

Acute Inhalation Toxicity

Subcategory I: Low Molecular Weight Phthalate Esters

1,2-Benzenedicarboxylic acid, diethyl ester (DEP, CASRN 84-66-2)
Rats (3/dose) were exposed whole body to CASRN 84-66-2 as a mixture of aerosol and vapor at 0 or 4.64 mg/L for 6 hours and observed for 14 days following dosing. No mortalities were observed.
LC_{50} > 4.64 mg/L

Subcategory II: Transitional Phthalate Esters

No data.

Subcategory III: High Molecular Weight Esters

1,2-benzenedicarboxylic acid, bis(2-ethylhexyl) ester (DEHP, CASRN 117-81-7; supporting chemical)
Rats (5 animals/sex/dose) were given a single dose of CASRN 117-81-7 at concentrations of 0, 3.39, 6.82 or 10.62 mg/L via inhalation for four hours. There were no mortalities observed.
LC_{50} = > 10.62 mg/L

Acute Dermal Toxicity

Subcategory I: Low Molecular Weight Phthalate Esters

1,2-Benzenedicarboxylic acid, diethyl ester (DEP, CASRN 84-66-2)
Guinea pigs (1/dose) were administered CASRN 84-66-2 via the dermal route at 0, 5, 10 or 20 mL/kg under occluded conditions for 24 hours and observed for 14 days following dosing. No mortalities were observed.
LD_{50} > 23,600 mg/kg-bw

No data.

Subcategory III: High Molecular Weight Phthalate Esters

1,2-benzenedicarboxylic acid, di-C_{6-8} branched alkyl ester, C_7 rich (DIHP, CASRN 71888-89-6)

(1) New Zealand White rabbits (2/sex/dose) were administered CASRN 71888-89-6 via the dermal route to a single dose (3160 mg/kg-bw) under occluded conditions for 24 hours and observed for 14 days following dosing. No mortalities were observed.

LD_{50} > 3160 mg/kg-bw

(2) New Zealand White rabbits (4/sex/dose) were administered CASRN 71888-89-6 via the dermal route to five different concentrations from 50 mg/kg-bw up to 3.16 g/kg-bw under occluded conditions for 24 hours and observed for 14 days following dosing. Mortalities were not noted. http://www.srcinc.com/what-we-do/databaseforms.aspx?id=384

LD_{50} > 3160 mg/kg-bw

1,2-benzenedicarboxylic acid, bis(2-ethylhexyl) ester (DEHP, CASRN 117-81-7; supporting chemical)

Guinea pigs (number, gender and age not specified) were given CASRN 117-81-7 via the dermal route of exposure (doses not provided). No details about test conditions or results were provided in the robust summary. (NOTE: Three other robust summaries were listed, two reported LD_{LO} values and the other reported an LD_{50} of 25,000 mg/kg-bw in rabbits.)

LD_{50} = 10,000 to 25,000 mg/kg-bw

1,2-benzenedicarboxylic acid, di-C_{8-10}-branched alkyl esters, C_9-rich (DINP, CASRN 68515-48-0, supporting chemical)

New Zealand White rabbits (unknown number per dose) were administered CASRN 68515-48-0 via the dermal route at 50, 200, 794 or 3160 mg/kg-bw under occluded conditions and observed for 14 days following dosing. No mortalities occurred.

LD_{50} > 3160 mg/kg-bw

1,2-benzenedicarboxylic acid, di-C_{9-11}-branched alkyl esters, C_{10}-rich (DIDP, CASRN 68515-49-1, supporting chemical)

Rabbits (4 per dose, sex unknown) were administered CASRN 68515-49-1 via the dermal route at concentrations of 200 or 3160 mg/kg-bw under occluded conditions for 24 hours and observed for 14 days following dosing. Mortalities were not noted.

LD_{50} > 3160 mg/kg-bw

1,2-benzenedicarboxylic acid, di-C_{11-14} branched alkyl esters, C_{13} rich (DTDP, CASRN 68515-47-9)

New Zealand White rabbits (2/sex/dose) were administered CASRN 68515-47-9 via the dermal route at 0, 50, 200, 794 or 3160 mg/kg-bw under occluded conditions for 24 hours and observed for 14 days following dosing. No mortalities were observed.

LD_{50} > 3160 mg/kg-bw

1,2-benzenedicarboxylic acid, benzyl C_{7-9} branched and linear alkyl esters (B79P, CASRN 68515-40-2)
New Zealand white rabbits (males and females, three animals used – assumed to be per sex/dose) were given two doses of CASRN 68515-40-2 (5010 or 7940 mg/kg-bw) via the dermal route of exposure. CASRN 68515-40-2 was applied to the clipped/intact skin and the area was covered with plastic strips for 24 hours. The animals were observed for 14 days. There were no mortalities, but there was reduced appetite and activity in treated animals for days 1-3.
LD_{50} > 7940 mg/kg-bw

1,2-benzenedicarboxylic acid, 2,2-dimethyl-1-(1-methylethyl)-3-(2-methyl-1-oxopropoxy) propyl phenylmethyl ester (B84P, CASRN 16883-83-3)
(1) New Zealand White rabbits (5/sex/dose) were administered CASRN 16883-83-3 via the dermal route at 2000, 3160, 5010 or 7940 mg/kg-bw under unspecified conditions for 24 hours and observed for 7 days following dosing. Mortalities were not noted.
LD_{50} > 7940 mg/kg-bw

(2) New Zealand White rabbits (1/sex/dose) were administered CASRN 16883-83-3 via the dermal route at 2510 or 10,000 mg/kg-bw under occluded conditions for 24 hours and observed for 14 days following dosing. No mortalities were observed.
LD_{50} > 10,000 mg/kg-bw

1,2-benzenedicarboxylic acid, butyl phenylmethyl ester (BBP, CASRN 85-68-7, supporting chemical)
Rabbits (unknown number or sex/dose) were administered CASRN 85-68-7 via the dermal route at 10,000 mg/kg-bw under unspecified conditions for an unknown period of time. Mortalities were not noted.
LD_{50} > 10,000 mg/kg-bw

Repeated-Dose Toxicity

Subcategory I: Low Molecular Weight Phthalate Esters

1,2-Benzenedicarboxylic acid, diethyl ester (DEP, CASRN 84-66-2)
Sprague-Dawley rats (15/sex/dose) were administered CASRN 84-66-2 for 16 weeks via the diet at doses of 0, 0.2, 1 or 5% (equivalent to approximately 0, 150, 750 or 3750 mg/kg/day). There were no effects observed at the lowest dose. Body weights and food consumption were statistically significantly decreased (magnitude not provided) at the mid (females only) and high (males and females) dose levels. Although body weight and food consumption were measured weekly, no details were provided in the robust summary about when or how long these decreases occurred. The relative weights of the following organs were elevated in both genders at the high dose level only: brain, liver, stomach and small intestine.
LOAEL = 750 mg/kg/day (females; decrease in food consumption and body weights); **3750 mg/kg/day** (males and females – decrease in food consumption and body weights and increased relative weights of various organs).
NOAEL = 150 mg/kg/day (females); **750 mg/kg/day** (males)

1,2-Benzenedicarboxylic acid, dimethyl ester (DMP, CASRN 131-11-3)
In a 90-day dermal study, rabbits (gender and number not specified) were exposed to CASRN 131-11-3 (multiple doses used, but not specified) at up to 4 ml/kg-bw/day (assuming a density of 1gram/ml, equivalent to 4000 mg/kg/day). Details regarding the study method were not provided in the robust summary. Unspecified systemic effects were observed at the highest tested dose level (4000 mg/kg/day), and kidney (nephritis) and lung (edema) effects were observed at the two highest doses.
NOAEL/LOAEL = Cannot be established with data provided

Subcategory II: Transitional Phthalate Esters

1,2-Benzenedicarboxylic acid, dihexyl ester, branched and linear (DHP, CASRN 68515-50-4)
(1) In a 13-week study, Sprague-Dawley rats (15/sex in controls; number of animals in treated groups unclear from robust summary) were fed CASRN 68515-50-4 at dietary concentrations of 0, 0.05, 0.10 or 0.5% (the 0.05% group was adjusted to 1% at seven weeks and then again to 3% at 12 weeks). Given this change in protocol[5], EPA is assigning the following dose groups for this study: 0, 0.10, 0.50 or 1%; which are equivalent to approximately 0, 75, 383 or 750 mg/kg/day). The following effects were observed in the high dose group: decreases in body weight gains and food consumption (males and females) over the last three weeks of the study; clinical signs (respiratory distress, stiff gait, rigid/arched tail; presumably in both males and females – all during the last three weeks on study); significant increase in total leukocyte counts (females only); significant increases in liver weights and significant decreases in spleen, kidneys, adrenals, and gonad weights (males and females); and microscopic changes in the testes (atrophy of spermatogenic epithelium) and liver (presence of eosinophils in cytoplasm and nuclear size variation). Males in all treated groups had significant increases in heart/body weight ratios and females had significantly increased thyroid weights in the low dose group only.
LOAEL = 75 mg/kg/day (increased heart weight in males)
NOAEL = Not established

(2) Beagle dogs (unknown number/sex/dose) were administered CASRN 68515-50-4 for 13 weeks via the feed at doses of 0, 0.1, 0.5 or 1% (the 0.1% group was adjusted to 5.0% at 9 weeks). Given this change in protocol, EPA is assigning the following dose groups for this study: 0, 0.5, 1 or 5%; which are equivalent to approximately 0, 90, 180 or 900 mg/kg/day). Mean liver weights and liver/body weight ratios for the dogs in the 5% group increased, and males exhibited decreased testes weight and ratio. Enlarged hepatic cells were observed in males in the 5% group. No changes in weight, clinical blood chemistry, hematology or urinalysis were observed. The LOAEL and NOAEL are based on data from exposure weeks 9-12.
LOAEL =900 mg/kg/day) (based on increases in absolute and relative (to body weight) liver weights, hepatic cell enlargement and testicular changes)
NOAEL = Cannot be assigned since only tissues from the control and high dose groups were microscopically evaluated.

Subcategory III: High Molecular Weight Phthalate Esters

1,2-benzenedicarboxylic acid, bis(2-ethylhexyl) ester (DEHP, CAS No. 117-81-7; supporting chemical)
Thirty robust summaries are provided in the dossier submitted by the sponsor. Most (29/30) are in German and the single robust summary in English is a 28-day oral feeding study in rats (number of animals not provided) fed 0, 50, 200 (summary lists 2000, assumed to be a typo) or 1000 mg/kg/day. The summary reports a dose-dependent increase in peroxisomes along with increases in other parameters associated with peroxisome proliferation (liver hypertrophy and increase in peroxisomal enzymes).

However, this Hazard Characterization uses the critical study identified in the ATSDR Toxicological Profile (David et al., 2000 as presented in the Profile – available at http://www.atsdr.cdc.gov/toxprofiles/tp9.html) to develop the Minimal Risk Level (MRL). This study was not provided in the dossier and is presented here because it provides an important reference point in the read-across for repeated-dose toxicity for the high molecular weight phthalate esters (see Table 4b).

[5] It seems unusual that the original lowest dose was altered to be the new highest dose. However, EPA notes that in another study with dogs (described next), the same protocol was followed. So, although it could be an error in transcription when developing the robust summaries, EPA is assuming the statements to be correct. Both studies date back to 1962 and are unpublished.

Briefly, F344 rats were fed a diet containing CASRN 117-81-7 at concentrations of 0, (80/sex), 100 (50/sex), 500 (55/sex), 2,500 (65/sex) or 12,500 (80/sex) ppm for up to 104 weeks. These concentrations are equivalent to 0, 5.8, 29, 147 or 789 mg/kg/day in males and 0, 7.3, 36, 182 or 939 mg/kg/day in females. There were no effects observed in the lowest dose group. Significant effects on the sperm (increased bilateral aspermatogenesis) were observed at the second lowest dose (29 mg/kg/day) and above. This was consistent with a significant reduction in relative testis weight that occurred at the highest dose (789 mg/kg/day). Liver effects were observed in males and females at doses of 147 (males) and 182 (females) and above and included significantly increased absolute and relative liver weights accompanied by increased peroxisome proliferation. Liver tumors were seen in males at 147 mg/kg/day and females at 939 mg/kg/day. Kidney effects were also seen in both males and females.
LOAEL = 29 mg/kg/day (sperm effects in males)
NOAEL = 5.8 mg/kg/day

1,2-benzenedicarboxylic acid, di-C_{7-9} branched and linear alkyl esters (in79P, CASRN 68515-41-3, supporting chemical)
CFE rats (15/sex/dose) were administered CASRN 68515-41-3 for 90 days via oral feed at doses of 0, 60, 120, 240 or 480 mg/kg/day. There were no changes at 60 mg/kg/day in hematology, serum chemistry, urinalysis or in a gross and microscopic examination of tissues. At ≥ 120 mg/kg-bw, there were indications of decreased hemoglobin levels and red blood cell counts, and increased urinary cell excretion. At ≥ 240 mg/kg/day, liver and kidney weights increased. At 480 mg/kg/day, males grew more slowly and were unable to concentrate urine normally, and two males produced renal casts. Relative weights of the brain and gonads were increased in males, and both sexes had increased haemosiderin in the spleen.
LOAEL = 120 mg/kg/day (based on changes in blood and serum chemistry and increased urinary output)
NOAEL = 60 mg/kg/day

1,2-benzenedicarboxylic acid, dioctyl ester (DnOP, CASRN 117-84-0)
Sprague-Dawley rats (unknown number/sex/dose) were administered CASRN 117-84-0 for 13 weeks via the feed at doses of 0, 0.4, 3.8, 38.8 or 376.5 mg/kg/day. No clinical signs of toxicity, reductions in body weights or food consumption were observed. At the highest dose, increased liver ethoxyresorufin-O-deethylase activity was observed. Mild histological changes were noted at the highest dose level in both the test substance and control groups, including reduced follicle size and colloid density in the thyroid, and endothelial nuclear prominence, nuclear hyperchromicity and anisokaryosis. Accentuation of zonation of hepatic lobules and increased perivenous cytoplasmic vacuolation was observed at the highest dose level. No testicular changes or increases in peroxisomes were observed.
LOAEL = 376.5 mg/kg/day (based on histopathological changes in the liver and thyroid)
NOAEL = 38.8 mg/kg/day

1,2-benzenedicarboxylic acid, diundecyl ester (DUP, CASRN 3648-20-2)
In a 21-day study, Fischer rats (5/sex/dose) were fed CASRN 3648-20-2 at dietary concentrations of 0, 0.3, 1.2 or 2.5% (equivalent to approximately 0, 282, 1145 or 2305 mg/kg/day). The following effects were observed in the mid and high dose groups: decreased body weight gain, increased liver and kidney weights, increases in indicators of peroxisome proliferation (increased palmitoyl-CoA oxidation), and males had increased relative testes weights (but no associated histopathology).
LOAEL = 1145mg/kg/day (decreased body weight gain, increased liver, kidney, and relative testes weights)
NOAEL = 282 mg/kg/day

1,2-benzenedicarboxylic acid, ditridecyl ester (DTP, CASRN 119-06-2; supporting chemical)

In a combined repeated-dose/reproductive/developmental toxicity screening test, Sprague-Dawley rats (13/sex/dose) were administered CASRN 119-06-2 for 42 days (males) or from 14 days prior to mating to day 3 of lactation (females) via gavage at doses of 0, 10, 50 or 250 mg/kg/day. No mortalities or testicular toxicity was observed. In the 50 and 250 mg/kg/day groups, increased salivation was observed, body weight gains were reduced, liver weights were increased and histopathological changes were observed. Additionally, in the 250 mg/kg/day group, kidney weights increased, additional histopathological changes were found, hyperplasia of the pelvic epithelium and transitional cells of the urinary bladder were observed, and alkaline phosphatase activity increased in males.

LOAEL = 50 mg/kg/day (based on histopathology, organ weights, blood chemistry)
NOAEL = 10 mg/kg/day

1,2-benzenedicarboxylic acid, butyl phenylmethyl ester (BBP, CASRN 85-68-7, supporting chemical)

(1) Wistar rats (unknown number per sex/dose) were administered CASRN 85-68-7 for 90 days via the diet at doses of 0, 151, 381 or 960 mg/kg/day. At ≥ 381 mg/kg/day, kidney weights increased, urinary pH decreased, liver weights increased and red blood cells decreased. Histopathology changes were noted in the liver and pancreas at 960 mg/kg/day.

LOAEL = 381 mg/kg/day (based on increased kidney weight)
NOAEL = 151 mg/kg/day

(2) Fischer 344 rats (50/sex/dose) were administered CASRN 85-68-7 for 103 days via the diet at doses of 0, 420 or 840 mg/kg/day. Food consumption and body weights decreased at the low- and high-dose levels. Survival of the high-dose males was lower than that of controls. Increased incidence of mononuclear cell leukemias affecting multiple organs was observed in the high-dose group. Incidence of fibroadenomas in the mammary glands of females decreased.

LOAEL = 840 mg/kg/day (based on survival, pathology)
NOAEL = 420 mg/kg/day

Reproductive Toxicity

Subcategory I: Low Molecular Weight Phthalate Esters

1,2-Benzenedicarboxylic acid, diethyl ester (DEP, CAS No. 84-66-2)

In a two generation study, Swiss CD-1mice (40 animals/sex/control group and 20 animals/sex/dose in the treated groups) were fed CASRN 84-66-2 at the following concentrations for seven days prior to mating and then for a 14 week cohabitation period: 0, 0.25, 1.25 or 2.5% in feed (equivalent to 0, 325, 1625 or 3250 mg/kg/day). There was a statistically significant decrease in body weight (males and females) in the parental generation at the highest dose only. The following effects were also noted (presumably in the parental generation and at the high dose only): increases in male prostate weight and liver weight (females only) and a decrease in female pituitary weight. Although no details (i.e., magnitude or statistical significance) were provided in the robust summary, it states that "….sperm concentration decreased *in the treated animals*" *(emphasis added).* This implies the effect was observed at all dose levels. In terms of reproductive endpoints, CASRN 84-66-2 had no effect on fertility, pup weight or sex determination. However, the number of live pups/litter was decreased in the high dose group (magnitude, significance not provided).

LOAEL (reproductive) = 3250 mg/kg/day (decrease in live pups/litter).
NOAEL (reproductive) = 1625 mg/kg/day

1,2-benzenedicarboxylic acid, dihexyl ester (DnHP, CASRN 84-75-3; supporting chemical)
In a one-generation study, Swiss CD-1 mice (40 animals/sex/control group and 20 animals/sex/concentration in the treated groups) were fed CASRN 84-75-3 at the following concentrations for seven days prior to mating and then for a 14-week cohabitation period: 0, 0.3, 0.6 or 1.2% in feed (equivalent to 0, 430, 880 or 1870 mg/kg/day). After the 14-week cohabitation period, a crossover experiment was run to determine whether any reproductive effects were either male or female-mediated (high dose male mice were mated with control females and high dose females were mated with control males). In the first part of the experiment, there was a dose related decrease in body weights (magnitude and associated dose levels not reported). Other systemic effects observed in the crossover experiment (only high dose animals examined) were: decreased sperm concentration and motility, significant decreases in testicular, epididymis, and seminal vesicle weights, and (microscopically) atrophy of the seminiferous tubules (males); significant decrease in uterine weight (31%, females); and decreases in kidney and adrenal weights and increased liver weights (both sexes). In addition, reproductive effects were observed at all dose levels in the first experiment: no litters were born in the high dose group, only one litter in the mid-dose group and a reduced number in the low dose group (14/17 versus 37/37 in controls). Also reported in the low dose group were decreases in the number of litters/pair, number of live pups/litter and proportion of live pups. The crossover study revealed similar reductions in fertility (only 1/18 high dose males sired a litter and none of the high dose females became pregnant).
LOAEL (reproductive) = 430 mg/kg/day (decreases in number of litters, number of live pups/pair and proportion of live pups).
NOAEL (reproductive) = not established

Subcategory III: High Molecular Weight Phthalate Esters

1,2-benzenedicarboxylic acid, bis(2-ethylhexyl) ester (DEHP, CASRN 117-81-7; supporting chemical)
Six robust summaries are provided in the dossier submitted by the sponsor. All of them are in German. As stated earlier, in this Hazard Characterization, EPA will rely on the ATSDR Toxicological Profile (available at http://www.atsdr.cdc.gov/toxprofiles/tp9.html) published in 2002. In their summary of reproductive and developmental toxicity, the ATSDR cites numerous studies in rodents showing that CASRN 117-81-7 is both a male and female reproductive toxicant. Studies in monkeys suggest that they are not as sensitive as rodents to testicular effects in males. Several studies identified a variety of effects on the male reproductive system in offspring following treatment of their parents. The ATSDR used a reproductive endpoint to derive their Minimal Risk Level (MRL) – a NOAEL of 5.8 mg/kg/day for testicular toxicity in rats (LOAEL = 29 mg/kg/day).

However, a reproductive study with CASRN 117-81-7 is reported in the CASRN 27554-26-3 dossier (see below). Although reported as a two-generation study in the submitted dossier, the original publication (*Toxicol. Appl. Pharm., 1987, Vol.88, pp.255-269)* describes a continuous breeding protocol used with four different phthalate esters and it appears that CASRN 117-81-7 was not carried through to a second generation (although there was a crossover mating study performed with high dose males and females of the F_0 generation). CD-1 mice (20/sex/dose) were administered CASRN 117-81-7 for via the diet at doses of 0, 0.01, 0.1 or 0.3% (equivalent to 0, 14, 140 or 420 mg/kg/day). A decrease in the number of litters/pair, live pups/litter, mean live pup weight and proportion of live pups was observed in both the mid and high dose group. Infertility was also observed in the high dose group. The following effects were observed in the high dose group (only control and high dose animals were examined for organ weight changes and histology analysis): reduced testis, epididymis, prostate weights, bilateral atrophy of the seminiferous tubules, decreased percentage motile sperm and abnormal sperm and sperm concentration in males; and reduced weight of ovaries, oviducts and uterus in females. Both sexes exhibited increased liver weights.

LOAEL (reproductive toxicity) = 140 mg/kg/day (based on decreased number of litters, live pups per litter, and live pup weights)
NOAEL (reproductive toxicity) = 14 mg/kg/day

1,2-benzenedicarboxylic acid, di-C_{7-9} branched and linear alkyl esters (in79P CASRN 68515-41-3, supporting chemical)
Sprague-Dawley rats (28/sex/dose) were administered CASRN 68515-41-3 daily over 2 generations via the feed at doses of 0, 0.1, 0.5 or 1.0% (corresponding to 0, 75, 375, or 750 mg/kg/day). Parameters measured included number of pups, body weights, food consumption sex, gross observations, necropsy, organ weights, sperm analysis, implantation sites, protein content of liver, clinical observations and CoA oxidase activity. The 1.0% males showed reduced body weights in the F0 and F1 generations. There was no impairment of fertility, fecundity or development in either generation, but pup body weights were reduced in the 1.0% group over the weaning period. Ovary weights were decreased in the 1.0% group for both generations, but ovarian function and mating behavior was not affected. Liver changes indicative of peroxisomal proliferation were noted in both generations and both sexes at the 1.0% dose, characterized by increased liver weight in young rats, histopathological changes, decreased weights in mature rats and increased CoA oxidase activity.
LOAEL (reproductive toxicity) = 750 mg/kg/day (based on reduced pup body weight, reduced ovary weights)
NOAEL (reproductive toxicity) = 375 mg/kg/day

1,2-benzenedicarboxylic acid, diisooctyl ester (DIOP, CASRN 27554-26-3)
The reproductive toxicity study reported in the CASRN 27554-26-3 robust summary is a CASRN 117-81-7 study and is summarized above under CASRN 117-81-7.

1,2-benzenedicarboxylic acid, dioctyl ester (DnOP, CASRN 117-84-0)
CD-1 mice (20/sex/dose) were administered CASRN 117-84-0 daily over two generations via oral feed at doses of 0, 1.8, 3.6 or 7.5 g/kg/day. No effect on any fertility or reproductive measure was observed. No treatment-related changes in parental clinical signs, body weight gains or food consumption was observed. Liver and kidney weights increased in the high-dose group.
LOAEL (reproductive toxicity) = Not established
NOAEL (reproductive toxicity) = 7500 mg/kg/day

1,2-benzenedicarboxylic acid, di-C_{8-10}-branched alkyl esters, C_9-rich (DINP, CASRN 68515-48-0, supporting chemical)
(1) In a two generation study, Fischer 344 rats (30 animals/sex/dose) were fed CASRN 68515-48-0 at the following concentrations for 10 weeks prior to mating and up to 26 weeks overall: 0, 0.2, 0.4 or 0.8% in feed (equivalent to approximately 0, 133, 266 or 532 mg/kg/day). The robust summary does not specify the treatment regimen during and following the mating of the F0 group. Also, the summary includes results from a one-generation study (reported separately here). In the two-generation study, there were no reported effects on the parental generation, reproductive capacity, or offspring. No other details were provided.
LOAEL (reproductive) = not established
NOAEL (reproductive) > 532 mg/kg/day (highest tested dose)

(2) In a one generation study, Sprague-Dawley rats (28 animals/sex/dose in the treated groups) were fed CASRN 68515-48-0 at the following concentrations for 10 weeks prior to mating: 0, 0.5, 1.0 or 1.5% in feed (equivalent to approximately 0, 333, 666 or 1000 mg/kg/day). The robust summary does not specify the treatment regimen during and following the mating of the F0 group. The results are presented along with those from the two-generation study reported above. Detailed results are not provided for systemic toxicity of parents, but it appears that there were none.

In terms of reproductive effects, the robust summary identifies a number of offspring effects at the highest dose (survival, decreased body weights, decreased liver and kidney weights); and the mid-dose (reduced body weights).
LOAEL (reproductive) = 666 mg/kg/day (reduced pup body weight)
NOAEL (reproductive) = 333 mg/kg/day

1,2-benzenedicarboxylic acid, di-C_{9-11} branched and linear alkyl esters (911P, CASRN 68515-43-5)
Sprague-Dawley rats (unknown number/sex/dose) were administered CASRN 68515-43-5 for 10 weeks prior to mating over two generations via oral feed at doses of 0, 0.1, 0.5 or 1.0% (corresponding to 0, 75, 375 or 750 mg/kg/day). The 1% group showed reduced body weights in the F0 and F1 generations. There was no impairment of fertility, fecundity or development in either generation. Pup body weights were reduced in the 1% group over the weaning period. Epididymal weights were decreased in the 1% group for both generations, but sperm concentration, motility and morphology was not affected. Liver changes in both sexes at the 1% dose occurred, characterized by increased liver weights, histopathological changes, decreased weights and increased palmitoyl CoA oxidase activity.
LOAEL (reproductive toxicity) = 750 mg/kg/day (reduced pup body weight)
NOAEL (reproductive toxicity) = 375 mg/kg/day

1,2-benzenedicarboxylic acid, ditridecyl ester (DTP, CASRN 119-06-2, supporting chemical)
In the combined repeated-dose/reproductive/developmental toxicity screening test described previously, no adverse effects were observed on copulation, fertility, pregnancy or delivery in any group. A decrease in live birth index on PND 0 was observed in the high-dose group. Maternal effects included body weight gain decreases in the high-dose group and increased liver:body weight ratios in the 50 and 250 mg/kg/day group. There were no adverse histopathologic findings, no effects on copulation or fertility and no effects on offspring sex ratio, body weight changes or morphological changes.
LOAEL (reproductive toxicity) = 250 mg/kg/day (reduced live birth index and effects on neonatal viability)
NOAEL (reproductive toxicity) = 50 mg/kg/day

1,2-benzenedicarboxylic acid, butyl phenylmethyl ester (BBP, CASRN 85-68-7; supporting chemical)
In a two-generation reproduction study in CD rats (30/sex/concentration), F0 and F1 generations were dosed for 10 weeks prior to mating, through mating, gestation, lactation, until scheduled sacrifice for adults; which occurred after the F2 generation was dosed through weaning. The following concentrations were given via the diet: 0, 750, 3750 or 11,250 ppm in food (target exposure levels were 0, 50, 250 or 750 mg/kg/day). Parental systemic toxicity at the high dose in both F0 and F1 parents were as follows: reduced body weights (male and female) and increased absolute and relative liver and kidney weights (males and females). There were also increases in liver/kidney weights in the mid-dose F0 and F1 animals and although the magnitude was reported (between 6-11% increase over controls); there was no mention in the robust summary whether this was statistically significant. There was evidence of reproductive toxicity in the males (F1) and females (F0 and F1) at the high dose level: males – reduced mating/fertility indices, reduced organ weights (testes, epididymes, seminal vesicles, and prostate), reductions in sperm concentration and motility, and an increase in gross and histopathological effects in the testes and epididymis; females – reduced absolute/relative weights of ovaries and uterus (F0 only), reduced mating/fertility indices, reduced uterine implantation sites, reduced ovarian weights, and reduced total and live pups/litter (F1only).

F1 and F2 pups were evaluated for developmental toxicity (sexual maturation) as well as a full analysis of organ weights (with emphasis on reproductive organs). Results showed a variety of effects in both male and female animals in both the F1 and F2 generations, at the high dose: reduced body weights; reduced organ weights (thymus and spleen, – both sexes; testes and epididymis – males; ovaries and uterus – females); increased relative brain weights (males and females); gross/histopathological effects (males – epididymis and testes), and

delayed/altered sexual maturation (reduced anogenital distance and increased nipple retention in males and delays in preputial separation (males) and vaginal patency (females). At the mid-dose, an increase (as opposed to a decrease as seen in the high dose group) in absolute and relative testes weight in F1 males was observed. Because this effect was not also seen in the F2 male pups, and because the direction of the effect (increase vs. decrease) was opposite of what was observed in the high dose group, these effects were not chosen to represent the LOAEL.
LOAEL (reproductive) = 750 mg/kg/day (decreases in reproductive organ weight [males and females], histopathological effects on reproductive organs [male], reduced mating/fertility indices [both sexes], reduced total and live pups/litter).
NOAEL (reproductive) = 250 mg/kg/day
LOAEL (offspring) = 750 mg/kg/day (reduced body weights, reduced organ weights, histopathological effects on male reproductive organs, delays/alterations in sexual maturation).
NOAEL (offspring) = 250 mg/kg/day

Developmental Toxicity

Subcategory I: Low Molecular Weight Phthalate Esters

1,2-Benzenedicarboxylic acid, dimethyl ester (DMP, CAS No. 131-11-3)
Pregnant Sprague-Dawley rats were given the following doses of CASRN 131-11-3 via the oral route (diet) during gestation days 6-15: 0, 0.25% 1.0% or 5.0% (corresponding to 0, 200, 840 and 3570 mg/kg-by/day). There were no mortalities among the pregnant animals. The only maternal toxicity observed was a decrease in food consumption and body weight and an increase in relative (ratio of absolute organ/body weight) kidney weight at the highest tested dose only. There was no corresponding pathological damage to the kidney. There were no effects observed in the fetuses (viability, body weight, skeletal/soft tissue effects).
LOAEL (maternal toxicity) = 3570 mg/kg/day (decrease in food consumption and body weight and increase in relative kidney weight).
NOAEL (maternal toxicity) = 840 mg/kg/day.
LOAEL (developmental toxicity) = Not established.
NOAEL (developmental toxicity) = 3570 mg/kg/day (highest dose tested).

1,2-Benzenedicarboxylic acid, diethyl ester (DEP, CAS No. 84-66-2)
(1) Pregnant Sprague-Dawley rats were given the following doses of CASRN 84-66-2 via the oral route (diet) during gestation days 6-15: 0, 0.25%, 2.5% or 5.0% (corresponding to 0, 200, 1910 and 3210 mg/kg/day). There were no mortalities among the pregnant animals. The only maternal toxicity observed was a decrease in food consumption and body weight in the mid and high dose groups. There were no effects observed in the fetuses for the following parameters: resorptions, viability, body weight, or litter size. There was a statistically significant increase in the incidence of fetuses with skeletal variations (particularly extra ribs) in the high dose group only.
LOAEL (maternal toxicity) = 1910 mg/kg/day (decrease in food consumption and body weight).
NOAEL (maternal toxicity) = 200 mg/kg/day.
LOAEL (developmental toxicity) = 3210 mg/kg/day (increase in skeletal variations).
NOAEL (developmental toxicity) =1910 mg/kg/day.

(2) New Zealand White rabbits (12 females/dose) were applied CASRN 84-66-2 to the skin from gestation day 6 through gestation day 18 at doses of 2 mL/kg at concentrations of 0.5, 5, 15 or 50% (density = 1/121 g/ml; doses correspond to 11.2, 112, 336 or 1120 mg/kg/day). No mortalities occurred. Slight erythemas, slight edema and atonia were observed in the 15% saturation group. There were no differences in maternal body weights or organ alterations. In offspring, there were no differences in the sex ratio, number of fetuses, uterine

position, fetal body weights, number of dead fetuses, number of resorptions, number of implantations, or number of corpora lutea or skeletal malformations. The mid-dose group contained two fetuses (separate litters) with external malformations; there were no such findings in any other group (including the high dose group) (http://www.srcinc.com/what-we-do/databaseforms.aspx?id=384).
NOAEL (maternal toxicity) = 1120 mg/kg/day
LOAEL (maternal toxicity) = Not established.
NOAEL (developmental toxicity) = 1120 mg/kg/day
LOAEL (developmental toxicity) = Not established.

Subcategory II: Transitional Phthalate Esters

The sponsor identified seven sponsored chemicals as members of this subcategory (see original submission at http://www.epa.gov/hpv/pubs/summaries/benzene/c13467tc.htm). Both the original EPA comments and this Hazard Characterization re-arranged this subcategory and there is currently one sponsored chemical (CASRN 68515-50-4) and one surrogate chemical (CASRN 84-75-3). Although no developmental toxicity data exist for either of these chemicals, EPA considers the information presented in the National Academy of Sciences (NAS) 2008 report entitled *Phthalates and Cumulative Risk Assessment: The Tasks Ahead* (pdf download available free at http://www.nap.edu/catalog.php?record_id=12528) and the recently posted Action Plan (see http://www.epa.gov/oppt/existingchemicals/pubs/ecactionpln.html) sufficient information to be acceptable for this endpoint for the purposes of the HPV Challenge Program.

Specifically, Chapter 3 in the NAS report presents both teratology and reproductive studies with various phthalate esters to show that many esters with side group carbon chain length backbones of C_{4-6} cause reproductive organ anomalies in developing male rats. The effects (male reproductive tract abnormalities including testicular atrophy, malformed external genitals, undescended testes and decreased sperm production) are seen only during early postnatal dosing of young male rats. Two of the phthalate esters referenced in the report that caused this toxicity in developing male rats were not identified as members of this HPV category (di-*n*-butyl phthalate [CASRN 84-74-2] and dipentyl phthalate [CASRN 131-18-0]. However, these chemicals fall within the boundaries of this subcategory (linear carbon chain lengths of C_{4-6}). Branching of the side groups appears to play a role in the development of this "phthalate syndrome" effect. For example, DEHP (CASRN 117-81-7) has a linear six-carbon moiety with an ethyl branch [total of eight carbon side chain] and is positive for the phthalate syndrome effect; whereas the DIOP (CASRN 27554-26-3) – which is a linear, eight carbon side chain with no branching - does not. Importantly, those with lower (C_{1-3}) or higher ($>C_7$) carbon chain lengths do not appear to be associated with the phthalate syndrome effects.

Subcategory III: High Molecular Weight Phthalate Esters

1,2-benzenedicarboxylic acid, diheptyl ester, branched and linear (DinHP, CASRN 68515-44-6)
Although no developmental toxicity data were provided in the HPV submission, EPA received a TSCA 8(e) notice in 1992 with preliminary results of a developmental screening study with three different phthalate esters (go to http://www.syrres.com/esc/tscats.htm and type in the CAS number to retrieve results; actual 8(e) notice is referenced as Fiche No. OTS0544569). One of the three phthalate esters tested was DEHP, which is evaluated separately below. The second and third phthalate esters were diisopentyl phthalate (CASRN 84777-06-0) and a "di-711-phthalate" (a phthalate ester reported to be identified under the following CASRNs: 68515-44-6; 111381-89-6; 111381-90-9; 111381-91-0; 3648-20-2 and 68515-40-7). The diisopentyl phthalate ester study results are not presented here because this ester would belong in Subcategory II (Transitional Phthalate Esters). In all three studies the following protocol was used: the chemical was given to pregnant Wistar rats (10/sex/dose) via gavage at dose levels of 0, 40, 200 or 1000 mg/kg/day on days 6-15 of gestation.

The following effects were reported in the pregnant females in the high dose group from the "di-711 phthalate" study: decreased body weight (statistically significant), decreased body weight gain, reduced gravid uterus weight, vaginal hemorrhage (6/10 animals), and increased relative liver and kidney weights (statistically significant). The following effects were reported for developmental toxicity: increased resorption rate (post-implantation loses of ~65%), decreased pup body weight, decreased number of live fetuses/dam (statistically significant), and statistically significant increases in external malformations (9/53 fetuses from 5/7 litters; primarily acaudia or filiformed tail).
LOAEL (maternal toxicity) = 1000 mg/kg/day (decreased body weight, vaginal hemorrhaging, increased relative liver and kidney weights).
NOAEL (maternal toxicity) = 200 mg/kg/day.
LOAEL (developmental toxicity) = 1000 mg/kg/day (increased resorptions, decreased number of live fetuses/dam, and increases in external malformations).
NOAEL (developmental toxicity) = 200 mg/kg/day.

1,2-benzenedicarboxylic acid, di-C_{6-8} branched alkyl ester, C_7 rich (DIHP, CASRN 71888-89-6)
(1) Crl:CDBr rats (25 females/dose) were administered CASRN 71888-89-6 on gestation days 6 through 20 via gavage at doses of 0, 250, 500, 750 or 1000 mg/kg/day. Maternal body weights and uterine weights decreased in the 750 and 1000 mg/kg/day dose groups. Fetal effects in the 750 and 1000 mg/kg/day groups included decreased body weights, increased number of resporptions per implantation site and per litter, increased percentage of post-implantation losses, decreased mean number of live fetuses per litter, change in the fetal sex ratio and increased number of fetal malformations (http://www.srcinc.com/what-we-do/databaseforms.aspx?id=384).
LOAEL (maternal toxicity) = 750 mg/kg/day (based on body weights, uterine weights)
NOAEL (maternal toxicity) = 500 mg/kg/day
LOAEL (developmental toxicity) = 750 mg/kg/day (based on fetal growth and survival)
NOAEL (developmental toxicity) = 500 mg/kg/day

(2) Sprague-Dawley rats (25 females/dose) were administered CASRN 71888-89-6 on gestation days 6 through 15 via gavage at doses of 0, 100, 300 or 750 mg/kg/day. There were dose-related increases in maternal liver weights in the 300 and 750 mg/kg/day groups. At doses of ≤ 300 mg/kg/day, there were no treatment-related or biologically important fetal malformations, embryolethality, or fetal weight reduction. Evidence of growth retardation and increased embryo/fetal death and increased incidence of external, visceral and skeletal malformations/variations was observed in the 750 mg/kg/day group
LOAEL (maternal toxicity) = 300 mg/kg/day (based on liver weights)
NOAEL (maternal toxicity) = 100 mg/kg/day
LOAEL (developmental toxicity) = 750 mg/kg/day (based on fetal growth and survival, skeletal malformations)
NOAEL (developmental toxicity) = 300 mg/kg/day

1,2-benzenedicarboxylic acid, bis(2-ethylhexyl) ester (DEHP, CASRN 117-81-7; supporting chemical)
Ten robust summaries are provided in the dossier submitted by the sponsor. All of them are in German. As stated earlier, in this Hazard Characterization, EPA will rely on the ATSDR Toxicological Profile (available at http://www.atsdr.cdc.gov/toxprofiles/tp9.html) published in 2002. In their summary of developmental toxicity, the ATSDR cites numerous studies in rodents showing that CASRN 117-81-7 caused a variety of developmental effects. In conventional developmental studies (pregnant animals dosed during gestation only) there were pre-and post-natal deaths, malformations, and developmental delays – all at doses of between 750 and 2000 mg/kg/day to pregnant rats; mice were a little more sensitive with some effects observed at doses as low as 100 mg/kg/day (data taken from Table 3-2 in document identified above). In the same table, non-conventional developmental studies are presented (dosing of females during and around gestation [pre and

post], and effects were observed at lower doses in rats (range of 313 to 1700 mg/kg/day in rats). Thus for the purposes of this assessment, the lowest NOAEL/LOAEL for developmental effects provided in Table 3-2 will be used (a mouse study – number 140 in Table 3-2, Figure 3-2).
LOAEL (developmental toxicity) = 91 mg/kg/day (external, visceral and skeletal malformations).
NOAEL (developmental toxicity) = 44 mg/kg/day.

In addition, it appears that this study is presented in English in the CASRN 27554-26-3 dossier and the summary is presented here: CD-1 mice (unknown number of females/dose) were administered 1,2-benzenedicarboxylic acid diisooctyl ester from gestation day 0 through gestation day 17 via the diet at doses of 0, 44, 91, 190.6 or 292.5 mg/kg/day. No maternal mortalities occurred. Reduced maternal body weight gain was observed in the two highest dose groups. There were no effects on the number of corpora lutea, implantation sites per dam, percent pre-implantation loss or sex ratio of live pups. The number and percent of resorptions, late fetal deaths and dead and malformed fetuses were increased in the two highest dose levels. Female fetal weight and the number of live fetuses per litter were reduced at the two highest dose levels. There was an increase in the percentage of fetuses with malformations and the percentage of malformations per litter at the 91 mg/kg/day groups and higher.
LOAEL (maternal toxicity) = 190.6 mg/kg/day (based on body weight gains)
NOAEL (maternal toxicity) = 91 mg/kg/day
LOAEL (developmental toxicity) = 91 mg/kg/day (based on fetal malformations, fetal survival, fetal weights)
NOAEL (developmental toxicity) = 44 mg/kg/day

1,2-benzenedicarboxylic acid, heptyl nonyl ester, branched and linear (Din79P, CAS No. 113181-89-6)
Although no developmental toxicity data were provided in the HPV submission, EPA received a TSCA 8(e) notice in 1992 with preliminary results of a developmental screening study with three different phthalate esters (go to http://www.syrres.com/esc/tscats.htm and type in the CAS number to retrieve results; actual 8(e) notice is referenced as Fiche No. OTS0544569). In this study, "Di-711-phthalate" (a phthalate ester reported to be identified under a number of CAS numbers, including that listed here for CASRN 68515-44-6 and CASRN 111381-89-6) was given to pregnant Wistar rats (10/sex/dose) via gavage at dose levels of 0, 40, 200 or 1000 mg/kg/day on days 6-15 of gestation. The following effects were reported in the pregnant females in the high dose group: decreased body weight (statistically significant), decreased body weight gain, reduced gravid uterus weight, vaginal hemorrhage (6/10 animals), and increased relative liver and kidney weights (statistically significant). The following effects were reported for developmental toxicity: increased resorption rate (post-implantation loses of ~65%), decreased pup body weight, decreased number of live fetuses/dam (statistically significant), and statistically significant increases in external malformations (9/53 fetuses from 5/7 litters; primarily acaudia or filiformed tail).
LOAEL (maternal toxicity) = 1000 mg/kg/day (decreased body weight, vaginal hemorrhaging, increased relative liver and kidney weights).
NOAEL (maternal toxicity) = 200 mg/kg/day.
LOAEL (developmental toxicity) = 1000 mg/kg/day (increased resorptions, decreased number of live fetuses/dam, and increases in external malformations).
NOAEL (developmental toxicity) = 200 mg/kg/day.

1,2-benzenedicarboxylic acid, di-C_{7-9} branched and linear alkyl esters (in79P CASRN 68515-41-3, supporting chemical)
Sprague-Dawley rats (28/sex/dose) were administered CASRN 68515-41-3 from gestation day 1 through gestation day 19 via gavage at doses of 0, 250, 500 or 1000 mg/kg/day. There were no effects on external or visceral abnormalities. Increased incidence of dilated renal pelvis was observed in the 250 mg/kg-bw group. There were no differences in body weight, fertility, reproductive organs, litter size, placental weights or fetal survival. There were no remarkable macroscopic findings in maternal animals. Fetal, litter and placental

weights were unaffected. There were skeletal variations (e.g., increased incidence of supernumerary ribs) at the high dose level. Other variations were noted in the robust summary; some at the mid- and low-dose levels that were considered unrelated to treatment by the submitter; but without incidence data, the Agency could not confirm this conclusion.
LOAEL (maternal toxicity) = Not established
NOAEL (maternal toxicity) = 1000 mg/kg/day
LOAEL (developmental toxicity) = 1000 mg/kg/day (based on skeletal and visceral variations)
NOAEL (developmental toxicity) = 500 mg/kg/day

1,2-benzenedicarboxylic acid, heptyl undecyl ester, branched and linear (711P, CASRN 111381-90-9)
Wistar rats (8 – 10 females/dose) were administered CASRN 111381-90-9 on gestation days 6 through 15 via gavage at doses of 0, 40, 200 or 1000 mg/kg/day. There were no treatment-related effects in the 40 or 200 mg/kg/day groups either in the dams or fetuses. The 1000 mg/kg/day maternal body weights were decreased during gestation days 15 – 20 and relative liver and kidney weight was increased in the high-dose group dams. Dams also showed vaginal hemorrhage during the study. Fetal weights of the remaining viable litters were reduced and all litters contained malformations in the 1000 mg/kg/day group. The malformations affected mainly the brain, vertebral column, tail, scapula, sternum and urogenital tract.
LOAEL (maternal toxicity) = 1000 mg/kg/day (based on body weight, organ weights)
NOAEL (maternal toxicity) = 200 mg/kg/day
LOAEL (developmental toxicity) = 1000 mg/kg/day (based on increases in fetal malformations and reduced fetal weights)
NOAEL (developmental toxicity) = 200 mg/kg/day

1,2-benzenedicarboxylic acid, diisooctyl ester (DIOP, CASRN 27554-26-3)
The developmental toxicity study reported in the CASRN 27554-26-3 robust summary is a CASRN 117-81-7 study (see above).

1,2-benzenedicarboxylic acid, dioctyl ester (DnOP, CASRN 117-84-0)
CD-1 mice (50 females/dose) were administered CASRN 117-84-0 on gestation days 6 through 13 via gavage at doses of 0 or 9780 mg/kg/day. No treatment-related effects were observed in the number of live births per litter, pup weight gains, survival, number of live births, number of viable litters and total litter weight. NOAELs/LOAELs cannot be determined from this study because: (1) there was only one dose; (2) appropriate analyses for teratologic effects were not performed; and (3) specific information on the effects (including incidence) were not reported.

1,2-benzenedicarboxylic acid, di-C_{8-10}-branched alkyl esters, C_9-rich (DINP, CASRN 68515-48-0, supporting chemical)
Crl:CDBR rats (unknown number of females/dose) were administered CASRN 68515-48-0 on gestation days 6 through 15 via gavage at doses of 0, 100, 500 or 1000 mg/kg/day. No details on methodology or results were provided except that the highest dose level reduced maternal weight gains and increased the incidence of developmental variations.
LOAEL (maternal toxicity) = 1000 mg/kg/day (based on reduced weight gain)
NOAEL (maternal toxicity) = 500 mg/kg/day
LOAEL (developmental toxicity) = 1000 mg/kg/day (based on developmental variations)
NOAEL (developmental toxicity) = 500 mg/kg/day

1,2-benzenedicarboxylic acid, di-C_{9-11} branched and linear alkyl esters (911P, CASRN 68515-43-5)
Sprague-Dawley rats (unknown number/sex/dose) were administered CASRN 68515-43-5 on gestation days 1 through 19 via gavage at doses of 0, 250, 500 or 1000 mg/kg/day. An increased incidence of dilated renal

pelvis was observed in the 1000 mg/kg/day group. There were no differences in body weight, reproductive organs, litter size, placental weights or fetal survival between any treatment groups and the prospective control groups at any time during gestation. Skeletal and visceral variations were observed at the 500 and 1000 mg/kg/day groups.
LOAEL (maternal toxicity) = Not established
NOAEL (maternal toxicity) = 1000 mg/kg/day
LOAEL (developmental toxicity) = 500 mg/kg/day (based on skeletal and visceral variations)
NOAEL (developmental toxicity) = 250 mg/kg/day

1,2-benzenedicarboxylic acid, di-C_{9-11}-branched alkyl esters, C_{10}-rich (DIDP, CASRN 68515-49-1, supporting chemical)
Sprague-Dawley rats (unknown number per sex/dose) were administered 1,2-benzenedicarboxylic acid di-C9, C10 and C-11 branched alkyl ester, C10 rich on gestation days 6 through 15 via gavage at doses of 0, 0, 100, 500 or 1000 mg/kg/day. Body weight and food consumption were reduced at > 500 mg/kg/day. There were no effects on fetal toxicity.
LOAEL (maternal toxicity) = 1000 mg/kg/day (based on body weight)
NOAEL (maternal toxicity) = 500 mg/kg/day
LOAEL (developmental toxicity) = Not established
NOAEL (developmental toxicity) = 1000 mg/kg/day

1,2-benzenedicarboxylic acid, ditridecyl ester (DTP, CASRN 119-06-2, supporting chemical)
In the combined repeated-dose/reproductive/developmental toxicity screening test described previously (p. 28), a decrease in live birth index on PND 0 was observed in the high-dose group. Viability of neonates on PND 4 was decreased in the high-dose group. Maternal effects included body weight gain decreases in the high-dose group and increased liver:body weight ratios in the 50 and 250 mg/kg/day group. There were no adverse histopathologic findings, no effects on copulation or fertility and no effects on offspring sex ratio, body weight changes and morphological changes.
LOAEL (maternal toxicity) = 50 mg/kg/day (based on histopathology, organ weights)
NOAEL (maternal toxicity) = 10 mg/kg/day
LOAEL (developmental toxicity) = Not established
NOAEL (developmental toxicity) = 250 mg/kg/day

1,2-benzenedicarboxylic acid, butyl phenylmethyl ester (BBP, CASRN 85-68-7, supporting chemical)
CD-1 mice (14-18/sex/dose) were administered CASRN 85-68-7 from gestation day 6 through gestation day 15 via oral feed at doses of 0, 0.1, 0.5, 1.25 or 2.0% in the diet (0, 182, 910, 2330 or 4120 mg/kg/day). The following maternal effects were seen in all the treated animals except the low dose group: decreased body weight and increased liver and kidney weights. In addition, all litters from dams in the highest dose group were resorbed. The following embryo/fetal effects were observed in the 910 and 2330 mg/kg/day dose groups: increased resorptions, decreased litter size, reduced body weights and malformations (no specifics provided).
LOAEL (maternal toxicity) = 910 mg/kg/day (based on body weights, organ weights)
NOAEL (maternal toxicity) = 182 mg/kg/day
LOAEL (developmental toxicity) = 910 mg/kg/day (based on fetal survival)
NOAEL (developmental toxicity) = 182 mg/kg/day

In vitro

Subcategory I: Low Molecular Weight Phthalate Esters

1,2-Benzenedicarboxylic acid, dimethyl ester (DMP, CASRN 131-11-3)
CASRN 131-11-3 was tested in several *Salmonella* strains (TA98, TA100, TA1535 and TA1537) at concentrations of 0, 33, 100, 333, 1000, 2166, 3000, 333, 5000 or 6666 mg/plate, with and without metabolic activation. Both positive and negative controls were run. No mutagenic activity was observed. Control responses were not provided.
CASRN 131-11-3 was not mutagenic in this assay.

1,2-Benzenedicarboxylic acid, diethyl ester (DEP, CASRN 84-66-2)
(1) CASRN 84-66-2 was tested in several *Salmonella* strains (TA98, TA100, TA1535 and TA1537) at concentrations between 0 and 10 mg/plate, with and without metabolic activation. Both positive and negative controls were run. No mutagenic activity was observed. Control responses were not provided.
CASRN 84-66-2 was not mutagenic in this assay.

(2) CASRN 84-66-2 was tested in several *Salmonella* strains (TA98, TA100, TA1535 and TA1537) and *Escherichia coli* at concentrations between 20 and 5000 µg/plate, with and without metabolic activation. Positive and negative controls were used. No mutagenic activity was observed. Control responses responded appropriately (http://www.srcinc.com/what-we-do/databaseforms.aspx?id=384).
CASRN 84-66-2 was not mutagenic in this assay.

Subcategory II: Transitional Phthalate Esters

1,2-benzenedicarboxylic acid, dihexyl ester (DnHP, CASRN 84-75-3, supporting chemical)
CASRN 84-75-3 was tested in several *Salmonella* strains (TA98, TA100, TA1535 and TA1537) at five concentrations (not specified) between 0 and 10 mg/plate, with and without metabolic activation. Both positive and negative controls were run. No mutagenic activity was observed. Control responses were not provided.
CASRN 84-75-3 was not mutagenic in this assay.

Subcategory III: High Molecular Weight Phthalate Esters

1,2-benzenedicarboxylic acid, di-C_{6-8} branched alkyl ester, C_7 rich (DIHP, CASRN 71888-89-6)
CASRN 71888-89-6 was tested in several *Salmonella* strains (TA98, TA100, TA1535, TA1537and TA1538) at concentrations of 250, 500, 1000, 2500 or 5000 mg/mL, with and without metabolic activation. Both positive and negative controls were run. No mutagenic activity was observed. Control responses were not provided.
CASRN 71888-89-6 was not mutagenic in this assay.

1,2-benzenedicarboxylic acid, bis(2-ethylhexyl) ester (DEHP, CASRN 117-81-7; supporting chemical)
Thirty robust summaries identifying in vitro genetic toxicity studies are provided in the dossier submitted by the sponsor. Most of them are in German but still do not provide much information beyond the results. In this case, since CASRN 117-81-7 is a supporting chemical, EPA will rely on the 2002 ATSDR Toxicological Profile summary which concludes that CASRN 117-81-7 is likely not mutagenic or genotoxic (see http://www.atsdr.cdc.gov/toxprofiles/tp9.html)

1,2-benzenedicarboxylic acid, heptyl undecyl ester, branched and linear (711P, CASRN 111381-90-9)

CASRN 111381-90-9 was tested in mouse lymphoma cells at concentrations ranging from 0.125 to 6.0 µL/m, with and without metabolic activation. Both positive and negative controls were run. Concentrations of 0.75 – 6 µL/mL induced moderate to high toxicity, but only a slight increase in mutation frequency. Control responses were not provided.

CASRN 111381-90-9 was not mutagenic in this assay.

1,2-benzenedicarboxylic acid, diisooctyl ester (DIOP, CASRN 27554-26-3)

(1) CASRN 27554-26-3 was tested in several *Salmonella* strains at concentrations of 10, 100, 1000 or 2000 µg/plate, with and without metabolic activation. Both positive and negative controls were run. No mutagenic activity was observed. Control responses were not provided.

CASRN 27554-26-3 was not mutagenic in this assay.

(2) CASRN 27554-26-3 was tested in several *Salmonella* strains (TA98, TA100, TA1535 and TA1537), with and without metabolic activation. Positive and negative controls were used. No mutagenic activity was observed. Control responses responded appropriately (http://www.srcinc.com/what-we-do/databaseforms.aspx?id=384).

CASRN 27554-26-3 was not mutagenic in this assay.

1,2-benzenedicarboxylic acid, dioctyl ester (DnOP, CASRN 117-84-0)

CASRN 117-84-0 was tested in several *Salmonella* strains (TA98, TA100, TA1535 and TA1537) at concentrations ranging from 0 to 10 mg/plate, with and without metabolic activation. Both positive and negative controls were run. No mutagenic activity was observed. Control responses were not provided.

CASRN 117-84-0 was not mutagenic in this assay.

1,2-benzenedicarboxylic acid, dinonyl ester, branched and linear (DNP, CASRN 68515-45-7)

The robust summary presents a study with CASRN 111381-90-9 (the mouse lymphoma cell study summarized above under CASRN 111381-90-9).

1,2-benzenedicarboxylic acid, di-C_{8-10}-branched alkyl esters, C_9-rich (DINP, CASRN 68515-48-0, supporting chemical)

(1) 1,2-Benzenedicarboxylic acid, di-C8 – C10 branched alkyl esters, C9 rich was tested in several *Salmonella* strains (TA98, TA100, TA1535, TA1537 and TA1538) at concentrations of 0.5 – 5000 µg/plate, with and without metabolic activation. No other details were provided.

CASRN 68515-48-0 was not mutagenic in this assay.

(2) 1,2-Benzenedicarboxylic acid, di-C8 – C10 branched alkyl esters, C9 rich was tested in Chinese hamster ovary (CHO) cells at concentrations of 5 – 160 µg/mL, with and without metabolic activation. No other details were provided.

CASRN 68515-48-0 was not mutagenic in this assay.

(3) In 2 assays, a mixture of commercial CASRN 68515-48-0s tested in mouse lymphoma cells at concentrations of 500 – 10,000 nL/mL, with and without metabolic activation. No other details were provided.

Mixture of commercial CASRN 68515-48-0s was not mutagenic in this assay.

1,2-benzenedicarboxylic acid, di-C_{9-11}-branched alkyl esters, C_{10}-rich (DIDP, CASRN 68515-49-1, supporting chemical)

(1) CASRN 68515-49-1 was tested in several *Salmonella* strains (TA100, TA1535 and TA1537) at concentrations between 0 and 10,000 µg/plate, with and without metabolic activation. Positive and negative controls were used. No mutagenic activity was observed. Control responses were not provided.
CASRN 68515-49-1 was not mutagenic in this assay.

(2) CASRN 68515-49-1 was tested in mouse lymphoma cells at concentrations between 0.25 and 10 µL/mL, with and without metabolic activation. Positive and negative controls were used. No mutagenic activity was observed. Control responses were not provided.
CASRN 68515-49-1 was not mutagenic in this assay.

1,2-benzenedicarboxylic acid, diundecyl ester (DUP, CASRN 3648-20-2)

CASRN 3648-20-2 was tested in *Salmonella* strains TA98, TA100, TA1535; and TA 1537 at five concentrations (not specified) up to 10 mg/plate, with and without metabolic activation. Positive and negative controls were used in the study. Results indicated no increase in the number of revertant colonies for any test strain.
CASRN 3648-20-2 was not mutagenic in this assay.

1,2-benzenedicarboxylic acid, di-C_{11-14} branched alkyl esters, C_{13} rich (DTDP, CASRN 68515-47-9)

CASRN 68515-47-9 was tested in several *Salmonella* strains (TA98, TA100, TA1535 and TA1537) at concentrations between 0 and 10 mg/plate, with and without metabolic activation. Both positive and negative controls were run. No mutagenic activity was observed. Control responses were not provided.
CASRN 68515-47-9 was not mutagenic in this assay.

1,2-benzenedicarboxylic acid, ditridecyl ester (DTP, CASRN 119-06-2, supporting chemical)

(1) CASRN 119-06-2 was tested in several *Salmonella* strains (TA100, TA1535, TA1537 and TA1538) at concentrations between 0 and 5000 µg/plate, with and without metabolic activation. Positive and negative controls were used. No mutagenic activity was observed. Control responses were not provided.
CASRN 119-06-2 was not mutagenic in this assay.

(2) In a reverse mutation assay, CASRN 119-06-2 was tested in *Escherichia coli* WP2 uvrA at concentrations between 0 and 5000 µg/plate, with and without metabolic activation. Positive and negative controls were used. No mutagenic activity was observed. Control responses were not provided.
CASRN 119-06-2 was not mutagenic in this assay.

1,2-benzenedicarboxylic acid, benzyl C_{7-9} branched and linear alkyl esters (B79P, CAS No. 68515-40-2)

CASRN 68515-40-2 was tested in *Salmonella* strains TA98, TA100, TA1535, TA 1537 and TA 1538 at concentrations of 0.0.1, 0.04, 0.20, 1.0, 3.0 or 10 uL/plate, with and without metabolic activation. Appropriate positive and negative controls were used. Results indicated no increase in the number of revertant colonies for any test strain.
CASRN 68515-40-2 was not mutagenic in this assay.

1,2-benzenedicarboxylic acid, 2,2-dimethyl-1-(1-methylethyl)-3-(2-methyl-1-oxopropoxy) propyl phenylmethyl ester (B84P, CASRN 16883-83-3)

CASRN 16883-83-3 was tested in several *Salmonella* strains (TA98, TA100, TA1535, TA1537 and TA 1538) at concentrations of 0.01, 0.04, 0.2, 1.0, 3.0 or 10.0 µg/plate, with and without metabolic activation. Both positive and negative controls were run. No mutagenic activity was observed. Control responses were not provided.

CASRN 16883-83-3 was not mutagenic in this assay.

1,2-benzenedicarboxylic acid, butyl phenylmethyl ester (BBP, CASRN 85-68-7, supporting chemical)
The robust summaries submitted for CASRN 85-68-7 provided three in vitro mutagenicity tests with CASRN 131-11-3 – which is a member of Subcategory I and thus not appropriate for read-across to Subcategory IV phthalate esters. However, there are several reported assays on the NTP website in which CASRN 85-68-7 was tested in the Ames assay and in an in vitro mouse lymphoma cell assay. CASRN 85-68-7 was not mutagenic in either assay (http://ntp-apps.niehs.nih.gov/ntp_tox/index.cfm?fuseaction=ntpsearch.searchresults&searchterm=85-68-7).
CASRN 85-68-7 was not mutagenic in either assay.

Genetic Toxicity – Chromosomal Aberrations

In vitro

Subcategory I: Low Molecular Weight Phthalate Esters

1,2-Benzenedicarboxylic acid, dimethyl ester (DMP, CAS No. 131-11-3)
In a study by the National Toxicology Program (NTP), Chinese hamster ovary (CHO) cells were exposed to CASRN 131-11-3 at concentrations ranging from 150 ug/mL to 5100 ug/mL under various conditions (with and without metabolic activation and at various incubation times). Not all concentrations were used for every exposure scenario. Appropriate positive and negative controls were used. There was no induction of chromosomal aberrations in CHO cells from CASRN 131-11-3 exposures, with or without metabolic activation.
CASRN 131-11-3 did not induce chromosomal aberrations (with or without metabolic activation) in this assay.

1,2-Benzenedicarboxylic acid, diethyl ester (DEP, CAS No. 84-66-2)
In a study by the National Toxicology Program (NTP), Chinese hamster ovary (CHO) cells were exposed to CASRN 84-66-2 at concentrations of 70, 151, 324, 698 or 1500 ug/mL (NOTE: units incorrectly listed in the robust summary) under various conditions (with and without metabolic activation and at various incubation times). Not all concentrations were used for every exposure scenario. Appropriate positive and negative controls were used. Cytotoxicity was observed at the top two doses. There was no induction of chromosomal aberrations in CHO cells from CASRN 84-66-2 exposures, with or without metabolic activation.
CASRN 84-66-2 did not induce chromosomal aberrations (with or without metabolic activation) in this assay.

Subcategory II: Transitional Phthalate Esters

No data were available.

Subcategory III: High Molecular Weight Phthalate Esters

1,2-benzenedicarboxylic acid, di-C_{6-8} branched alkyl ester, C_7 rich (DIHP, CASRN 71888-89-6)
A chromosomal aberration test was evaluated in CHO cells following exposure to CASRN 71888-89-6 at concentrations of 499, 1250, 2500, 3750 or 4990 mg/mL with and without metabolic activation. No induction of chromosomal aberrations was observed in CHO cells with or without metabolic activation.
CASRN 71888-89-6 did not induce chromosomal aberrations in this assay.

1,2-benzenedicarboxylic acid, bis(2-ethylhexyl) ester (DEHP, CASRN 117-81-7; supporting chemical)

Thirty robust summaries identifying in vitro genetic toxicity studies are provided in the dossier submitted by the sponsor. Most of them are in German but still do not provide much information beyond the results. In this case, since CASRN 117-81-7 is a supporting chemical, EPA will rely on the 2002 ATSDR Toxicological Profile summary which concludes that CASRN 117-81-7 is likely not mutagenic or genotoxic (see http://www.atsdr.cdc.gov/toxprofiles/tp9.html)

1,2-benzenedicarboxylic acid, di-C_{8-10}-branched alkyl esters, C_9-rich *(DINP, CASRN 28553-12-0/68515-48-0; supporting chemical)*

In a mammalian cell in vitro test, Chinese hamster ovary cells (CHO) were exposed to CASRN 68515-48-0 at concentrations ranging from 5 to 160 ug/mL, both with and without activation. No other details were provided in the robust summary except the results (negative).

CASRN 68515-48-0 did not induce chromosomal aberrations (with or without metabolic activation) in this assay.

1,2-benzenedicarboxylic acid, ditridecyl ester (DTP, CASRN 119-06-2, supporting chemical)

A chromosomal aberration test was evaluated in CHO cells following exposure to CASRN 119-06-2 at concentrations ranging from 1188 to 4750 µg/mL with and without metabolic activation. No induction of chromosomal aberrations was observed in CHO cells with or without metabolic activation.

CASRN 119-06-2 did not induce chromosomal aberrations in this assay.

1,2-benzenedicarboxylic acid, butyl phenylmethyl ester (BBP, CASRN 85-68-7; supporting chemical)

Again, a CASRN 131-11-3 study was reported for this endpoint in the CASRN 85-68-7 robust summaries. However, details of a CASRN 85-68-7 CHO/chromosomal aberration assay was found on the NTP website which had negative results (http://ntp-apps.niehs.nih.gov/ntp_tox/index.cfm?fuseaction=ntpsearch.searchresults&searchterm=85-68-7).

CASRN 85-68-7 did not induce chromosomal aberrations (with or without metabolic activation) in this assay.

In vivo

Subcategory I: Low Molecular Weight Phthalate Esters

1,2-Benzenedicarboxylic acid, dimethyl ester (DMP, CAS No. 131-11-3)

In another NTP study (http://ntp-apps.niehs.nih.gov/ntp_tox/index.cfm?fuseaction=micronucleus.micronucleusData&current%5Fstrain%5Fid=B6C3F1&endpointlist=MN&cas%5Fno=131%2D11%2D3&study%5Fno=A47213&activetab=detail) not provided in the HPV Submission, male B6C3F1 mice were given the following doses of CASRN 131-11-3 via intraperitoneal injection daily for three days: 0, 750, 1500, 2250 and 3000 mg/kg/day. Blood cells were harvested 24 hours after the last dose and assessed for the presence of micronuclei. Appropriate positive and negative controls were used. There was no increase in micronuclei from CASRN 131-11-3 exposure in this assay.

CASRN 131-11-3 was negative for micronuclei induction in this assay.

Subcategory II: Transitional Phthalate Esters

1,2-Benzenedicarboxylic acid, dihexyl ester, branched and linear (DHP, CASRN 68515-50-4)
In a mammalian erythrocyte micronucleus assay, CASRN 68515-50-4 was tested in CD-1 mice (15/sex/dose) at concentrations of 0, 1250, 2500 or 5000 mg/kg/day administered by gavage. CASRN 68515-50-4 did not induce an increase in bone marrow micronucleated polychromatic erythrocytes in male or female mice and was considered negative in this assay.
CASRN 68515-50-4 did not induce micronuclei in this assay.

Subcategory III: High Molecular Weight Phthalate Esters

1,2-benzenedicarboxylic acid, bis(2-ethylhexyl) ester (DEHP, CASRN 117-81-7; supporting chemical)
Fifteen robust summaries identifying in vivo genetic toxicity studies are provided in the dossier submitted by the sponsor. Most of them are in German but still do not provide much information beyond the results. In this case, since CASRN 117-81-7 is a supporting chemical, EPA will rely on the 2002 ATSDR Toxicological Profile summary which concludes that CASRN 117-81-7 is likely not mutagenic or genotoxic (see http://www.atsdr.cdc.gov/toxprofiles/tp9.html)

1,2-benzenedicarboxylic acid, di-C_{8-10}-branched alkyl esters, C_9-rich *(DINP, CASRN 68515-48-0, supporting chemical)*
In a mammalian bone marrow micronucleus assay, CASRN 68515-48-0 was tested in CD-1 mice at concentrations of 0, 500, 1000 or 2000 mg/kg/day administered by gavage. The test substance did not induce an increase in bone marrow micronucleated polychromatic erythrocytes in male or female mice and was considered negative in this assay.
CASRN 68515-48-0 did not induce micronuclei in this assay.

1,2-benzenedicarboxylic acid, di-C_{9-11}-branched alkyl esters, C_{10}-rich (DIDP, CASRN 68515-49-1, supporting chemical)
A micronucleus assay was performed for CASRN 68515-49-1 in CD-1 mice at concentrations of 0, 1250, 2500 or 5000 mg/kg/day administered by gavage. 1,2-benzenedicarboxylic acid, di-C9, C10 and C-11 branched alkyl ester, C10 rich did not induce differences between treatment groups and controls.
CASRN 68515-49-1 did not induce chromosomal aberrations in this assay.

1,2-benzenedicarboxylic acid, butyl phenylmethyl ester (BBP, CAS No. 85-68-7; supporting chemical)
Although not reported in the HPV submission, the NTP reported two in vivo genotoxicity experiments with CASRN 85-68-7 (both found at http://ntp-apps.niehs.nih.gov/ntp_tox/index.cfm?fuseaction=ntpsearch.searchresults&searchterm=85-68-7):

(1) In a mouse micronucleus test, male B6C3F1 mice given intraperitoneal injections of up to 2500 mg/kg-bw showed no increases in micronuclei of bone marrow cells.
CASRN 85-68-7 was negative for micronuclei induction in this assay.

(2) In a mouse bone marrow cytogenetics test examining chromosomal aberrations, male B6C3F1 mice were given single intraperitoneal injections of up to 5000 mg/kg-bw. Two of the three trials were positive for an increase in the percent of harvested cells with aberrations.
CASRN 85-68-7 was positive for chromosomal aberrations in this assay.

In vitro/In vivo

Subcategory I: Low Molecular Weight Phthalate Esters

1,2-Benzenedicarboxylic acid, dimethyl ester (DMP, CAS No. 131-11-3)
In an NTP study (http://ntp-apps.niehs.nih.gov/ntp_tox/index.cfm?fuseaction=invitrosce.scedata&study_no=970550&cas_no=131%2D11%2D3&endpointlist=SCE) not provided in the HPV Submission, Chinese hamster ovary (CHO) cells were exposed to CASRN 131-11-3 at concentrations ranging from 50 ug/L to 1510 ug/mL without metabolic activation (one test) and from 151 to 5010 ug/mL with metabolic activation (three separate tests) to assess the induction of sister chromatid exchange (SCE). Appropriate positive and negative controls were used. There was no induction of SCEs in the no activation test and the results of the three activation tests were questionable, weak positive, and positive.
CASRN 131-11-3 did not induce SCEs without metabolic activation, but was overall positive for SCE induction following metabolic activation in this assay.

1,2-Benzenedicarboxylic acid, diethyl ester (DEP, CAS No. 84-66-2)
In an NTP study (http://ntp-apps.niehs.nih.gov/ntp_tox/index.cfm?fuseaction=invitrosce.scedata&study_no=913646&cas_no=84%2D66%2D2&endpointlist=SCE) not provided in the HPV Submission, Chinese hamster ovary (CHO) cells were exposed to CASRN 84-66-2 at concentrations ranging from 5 ug/mL to 500 ug/mL without metabolic activation (one test) and from 50 to 1667 ug/mL with metabolic activation (three separate tests) to assess the induction of sister chromatid exchange (SCE). Appropriate positive and negative controls were used. There was no induction of SCEs in the no activation test and the results of the three activation tests were positive.
CASRN 84-66-2 did not induce SCEs without metabolic activation, but was positive for SCE induction following metabolic activation in this assay.

Subcategory II: Transitional Phthalate Esters

No data

Subcategory III: High Molecular Weight Phthalate Esters

1,2-benzenedicarboxylic acid, bis(2-ethylhexyl) ester (DEHP, CASRN 117-81-7; supporting chemical)
Many robust summaries identifying other genetic toxicity studies are provided in the dossier submitted by the sponsor. Most of them are in German but still do not provide much information beyond the results. In this case, since CASRN 117-81-7 is a supporting chemical, EPA will rely on the 2002 ATSDR Toxicological Profile summary which concludes that CASRN 117-81-7 is likely not mutagenic or genotoxic (see http://www.atsdr.cdc.gov/toxprofiles/tp9.html)

1,2-benzenedicarboxylic acid, butyl phenylmethyl ester (BBP, CAS No. 85-68-7; supporting chemical)
Although not reported in the HPV submission, the NTP reported two other genotoxicity experiments with CASRN 85-68-7 (found at http://ntp-apps.niehs.nih.gov/ntp_tox/index.cfm?fuseaction=ntpsearch.searchresults&searchterm=85-68-7):

(1) Chinese hamster ovary (CHO) cells were exposed to CASRN 85-68-7 at concentrations ranging from 0.4 ug/mL to 12.5 ug/mL without metabolic activation (two tests) and from 125 to 1250 ug/mL with metabolic

activation (one test) to assess the induction of sister chromatid exchange (SCE). Appropriate positive and negative controls were used. There was no induction of SCEs in the activation test and the results of the two no activation tests were questionable and negative.
CASRN 85-68-7 did not induce SCEs with or without metabolic activation in this assay.

(2) In an in vivo mouse bone marrow cytogenetics test examining sister chromatid exchanges, male B6C3F1 mice were given single intraperitoneal injections of up to 5000 mg/kg-bw. Two trials were done and both were positive for an increase in the mean number of SCEs/cell; however, the response was not dose-related.
CASRN 85-68-7 was positive for chromosomal aberrations in this assay.

Additional Information (Eye Irritation, Skin Irritation, Sensitization, Carcinogenicity)

Skin Irritation

Subcategory I: Low Molecular Weight Phthalate Esters

1,2-Benzenedicarboxylic acid, diethyl ester (DEP, CASRN 84-66-2)
Although not reported in the HPV submission, according to the EPA Office of Pesticide Program (OPP) inert reassessment for CASRN 84-66-2 (found at http://www.epa.gov/opprd001/inerts/lists.html), the chemical is reported to cause mild or slight skin irritation in the rabbit (as presented in Table 4 of the inerts document).

Subcategory III: High Molecular Weight Phthalate Esters

1,2-benzenedicarboxylic acid, di-C_{7-9} branched and linear alkyl esters (in79P CASRN 68515-41-3, supporting chemical)
New Zealand White rabbits (number unspecified) were administered 1 ml of undiluted CASRN 68515-41-3 to intact skin under unspecified conditions daily for 3 days and observed for 7 days.
CASRN 68515-41-3 was not irritating to rabbit skin in this assay.

1,2-benzenedicarboxylic acid, 2,2-dimethyl-1-(1-methylethyl)-3-(2-methyl-1-oxopropoxy) propyl phenylmethyl ester (B84P, CASRN 16883-83-3)
New Zealand rabbits (3/sex) were administered an unspecified amount of undiluted CASRN 16883-83-3 to intact skin under occluded conditions for 24 hours and observed for 7 days. The dermal reaction was scored by the method of Draize.
CASRN 16883-83-3 was not irritating to rabbit skin in this assay.

Eye Irritation

Subcategory I: Low Molecular Weight Phthalate Esters

1,2-Benzenedicarboxylic acid, diethyl ester (DEP, CASRN 84-66-2)
Although not reported in the HPV submission, according to the EPA Office of Pesticide Program (OPP) inert reassessment for CASRN 84-66-2 (found at http://www.epa.gov/opprd001/inerts/lists.html), the chemical is reported to cause minimal eye irritation in the rabbit (as presented in Table 4 of the inerts document).

1,2-benzenedicarboxylic acid, di-C_{6-8} branched alkyl ester, C_7 rich (DIHP, CASRN 71888-89-6)
Six New Zealand White rabbits were administered 0.1 ml CASRN 71888-89-6 into the lower conjunctive sac of the right eye and observed at 1, 4 24 and 72 hours and 4 and 7 days.
Eye irritation was scored according to the method of Draize (http://www.srcinc.com/what-we-do/databaseforms.aspx?id=384).
CASRN 71888-89-6 was not irritating to rabbit eyes in this assay.

1,2-benzenedicarboxylic acid, 2,2-dimethyl-1-(1-methylethyl)-3-(2-methyl-1-oxopropoxy) propyl phenylmethyl ester (B84P, CASRN 16883-83-3)
New Zealand rabbits (3/sex) were administered 0.1 ml of 1,2-benzenedicarboxylic acid, benzyl 3-hydroxy-1-isopropyl-2,2-dimethylpropyl ester isobutyrate into the conjunctival sac for 24 hours and observed at 1 hour and 7 days. The ocular reaction was scored by the method of Draize.
CASRN 16883-83-3 was slightly irritating to rabbit eyes in this assay.

Carcinogenicity

1,2-Benzenedicarboxylic acid, dimethyl ester (DMP, CAS No. 131-11-3) and 1,2-Benzenedicarboxylic acid, diethyl ester (DEP, CAS No. 84-66-2)
In a one-year cancer study in 50 male Swiss (CD-1) mice by the NTP, CASRN 131-11-3 and CASRN 84-66-2 were both assessed for the ability to be either a cancer initiator or promoter (not provided by submitter, available at http://ntp-apps.niehs.nih.gov/ntp_tox/index.cfm?fuseaction=abstracts.abstract&chemical_name=Diethyl%20phthalate/dimethyl%20phthalate&cas_no=DIETH/DIMETH&study_no=C55914&study_length=2%20Years&abstract_url=0709D9F1-03F8-85B0-C5ADABDB95AC61F6&next=longtermbioassaydata.datasearch) . Animals were dosed dermally (number and dose level not provided). The NTP concluded that neither CASRN 131-11-3 nor CASRN 84-66-2 acted as either initiators or promoters in this test.
CASRN 131-11-3 and CASRN 84-66-2 were negative for cancer initiation/promotion activity in this assay.

1,2-Benzenedicarboxylic acid, diethyl ester (DEP, CAS No. 84-66-2)
The NTP conducted two-year dermal cancer bioassays with CASRN 84-66-2 in both rats and mice which were not reported in the HPV submission and are available at http://ntp-apps.niehs.nih.gov/ntp_tox/index.cfm?fuseaction=abstracts.abstract&chemical_name=Diethyl%20phthalate&cas_no=84-66-2&study_no=C60048B&study_length=2%20Years&abstract_url=0709D9F1-03F8-85B0-C5ADABDB95AC61F6&next=longtermbioassaydata.datasearch . Sixty male and female rats (F344/N) and the same number of mice (B6C3F1) were dosed via the dermal route five days/week with doses of 0, 100, or 300 uL (rats, equivalent to approximately 400 and 1200 mg/kg/day, respectively) or 0, 7.5, 15, or 30 uL (mice, equivalent to approximately 350, 700, and 1400 mg/kg/day, respectively). The NTP concluded there was no evidence of carcinogenic activity in male or female rats, although the sensitivity for detection in the males was reduced due to low survival in all groups. The NTP concluded there was equivocal evidence of carcinogenic activity in male and female mice based on an increased incidence of liver cancer (primarily benign adenomas).
CASRN 84-66-2 was negative for carcinogenicity in rats and equivocal for carcinogenicity in mice in these NTP bioassays.

1,2-benzenedicarboxylic acid, bis(2-ethylhexyl) ester (DEHP, CAS No. 117-81-7; supporting chemical)
A number of studies are in the NTP database **(http://ntp-apps.niehs.nih.gov/ntp_tox/index.cfm?fuseaction=ntpsearch.searchresults&searchterm=117-81-7**) the evidence shows that CASRN 117-81-7 is a rodent carcinogen (see ATSDR conclusion at http://www.atsdr.cdc.gov/toxprofiles/tp9.html)
CASRN 117-81-7 was found to be positive for carcinogenicity in both rats and mice.

1,2-benzenedicarboxylic acid, butyl phenylmethyl ester (BBP, CAS No. 85-68-7; supporting chemical)
A number of studies are in the NTP database (http://ntp-apps.niehs.nih.gov/ntp_tox/index.cfm?fuseaction=ntpsearch.searchresults&searchterm=85-68-7) and the NTP has concluded that CASRN 85-68-7 is a carcinogen in rats but not mice.
CASRN 85-68-7 was found to be positive for carcinogenicity in rats (some evidence in males and equivocal evidence in females) and was negative for carcinogenicity in mice.

Conclusions:

Subcategory I: Low Molecular Weight Phthalate Esters (CASRNs 131-11-3 and 84-66-2)

The acute oral (rats and mice), dermal (guinea pigs) and inhalation (rats) toxicity of low molecular weight phthalate esters in animal studies is low. Oral repeated-dose and reproductive toxicity data in rats and mice are available for CASRN 84-66-2 and show effects at 750 mg/kg/day (decreases in body weight) and 3250 mg/kg/day (reduced litter size), respectively. The NOAELs for these studies were 150 mg/kg/day and 1625 mg/kg/day, respectively. These data may also reasonably represent CASRN 131-11-3. Prenatal developmental toxicity data in rats are available for both members of this subcategory. Maternal toxicity is seen at oral (dietary) doses of 1910 mg/kg/day (CASRN 84-66-2, decreased body weight) and 3570 mg/kg/day (CASRN 131-11-3, decreased body weight and kidney effects), with the NOAELs of 200 and 840 mg/kg/day, respectively. There are no developmental effects following exposure to CASRN 131-11-3 (highest dose of 3570 mg/kg/day) and skeletal variations are observed at the highest tested dose of CASRN 84-66-2 (3210 mg/kg/day). Both members of the low molecular weight phthalate esters category are not mutagenic when tested *in vitro* in bacteria and do not induce chromosomal aberrations when tested *in vitro.* CASRN 84-66-2 is not a skin or eye irritant in rabbits. Both CASRN 131-11-3 and CASRN 84-66-2 are negative in one-year initiation/promotion cancer studies (dermal route of exposure) in mice. The NTP reported negative results in rats and equivocal results in mice in separate two-year dermal cancer studies with CASRN 84-66-2.

Subcategory II: Transitional Phthalate Esters (CASRN 68515-50-4)

The acute oral and dermal toxicity of CASRN 68515-50-4 in rats and rabbits, respectively, is low. Available repeated-dose toxicity studies with CASRN 68515-50-4 show increased heart weights at 76.6 mg/kg/day (highest tested dose in rats) and changes in body, liver and testes weights at 900 mg/kg/day (highested tested dose in dogs). Reproductive toxicity data exist for the supporting compound CASRN 84-75-3 (decreased pregnancy rates, fetal survival and testicular effects all at the highest tested dose of 430 mg/kg/day). There are no prenatal developmental toxicity data with either CASRN 68515-50-4 or the supporting chemical CASRN 84-75-3; however available data exist for phthalate esters that fall within the boundaries of this subcategory (i.e., dibutyl phthalate and dipentyl phthalate; CASRNs 84-74-2 and 131-18-0, respectively). Both of these phthalate esters are known to cause male reproductive tract abnormalities following neonatal and early postnatal exposures (known as the phthalate syndrome). CASRN 68515-50-4 is not mutagenic when tested in bacteria *in vitro* and has not induced chromosomal aberrations when tested *in vitro* in mammalian cell lines.

Subcategory III: High Molecular Weight Phthalate Esters (CASRNs 68515-44-6, 71888-89-6, 111381-89-6, 27554-26-3, 117-84-0,111381-90-9, 68515-45-7, 68515-43-5, 84-77-5, 111381-91-0, 16883-83-3, 3648-20-2, 85507-79-5, 68515-40-2, 68648-93-1 and 68515-47-9)

Acute oral toxicity data in rats and mice are available for 4/16 sponsored members and for 5/6 supporting data and all show a low order of toxicity. Dermal acute toxicity data in rabbits are available for 4/16 sponsored members and 4/6 supporting members, again showing low toxicity. There is only one acute inhalation study (with a supporting chemical) in rats which also shows a low order of toxicity.

Repeated-dose toxicity data exist for only one (CASRN 117-84-1) of the 16 members of this subcategory; however, there are four different studies in supporting chemicals which are used to read-across to untested sponsored members of this subcategory. The range in doses and effects across the subcategory are from 29 mg/kg/day (sperm effects, CASRN 117-81-7, a supporting chemical) to 381 mg/kg/day (liver and thyroid effects, CASRN 85-68-7). The range in reported NOAELs for these same studies is 5.8 mg/kg/day (CASRN 117-81-7) to 151 mg/kg/day (CASRN 85-68-7). Reproductive toxicity studies (one-generation, two generation, or combined repeated-dose/reproductive/developmental toxicity protocols) are available for two sponsored subcategory members (CASRN 117-84-0 and CASRN 68515-43-5) and data are also available for five supporting chemicals. The range in doses and effects observed are from 140 mg/kg/day (decreased number of litters, live pups per litter, and live pup weights,CASRN 117-81-7, a supporting chemical) to 750 mg/kg/day (decreased pup body weight in both CASRN 68515-41-3 [a supporting chemical] and CASRN 68515-43-5 studies). The range in reported NOAEL values is 14 mg/kg/day (CASRN 117-81-7, supporting chemical) to the highest tested dose in the CASRN 117-84-0 reproductive study (7500 mg/kg/day).

Five prenatal developmental studies in rats with sponsored Subcategory III members exist and there are additional data for all six supporting chemicals. Overall, maternal toxicity is seen at doses of between 50 mg/kg/day (liver effects, CASRN 119-06-2, a supporting chemical) to 1000 mg/kg/day (multiple effects in studies with CASRNs 68515-44-6, 111381-89-6 111381-90-9, 68515-48-0 [a supporting chemical], and 68515-49-1 [a supporting chemical]). The lowest reported NOAEL for maternal toxicity is 10 mg/kg/day (CASRN 119-06-2, supporting chemical). Two studies show no maternal toxicity at the highest dose tested (CASRN 68515-43-5 and CASRN 68515-41-3 [a supporting chemical], both at 1000 mg/kg/day). In 9/11 studies, developmental toxicity is observed (the two for which no developmental toxicity is seen at the highest tested dose of 1000 mg/kg/day are for the two supporting chemicals CASRNs 68515-49-1 and 119-06-2). A variety of developmental effects (most frequently reported are malformations and skeletal variations) are seen in the other nine studies from doses of 91 mg/kg/day (CASRN 117-81-7, a supporting chemical), to 500 mg/kg/day (CASRN 68515-43-5) and from 750 mg/kg/day to 1000 mg/kg/day (CASRNs 85-68-7 [a supporting chemical], 71888-89-6, 68515-44-6, 111381-89-6, 68515-41-3 [a supporting chemical], 111381-90-9, and 68515-48-0 [a supporting chemical]). The lowest reported NOAEL for developmental toxicity is 44 mg/kg/day (CASRN 117-81-7, supporting chemical). Many sponsored subcategory members (and supporting chemicals) are negative for mutagenicity following testing at both the gene and chromosome level.

Assumptions for Read-Across in Table 3

Read across is performed only within a subcategory. Where possible, read-across is done by interpolation. For example, in Table 3b for the repeated-dose endpoint, available data for CASRN 85-68-7 and CASRN 117-81-7 bracket four sponsored chemicals. Thus, the range of possible NOAELs/LOAELs for those four sponsored chemicals is represented by these "bounding substances". Extrapolation is used where such bracketing data does not exist.

Table 4a. Summary of Human Health Data: Subcategories I and II				
	Subcategory I: Low Molecular Weight Phthalate Esters (C_{1-3} Backbone)		**Subcategory II: Transitional Phthalate Esters Subcategory (C_{4-6} Backbone)**	
Endpoints	**CASRN 131-11-3 (C1, 194)**	**CASRN 84-66-2 (C2, 222)**	**CASRN 68515-50-4 (C6, 336)**	**CASRN 84-75-3 (C6, 334; supporting chemical)**
Acute Oral Toxicity LD_{50} (mg/kg-bw)	**6900**	**> 5900**	**>15,800**	**30,000**
Acute Inhalation Toxicity LC_{50} (mg/L)	No Data > 4.64 (RA)	**> 4.64**	–	–
Acute Dermal Toxicity LD_{50} (mg/kg-bw)	**>23,600**	**> 23,600**	**-**	–
Repeated-Dose Toxicity NOAEL/LOAEL Oral (mg/kg/day)	No Data NOAEL = 150 LOAEL = 750 (RA)	**NOAEL = 150** **LOAEL = 750**	**NOAEL = NE** **LOAEL = 76.6**	**-**
Reproductive Toxicity NOAEL/LOAEL Oral (mg/kg/day)	No Data NOAEL = 1625 LOAEL = 3250 (RA)	**NOAEL = 1625** **LOAEL = 3250**	No Data NOAEL = NE LOAEL = 430 (RA)	**NOAEL = NE** **LOAEL = 430**
Developmental Toxicity NOAEL/LOAEL Oral (mg/kg/day) **Maternal Toxicity** **Developmental Toxicity**	**NOAEL = 840** **LOAEL = 3570** **NOAEL = 3570** **LOAEL = NE**	**NOAEL = 200** **LOAEL = 1910** **NOAEL = 1910** **LOAEl = 3210**	Endpoint Met With Other, Non-Submitted Data (see text under Developmental Toxicity)	**-**
Genetic Toxicity – Gene Mutation *In vitro*	**Negative**	**Negative**	**Negative**	**-**
Genetic Toxicity – Chromosomal Effects *In vitro*	**Negative**	**Negative**	–	–
Genetic Toxicity – Chromosomal Effects *In vivo*	**Negative**	No Data Negative (RA)	**Negative**	–
Genetic Toxicity – Other	**Equivocal**	**Equivocal**	**-**	–
Additional Information **Skin Irritation** **Eye Irritation** **Sensitization** **Cancer**	 - - - **Negative**	 **Non-irritating** **Non-irritating** – **Negative (see text)** **Equivocal (see text)**	–	–

Under the CASRN is the carbon chain backbone length and molecular weight. Supporting chemicals are shaded. **Bold = experimental values.** RA=read across. NE=not established. (-) = endpoint not evaluated for this substance.

Table 4b. Summary of Human Health Data: Subcategory III – High Molecular Weight Phthalate Esters: Acute and Repeated-Dose Toxicity Endpoints				
Chemical (Carbon backbone and molecular wt.)	**Acute Oral Toxicity LD_{50} (mg/kg-bw)**	**Acute Dermal Toxicity LD_{50} (mg/kg-bw)**	**Acute Inhalation Toxicity LC_{50} (mg/L)**	**Repeated-Dose Toxicity NOAEL/LOAEL Oral (mg/kg/day)**
CASRN 85-68-7 (C4/ring, 312, supporting chemical)	**2330**	**> 10,000**	-	**NOAEL = 151 LOAEL = 381**
CASRN 68515-44-6 (C7, 364)	No Data >2000 (RA)	No Data >3000 (RA)	No Data 10.6 (RA)	No Data NOAEL=5.8 to 151; LOAEL=29 to 381 (RA)
CASRN 71888-89-6 (C7, 393)	**> 10,000**	**> 3160**	-	No Data NOAEL=5.8 to 151; LOAEL=29 to 381 (RA)
CASRN 111381-89-6 (C7,C9; 391)	No Data >2000 (RA)	No Data >3000 (RA)	No Data 10.6 (RA)	No Data NOAEL=5.8 to 151; LOAEL=29 to 381 (RA)
CASRN 27554-26-3 (C8, 391)	No Data >2000 (RA)	No Data >3000 (RA)	No Data 10.6 (RA)	No Data NOAEL=5.8 to 151; LOAEL=29 to 381 (RA)
CASRN 117-81-7 (C8, 391, supp. chemical)	**6860 – 49,000**	**10,000**	**10.6**	**NOAEL = 5.8 LOAEL = 29**
CASRN 117-84-1 (C8, 391)	**13,000**	-	-	**NOAEL = 39 LOAEL = 377**
CASRN 68515-41-3 (C7, C9; 405, supp. chemical)	**19,300**	-	-	**NOAEL = 60 LOAEL = 120**
CASRN 111381-90-9 (C7, C11; 419)	No Data >2000 (RA)	No Data >3000 (RA)	No Data 10.6 (RA)	No Data NOAEL=10-60; LOAEL=50-120 (RA)
CASRN 68515-48-0 (C9, 419, supporting chemical)	**> 10,000**	**> 3160**	-	-
CASRN 68515-45-7 (C9, 421)	No Data >2000 (RA)	No Data >3000 (RA)	No Data 10.6 (RA)	No Data NOAEL=10-60; LOAEL=50-120 (RA)
CASRN 68515-43-5 (C10, 447)	No Data >2000 (RA)	No Data >3000 (RA)	No Data 10.6 (RA)	No Data NOAEL=10-60; LOAEL=50-120 (RA)
CASRN 84-77-5 (C10, 447)	No Data >2000 (RA)	No Data >3000 (RA)	No Data 10.6 (RA)	No Data NOAEL=10-60; LOAEL=50-120 (RA)
CASRN 68515-49-1 (C10, 447, supporting chemical)	-	**> 3160**	-	-
CASRN 111381-91-0 (C9, C11; 447)	No Data >2000 (RA)	No Data >3000 (RA)	No Data 10.6 (RA)	No Data NOAEL=10-60; LOAEL=50-120 (RA)
CASRN 16883-83-3 (C12, ring; 455)	**> 15,800**	**> 7940**	No Data (RA)	No Data NOAEL=10-60; LOAEL=50-120 (RA)
CASRN 3648-20-2 (C11, 475)	No Data >2000 (RA)	No Data >3000 (RA)	No Data 10.6 (RA)	No Data NOAEL=10-60; LOAEL=50-120 (RA)
CASRN 85507-79-5 (C11, 489)	No Data >2000 (RA)	No Data >3000 (RA)	No Data 10.6 (RA)	No Data NOAEL=10-60; LOAEL=50-120 (RA)
CASRN 119-06-2 (C13, 531, supporting chemical)	**> 2,000**	-	-	**NOAEL = 10 LOAEL = 50**
CASRN 68515-40-2 (C7, C9, ring; 550)	-	**> 7940**	-	No Data NOAEL=10; LOAEL=50 (RA)
CASRN 68648-93-1 (C6, C8, C10; 557)	No Data >2000 (RA)	No Data >3000 (RA)	No Data 10.6 (RA)	No Data NOAEL=10; LOAEL=50 (RA)
CASRN 68515-47-9 (C13, 561)	**> 10,000**	**> 3160**	-	No Data NOAEL=10; LOAEL=50 (RA)

Supporting chemicals are shaded. **Bold = experimental values.** RA=read across. NE=not established. (-) = endpoint not evaluated for this substance.

Table 4c. Summary of Human Health Data: Subcategory III – High Molecular Weight Phthalate Esters: Reproductive and Developmental Toxicity Endpoints			
Chemical (Carbon backbone and molecular wt.)	**Reproductive Toxicity NOAEL/LOAEL Oral (mg/kg/day))**	**Developmental Toxicity**	
		Maternal Toxicity NOAEL/LOAEL Oral (mg/kg/day)	**Developmental Toxicity NOAEL/LOAEL Oral (mg/kg/day)**
CASRN 85-68-7 (C4/ring, 312, supp. chemical)	**NOAEL = 250 LOAEL = 750**	**NOAEL = 182 LOAEL = 910**	**NOAEL = 182 LOAEL = 910**
CASRN 68515-44-6 (C7, 364)	No Data NOAEL=14 to 250/LOAEL=140 to 750 (RA)	**NOAEL = 200 LOAEL = 1000**	**NOAEL = 200 LOAEL = 1000**
CASRN 71888-89-6 (C7, 393)	No Data NOAEL=14 to 250/LOAEL=140 to 750 (RA)	**NOAEL = 100 LOAEL = 300**	**NOAEL = 300 LOAEL = 750**
CASRN 111381-89-6 (C7,C9; 391)	No Data NOAEL=14 to 250/LOAEL=140 to 750 (RA)	**NOAEL = 200 LOAEL = 1000**	**NOAEL = 200 LOAEL = 1000**
CASRN 27554-26-3 (C8, 391)	No Data NOAEL=14 to 250/LOAEL=140 to 750 (RA)	No Data NOAEL=200 to 1000/LOAEL>1000 (RA)	No Data NOAEL=44 to 200/LOAEL=91 to 1000 (RA)
CASRN 117-81-7 (C8, 391, supp. chemical)	**NOAEL = 14 LOAEL = 140**	-	**NOAEL = 44 LOAEL = 91**
CASRN 117-84-0 (C8, 391)	**NOAEL = 7500 LOAEL = NE**	No Data NOAEL=200 to 1000/LOAEL>1000 (RA)	No Data NOAEL=44 to 500/LOAEL=91 to 1000 (RA)
CASRN 68515-41-3 (C7, C9; 405, supp. chemical)	**NOAEL = 375 LOAEL = 750**	**NOAEL = 1000 LOAEL = NE**	**NOAEL = 500 LOAEL = 1000**
CASRN 111381-90-9 (C7, C11; 419)	No Data NOAEL=333 to 375/LOAEL=666 to 750 (RA)	**NOAEL = 200 LOAEL = 1000**	**NOAEL = 200 LOAEL = 1000**
CASRN 68515-48-0 (C9, 419, supporting chemical)	**NOAEL = 333 LOAEL = 666**	**NOAEL = 500 LOAEL = 1000**	**NOAEL = 500 LOAEL = 1000**
CASRN 68515-45-7 (C9, 421)	No Data NOAEL=333 to 375/LOAEL=666 to 750 (RA)	No Data NOAEL=500 to 1000/LOAEL>1000 (RA)	No Data NOAEL=250 to 500/LOAEL=500 to 1000 (RA)
CASRN 68515-43-5 (C10, 447)	**NOAEL = 375 LOAEL = 750**	**NOAEL = 1000 LOAEL = NE**	**NOAEL = 250 LOAEL = 500**
CASRN 84-77-5 (C10, 447)	No Data NOAEL=50 to 375/LOAEL=250 to 750 (RA)	No Data NOAEL=500 to 1000/LOAEL>1000 (RA)	No Data NOAEL=250 to 1000/LOAEL=500 to>1000 (RA)
CASRN 68515-49-1 (C10, 447, supporting chemical)	-	**NOAEL = 500 LOAEL = 1000**	**NOAEL = 1000 LOAEL = NE**
CASRN 111381-91-0 (C9, C11; 447)	No Data NOAEL=50 to 375/LOAEL=250 to 750 (RA)	No Data NOAEL=10 to 500/LOAEL=50 to 1000 (RA)	No Data NOAEL=250 to 1000/LOAEL>1000 (RA)
CASRN 16883-83-3 (C12, ring; 455)	No Data NOAEL=50 to 375/LOAEL=250 to 750 (RA)	No Data NOAEL=10 to 500/LOAEL=50 to 1000 (RA)	No Data NOAEL=250 to 1000/LOAEL>1000 (RA)
CASRN 3648-20-2 (C11, 475)	No Data NOAEL=50 to 375/LOAEL=250 to 750 (RA)	No Data NOAEL=10 to 500/LOAEL=50 to 1000 (RA)	No Data NOAEL=250 to 1000/LOAEL>1000 (RA)
CASRN 85507-79-5 (C11, 489)	No Data NOAEL=50 to 375/LOAEL=250 to 750 (RA)	No Data NOAEL=10 to 500/LOAEL=50 to 1000 (RA)	No Data NOAEL=250 to 1000/LOAEL>1000 (RA)
CASRN 119-06-2 (C13, 531, supporting chemical)	**NOAEL = 50 LOAEL = 250**	**NOAEL = 10 LOAEL = 50**	**NOAEL = 250 LOAEL = NE**
CASRN 68515-40-2 (C7, C9, ring; 550)	No Data NOAEL=50/LOAEL=250 (RA)	No Data NOAEL=10/LOAEL=50 (RA)	No Data NOAEL=250/LOAEL=NE (RA)
CASRN 68648-93-1 (C6, C8, C10; 557)	No Data NOAEL=50/LOAEL=250 (RA)	No Data NOAEL=10/LOAEL=50 (RA)	No Data NOAEL=250/LOAEL=NE (RA)
CASRN 68515-47-9 (C13, 561)	No Data NOAEL=50/LOAEL=250 (RA)	No Data NOAEL=10/LOAEL=50 (RA)	No Data NOAEL=250/LOAEL=NE (RA)

Supporting chemicals are shaded. **Bold = experimental values.** RA=read across. NE=not established. (-) = endpoint not evaluated for this substance.

Table 4d. Summary of Human Health Data: Subcategory III – High Molecular Weight Phthalate Esters: Genetic Toxicity and Additional Information							
Chemical (Carbon backbone and molecular wt.)	**Genetic Toxicity – Gene Mutation**		**Genetic Toxicity – Chromosomal Effects**		**Additional Information**		
	In Vitro	**In Vivo**	**In Vitro**	**In Vivo**	**Skin**	**Eye**	**Cancer**
CASRN 85-68-7 (C4/ring, 312, supp. chemical)	-	-	**Negative**	**Equivocal**	-	-	**Pos**
CASRN 68515-44-6 (C7, 364)	No Data Negative (RA)	No Data Negative (RA)	No Data Negative (RA	No Data Negative to Equivocal (RA)	-	-	-
CASRN 71888-89-6 (C7, 393)	**Negative**	-	**Negative**	No Data Negative to Equivocal (RA)-	-	-	-
CASRN 111381-89-6 (C7,C9; 391)	No Data Negative (RA)	No Data Negative (RA)	No Data Negative (RA	No Data Negative to Equivocal (RA)	-	**None**	-
CASRN 27554-26-3 (C8, 391)	**Negative**	-	No Data Negative (RA)	No Data Negative to Equivocal (RA)	-	-	-
CASRN 117-81-7 (C8, 391, supp. chemical)	**Negative**	**Negative**	**Negative**	**Negative**	-	-	**Pos**
CASRN 117-84-1 (C8, 391)	**Negative**	-	No Data Negative (RA)	No Data Negative (RA)	-	-	-
CASRN 68515-41-3 (C7, C9; 405, supp. chemical)	-	-	**Negative**	-	**None**	**None**	-
CASRN 111381-90-9 (C7, C11; 419)	**Negative**	-	No Data Negative (RA)	No Data Negative (RA)	-	-	-
CASRN 68515-48-0 (C9, 419, supporting chemical)	**Negative**	-	**Negative**	**Negative**	-	-	-
CASRN 68515-45-7 (C9, 421)	No Data Negative (RA)	No Data Negative (RA)	No Data Negative (RA)	No Data Negative (RA)	-	-	-
CASRN 68515-43-5 (C10, 447)	No Data Negative (RA)	No Data Negative (RA)	No Data Negative (RA)	No Data Negative (RA)	-	-	-
CASRN 84-77-5 (C10, 447)	No Data Negative (RA)	No Data Negative (RA)	No Data Negative (RA)	No Data Negative (RA)	-	-	-
CASRN 68515-49-1 (C10, 447, supporting chemical)	**Negative**	-	-	-	-	-	-
CASRN 111381-91-0 (C9, C11; 447)	No Data Negative (RA)	No Data Negative (RA)	No Data Negative (RA)	No Data Negative (RA)	-	-	-
CASRN 16883-83-3 (C12, ring; 455)	**Negative**	-	No Data Negative (RA)	No Data Negative (RA)	**None**	**Slight**	-
CASRN 3648-20-2 (C11, 475)	**Negative**	-	**Negative**	-	-	-	-
CASRN 85507-79-5 (C11, 489)	No Data Negative (RA)	No Data Negative (RA)	No Data Negative (RA)	No Data Negative (RA)	-	-	-
CASRN 119-06-2 (C13, 531, supporting chemical)	**Negative**	-	-	-	-	-	-
CASRN 68515-40-2 (C7, C9, ring; 550)	**Negative**	-	No Data Negative (RA)	No Data Negative (RA)	-	-	-
CASRN 68648-93-1 (C6, C8, C10; 557)	No Data Negative (RA)	No Data Negative (RA)	No Data Negative (RA)	No Data Negative (RA)	-	-	-
CASRN 68515-47-9 (C13, 561)	**Negative**	-	No Data Negative (RA)	No Data Negative (RA)	-	-	-

Supporting chemicals are shaded. **Bold = experimental values.** RA=read across. NE=not established. (-) = endpoint not evaluated for this substance.

4. Hazards to the Environment

Environmental Effects – Aquatic Toxicity

A summary of aquatic toxicity data submitted for SIDS endpoints is provided in Table 4. The table also indicates where data for tested category members are read-across (RA) to untested members of the category.

Acute Toxicity to Fish

Subcategory I: Low Molecular Weight Phthalate Esters

1,2-Benzenedicarboxylic acid, dimethyl ester (CASRN 131-11-3)
Rainbow trout (*Oncorrhynchus mykiss*) were exposed to 1,2-benzenedicarboxylic acid dimethyl ester at measured concentrations of < 0.036, 6.1, 10, 19, 38 and 83 mg/L under flow-through conditions for 96 hours. Mortalities were observed at 19 and 83 mg/L.
96-h LC_{50} = 56 mg/L

1,2-Benzenedicarboxylic acid, diethyl ester (CASRN 84-66-2)
Steelhead trout (*Salmo gairdneri*) were exposed to 1,2-benzenedicarboxylic acid diethyl ester at measured concentrations of < 0.0067, 1.9, 3.8, 8.4, 16 and 33 mg/L under flow-through conditions for 96 hours. Mortalities were observed at ≥ 8.4 mg/L.
96-h LC_{50} = 12 mg/L

Subcategory II: Transitional Phthalate Esters

1,2-Benzenedicarboxylic acid, butyl phenylmethyl ester (CASRN 85-68-7, supporting chemical)
Rainbow trout (*Oncorhynchus mykiss*) were exposed to 1,2-benzenedicarboxylic acid butyl phenylmethyl ester at measured concentrations of < 0.016, 0.17, 0.28, 0.48, 1.4 and 3.1 mg/L under flow-through conditions for 96 hours. Mortalities were observed at ≥ 0.48 mg/L.
96-h LC_{50} = 0.82 mg/L

1,2-Benzenedicarboxylic acid, dihexyl ester, branched and linear (CASRN 68515-50-4)
Rainbow trout (*Oncorhynchus mykiss*) were exposed to 1,2-benzenedicarboxylic acid, dihexyl ester, branched and linear at measured concentrations of < 0.0042, 0.014, 0.040, 0.057, 0.093 and 0.20 mg/L under flow-through conditions for 96 hours. The maximum dose exceeded the calculated water solubility value, which ranges from 0.023 to 0.159 mg/L. No mortality was observed.
No effects at saturation.

1,2-Benzenedicarboxylic acid, di-C6 – 8 branched alkyl ester, C7 rich (CASRN 71888-89-6)
Rainbow trout (*Oncorhynchus mykiss*) were exposed to 1,2-benzenedicarboxylic acid di-C6 – 8 branched alkyl ester, C7 rich as a water accommodated fraction (WAF) under semi-static conditions for 96 hours. Measured concentrations were 0.0 and 0.2 mg/L. The calculated water solubility value for 1,2-benzenedicarboxylic acid di-C6-8 branched alkyl ester, C7 rich ranges from 0.00245 to 0.017 mg/L. No mortality was observed.
No effects at saturation.

Subcategory III: High Molecular Weight Phthalate Esters

1,2-Benzenedicarboxylic acid (C7, C11) ester, branched and linear (CASRN 111381-90-9)
Rainbow trout (*Oncorhynchus mykiss*) were exposed to 1,2-benzenedicarboxylic acid (C7, C11) ester, branched and linear at measured concentrations of < 0.0083, 0.019, 0.041, 0.049, 0.092 and 0.21 mg/L under flow-through conditions for 96 hours. All doses exceeded the calculated water solubility value, which ranges from 0.00002 to 0.00031 mg/L. Separation of the chemical from the test solution was observed at 24 hours. No mortality was observed.
No effects at saturation.

1,2-Benzenedicarboxylic acid, diisooctyl ester (CASRN 27554-26-3)
Rainbow trout (*Oncorhynchus mykiss*) were exposed to 1,2-benzenedicarboxylic acid diisooctyl ester at measured concentrations of 0, 0.017, 0.031, 0.060, 0.11 and 0.23 mg/L under flow-through conditions for 96 hours. The minimum dose exceeded the calculated water solubility value, which ranges from 0.00024 to 0.00249 mg/L. No mortality was observed.
No effects at saturation.

1,2-Benzenedicarboxylic acid, mixed decyl and hexyl and octyl diesters (CASRN 68648-93-1)
Rainbow trout (*Oncorhynchus mykiss*) were exposed to 1,2-benzenedicarboxylic acid, mixed decyl and hexyl and octyl diesters at measured concentrations of 0, 0.018, 0.030, 0.060, 0.11 or 0.24 mg/L under flow-through conditions for 96 hours. All doses exceeded the calculated water solubility value, which ranges from 0.00042 to 0.00088 mg/L. No mortality was observed.
No effects at saturation.

1,2-Benzenedicarboxylic acid, benzyl C7 – 9 branched and linear alkyl esters (CASRN 68515-40-2)
Rainbow trout (*Oncorhynchus mykiss*) were exposed to 1,2-benzenedicarboxylic acid, benzyl C7 – 9 branched and linear alkyl esters with acetone as a carrier solvent at nominal concentrations of 0, 100, 180, 320, 560 or 1000 mg/L under static conditions for 96 hours. All doses far exceeded the calculated water solubility value, which is 0.00847 mg/L. No mortality was observed.
No effects at saturation.

1,2-Benzenedicarboxylic acid, diundecyl ester (CASRN 3648-20-2)
Rainbow trout (*Oncorhynchus mykiss*) were exposed to 1,2-benzenedicarboxylic acid, diundecyl ester at measured concentrations of < 0.0091, 0.11, 0.20, 0.35, 0.88 and 1.4 mg/L under flow-through conditions for 96 hours. All doses exceeded the calculated water solubility value, which ranges from 0.16×10^{-6} to 4.41×10^{-6} mg/L. No mortality was observed.
No effects at saturation.

1,2-Benzenedicarboxylic acid, di-C11– 14-branched alkyl esters, C13 rich (CASRN 68515-47-9)
Rainbow trout (*Oncorhynchus mykiss*) were exposed to 1,2-benzenedicarboxylic acid di-C11 – 14-branched alkyl esters, C13 rich at measured concentrations of < 0.0094, 0.013, 0.023, 0.039, 0.067 and 0.15 mg/L under flow-through conditions for 96 hours. All doses exceeded the calculated water solubility, which ranges from 2×10^{-8} to 7×10^{-8} mg/L. No treatment-related mortality was observed.
No effects at saturation.

1,2-Benzenedicarboxylic acid, di-C7 – 9-branched and linear alkyl esters (CASRN 68515-41-3, supporting chemical)
Rainbow trout (*Oncorhynchus mykiss*) were exposed to 1,2-benzenedicarboxylic acid, di-C7 – 9-branched and linear alkyl esters with acetone as a carrier solvent at nominal concentrations of 0, 100, 180, 320, 560 and 1000 mg/L under static conditions for 96 hours. Measured concentrations were not reported. All doses exceeded the calculated water solubility, which is 0.000206 mg/L. No mortality was observed.
No effects at saturation.

1,2-Benzenedicarboxylic acid, di-C8 – C10 branched alkyl esters, C9 rich (CASRN 68515-48-0, supporting chemical)
Rainbow trout (*Oncorhynchus mykiss*) were exposed to 1,2-benzenedicarboxylic acid di-C8 – C10 branched alkyl esters, C9 rich at measured concentrations of < 0.0068, 0.0087, 0.019, 0.032, 0.062 and 0.16 mg/L under flow-through conditions for 96 hours. All doses exceeded the calculated water solubility, which ranges from 0.000308 to 0.00061 mg/L. No mortality was observed.
No effects at saturation.

1,2-Benzenedicarboxylic acid, di-C9, C10 and C-11 branched alkyl ester, C10 rich (CASRN 68515-49-1, supporting chemical)
Rainbow trout (*Oncorhynchus mykiss*) were exposed to 1,2-benzenedicarboxylic acid di-C9, C10 and C-11 branched alkyl ester, C10 rich at measured concentrations of < 0.021, 0.043, 0.075, 0.14, 0.25 and 0.62 mg/L under flow-through conditions for 96 hours. All doses exceeded the calculated water solubility, which is 0.00004 mg/L. Droplets of undissolved test material were observed at all doses and a film of dissolved test material was observed at ≥ 0.25 mg/L. No mortalities occurred.
No effects at saturation.

1,2-Benzenedicarboxylic acid, benzyl 3-hydroxy-1-isopropyl-2,2-dimethylpropyl ester isobutyrate (CASRN 16883-83-3)
(1) Fathead minnows (*Pimephales promelas*) were exposed to 1,2-benzenedicarboxylic acid, benzyl 3-hydroxy-1-isopropyl-2,2-dimethylpropyl ester isobutyrate at nominal concentrations of 0 and 1000 mg/L under static conditions for 96 hours. Measured concentrations were not reported. The dose concentration far exceeded the calculated water solubility, which is 0.00147 mg/L. An oily sheen was observed on the surface of the test solution during the study. No mortality was observed.
No effects at saturation.

(2) Steelhead trout (*Salmo gairdneri*) were exposed to 1,2-benzenedicarboxylic acid, benzyl 3-hydroxy-1-isopropyl-2,2-dimethylpropyl ester isobutyrate at nominal concentrations of 0 or 1000 mg/L under static conditions for 96 hours. Measured concentrations were not reported. The dose concentration far exceeded the calculated water solubility, which is 0.00147 mg/L. No mortality was observed.
No effects at saturation.

Acute Toxicity to Aquatic Invertebrates

Subcategory I: Low Molecular Weight Phthalate Esters

1,2-Benzenedicarboxylic acid, dimethyl ester (CASRN 131-11-3)
Daphnia magna were exposed to 1,2-benzenedicarboxylic acid, dimethyl ester at measured concentrations of < 0.0007, 23.5, 38, 62.5, 132 and 225 mg/L under static conditions for 48 hours. Immobilities were observed at ≥ 23.5 mg/L.
48-h LC_{50} = 45.9 mg/L

1,2-Benzenedicarboxylic acid, diethyl ester (CASRN 84-66-2)
Daphnia magna were exposed to 1,2-benzenedicarboxylic acid, diethyl ester at measured concentrations of < 0.007, 37.5, 69, 115, 195 and 335 mg/L under static conditions for 48 hours. Immobilities were observed at ≥ 69 mg/L.
48-h LC_{50} = 86 mg/L

Subcategory II: Transitional Phthalate Esters

1,2-Benzenedicarboxylic acid, dihexyl ester, branched and linear (CASRN 68515-50-4)
Daphnia magna were exposed to 1,2-benzenedicarboxylic acid, dihexyl ester, branched and linear at measured concentrations of < 0.0083, 0.019, 0.028, 0.059, 0.104 and 0.18 mg/L under static conditions for 48 hours. The maximum dose exceeded the calculated water solubility, which ranges from 0.023 to 0.159 mg/L. Immobilities were observed at ≥ 0.059 mg/L.
48-h LC_{50} ≥ 0.059 mg/L

1,2-Benzenedicarboxylic acid, butyl phenylmethyl ester (CASRN 85-68-7, supporting chemical)
Daphnia magna were exposed to 1,2-benzenedicarboxylic acid, butyl phenylmethyl ester at measured concentrations of < 0.0033, 0.18, 0.21, 0.56, 0.47 and 0.96mg/L under static renewal conditions for 48 hours. No immobilities were observed.
No effects at saturation.

Subcategory III: High Molecular Weight Phthalate Esters

1,2-Benzenedicarboxylic acid (C7, C11) ester, branched and linear (CASRN 111381-90-9)
Daphnia magna were exposed to 1,2-benzenedicarboxylic acid (C7, C11) ester, branched and linear at measured concentrations of < 0.0096, 0.014, 0.023, 0.037, 0.082 or 0.122 mg/L under static conditions for 48 hours. At concentrations greater than or equal to 0.037 mg/L, daphnids were trapped at the surface due to the presence of unsolubilized test chemical. Consequently, the study was repeated at nominal concentrations of < 0.015 and 0.04 mg/L. All doses exceeded the calculated water solubility value, which ranges from 0.00002 to 0.00031 mg/L. No immobilizations occurred at the maximum dose.
No effects at saturation.

1,2-Benzenedicarboxylic acid, diisooctyl ester (CASRN 27554-26-3)
Daphnia magna were exposed to 1,2-benzenedicarboxylic acid diisooctyl ester at measured concentrations of <0.0040, 0.017, 0.031, 0.060, 0.11 and 0.23 mg/L under static conditions for 48 hours. Immobilities were observed at ≥ 0.031 mg/L. However, more than 50% of the organisms were trapped at the surface. Consequently, the study was repeated at measured concentrations of < 0.0037 and 0.16

mg/L. No immobilizations occurred at 0.16 mg/L. This dose exceeded the calculated water solubility value, which ranges from 0.00024 to 0.00249 mg/L.
No effects at saturation.

1,2-Benzenedicarboxylic acid, mixed decyl and hexyl and octyl diesters (CASRN 68648-93-1)
Daphnia magna were exposed to 1,2-benzenedicarboxylic acid, mixed decyl and hexyl and octyl diesters at measured concentrations of 0 or 0.33 mg/L under static conditions for 48 hours. The dose concentration exceeded the calculated water solubility value, which ranges from 0.00042 to 0.00088 mg/L. No immobilization was observed.
No effects at saturation.

1,2-Benzenedicarboxylic acid, benzyl C7 – 9 branched and linear alkyl esters (CASRN 68515-40-2)
Daphnia magna were exposed to 1,2-benzenedicarboxylic acid, benzyl C7 – 9 branched and linear alkyl esters with acetone as a carrier solvent at nominal concentrations of 0, 1.0, 180 either this is out of order or it should be 1.80 mg/L, 3.2, 5.6 or 10 mg/L under static conditions for 48 hours. All doses exceeded the calculated water solubility value, which is 0.00847 mg/L. No mortalities were observed.
No effects at saturation.

1,2-Benzenedicarboxylic acid, diundecyl ester (CASRN 3648-20-2)
Daphnia magna were exposed to 1,2-benzenedicarboxylic acid, diundecyl ester at measured concentrations of 0, 0.015, 0.026, 0.048, 0.064 or 0.095 mg/L under static conditions for 48 hours. Immobilities were observed at ≥ 0.026 mg/L. However, more than 50% of the organisms were trapped at the surface at ≥ 0.026 mg/L. Consequently, the study was repeated at 0 and 0.02 mg/L. No immobilizations occurred at this level. All doses exceeded the calculated water solubility value, which ranges from 0.16×10^{-6} to 4.41×10^{-6} mg/L.
No effects at saturation.

1,2-Benzenedicarboxylic acid, di-C11 – 14-branched alkyl esters, C13 rich (CASRN 68515-47-9)
Daphnia magna were exposed to 1,2-benzenedicarboxylic acid, di-C11 – 14-branched alkyl esters, C13 rich at measured concentrations of < 0.0088, < 0.0088, 0.011, 0.017, 0.029 and 0.055 mg/L under static conditions for 48 hours. All doses exceeded the calculated water solubility, which ranges from 2×10^{-8} to 7×10^{-8} mg/L. Immobilities were observed at 0.029 mg/L.
No effects at saturation.

1,2-Benzenedicarboxylic acid, di-C7 – 9-branched and linear alkyl esters (CASRN 68515-41-3, supporting chemical)
Daphnia magna were exposed to 1,2-benzenedicarboxylic acid, di-C7 – 9-branched and linear alkyl esters at nominal concentrations of 0 or 1 mg/L with a castor oil 40-ethoxylate dispersant under static conditions for 48 hours. Measured concentrations were not reported. The measured concentration was 0.8 mg/L in a chronic study run subsequently with the same loading level. The dose concentration exceeded the calculated water solubility, which is 0.000206 mg/L. No immobilization or floating organisms were observed.
No effects at saturation.

1,2-Benzenedicarboxylic acid, di-C8 – C10 branched alkyl esters, C9 rich (CASRN 68515-48-0, supporting chemical)
Daphnia magna were exposed to 1,2-benzenedicarboxylic acid, di-C8 – C10 branched alkyl esters, C9 rich at nominal concentrations of 0 and 0.2 mg/L under static conditions for 48 hours. Measured

concentrations were < 0.014 and 0.06 mg/L. The dose concentration exceeded the calculated water solubility, which ranges from 0.000308 to 0.00061 mg/L. No immobilities were observed.
No effects at saturation.

1,2-Benzenedicarboxylic acid, di-C9, C10 and C-11 branched alkyl ester, C10 rich (CASRN 68515-49-1, supporting chemical)
Daphnia magna were exposed to 1,2-benzenedicarboxylic acid, di-C9, C10 and C-11 branched alkyl ester, C10 rich at measured concentrations of 0, 0.074, 0.12, 0.22, 0.34 or 0.61 mg/L under static conditions for 48 hours. Immobilities were observed at ≥ 0.074 mg/L, but > 50% of the organisms were trapped at the surface by a film of the test material. The test was re-run using a WAF at a measured concentration of 0.02 mg/L. This dose exceeded the calculated water solubility, which is 0.00004 mg/L. No immobilities were observed.
No effects at saturation.

1,2-Benzenedicarboxylic acid, benzyl 3-hydroxy-1-isopropyl-2,2-dimethylpropyl ester isobutyrate (CASRN 16883-83-3)
Daphnia magna were exposed to 1,2-benzenedicarboxylic acid, benzyl 3-hydroxy-1-isopropyl-2,2-dimethylpropyl ester isobutyrate at nominal concentrations of 0, 1.0, 1.8, 3.2, 5.6 or 10.0 mg/L with acetone as a carrier solvent under static conditions for 48 hours. Measured concentrations were not reported. The dose concentration far exceeded the calculated water solubility value, which is 0.00147 mg/L. This dose exceeded the calculated water solubility, which is 0.00004 mg/L. However, immobilizations were observed at nominal concentrations of ≥ 5.6 mg/L.
48-h LC_{50} = 7.5 mg/L

Toxicity to Aquatic Plants

Subcategory I: Low Molecular Weight Phthalate Esters

1,2-Benzenedicarboxylic acid, dimethyl ester (CASRN 131-11-3)
Algae (*Pseudokirchneriella subcapitata*) were exposed to 1,2-benzenedicarboxylic acid dimethyl ester at measured concentrations of 64.7, 133, 292.6, 597.7 and 1329.6 mg/L under static conditions for 6 days. Measured concentrations were 64.7, 133, 292.6, 597.7 and 1329.6 mg/L. Negative chlorophyll changes were observed at ≥ 292.6 mg/L. 1,2-Benzenedicarboxylic acid dimethyl ester was toxic to algae below its water solubility level.
6-d EC_{50} = 142 mg/L

1,2-Benzenedicarboxylic acid, diethyl ester (CASRN 84-66-2)
Algae (*Pseudokirchneriella subcapitata*) were exposed to 1,2-benzenedicarboxylic acid diethyl ester at nominal concentrations of 0, 6.3, 12.5, 25, 50 and 100 mg/L under static conditions for 8 days. Measured concentrations were: not detected, 3.65, 7.4, 15.2, 30.3 and 58.8 mg/L. 1,2-Benzenedicarboxylic acid diethyl ester was toxic to algae below its water solubility level.
8-d EC_{50} = 16 mg/L

Subcategory II: Transitional Phthalate Esters

1,2-Benzenedicarboxylic acid, dihexyl ester, branched and linear (CASRN 68515-50-4)
Algae *(Pseudokirchneriella subcapitata)* were exposed to 1,2-benzenedicarboxylic acid, dihexyl ester, branched and linear at measured concentrations of 0.1, 0.1, 0.1, 0.2 and 0.33 mg/L under static

conditions for 7 days. The two highest doses exceeded the calculated water solubility, which ranges from 0.023 to 0.159 mg/L. A decrease in chlorophyll concentration was observed at 0.33 mg/L.
7-d EC_{50} > 0.33 mg/L

1,2-Benzenedicarboxylic acid, butyl phenylmethyl ester (CASRN 85-68-7, supporting chemical)
Algae (*Pseudokirchneriella subcapitata*) were exposed to 1,2-benzenedicarboxylic acid, butyl phenylmethyl ester at 0, 3.125, 6.25, 12.5, 25, 50 and 100% of saturation under static conditions for 6 days. Measured concentrations were < 0.01, < 0.05, 0.05, 0.2, 0.3, 0.8 and 1.3 mg/L. At all test concentrations, the chlorophyll concentration was reduced compared to the control.
5-d EC_{50} = 0.21 mg/L

Subcategory III: High Molecular Weight Phthalate Esters

1,2-Benzenedicarboxylic acid (C7, C11) ester, branched and linear (CASRN 111381-90-9)
Algae (*Pseudokirchneriella subcapitata*) were exposed to 1,2-benzenedicarboxylic acid (C7, C11) ester, branched and linear as a WAF at measured concentrations of 0 or 1.6 mg/L under static conditions for 7 days. The calculated water solubility value for 1,2-benzenedicarboxylic acid (C7, C11) ester, branched and linear ranges from 0.00002 to 0.00031 mg/L. 1,2-Benzenedicarboxylic acid (C7, C11) ester, branched and linear was not toxic to algae at or below its water solubility level.
No effects at saturation.

1,2-Benzenedicarboxylic acid, diisooctyl ester (CASRN 27554-26-3)
Algae (*Pseudokirchneriella subcapitata*) were exposed to 1,2-benzenedicarboxylic acid diisooctyl ester as a WAF at measured concentrations of 0 or 1.3 mg/L under static conditions for 6 days. The calculated water solubility value for 1,2-benzenedicarboxylic acid, diisooctyl ester ranged from 0.00024 to 0.00249 mg/L. 1,2-Benzenedicarboxylic acid diisooctyl ester was not toxic to algae at or below its water solubility level.
No effects at saturation.

1,2-Benzenedicarboxylic acid, mixed decyl and hexyl and octyl diesters (CASRN 68648-93-1)
Algae (*Pseudokirchneriella subcapitata*) were exposed to 1,2-benzenedicarboxylic acid, mixed decyl and hexyl and octyl diesters as a WAF at measured concentrations of < 0.10 and 0.08 mg/L under static conditions for 6 days. The calculated water solubility value for 1,2-benzenedicarboxylic acid, mixed decyl and hexyl and octyl diesters ranges from 0.00042 to 0.00088 mg/L. 1,2-Benzenedicarboxylic acid, mixed decyl and hexyl and octyl diesters was not toxic to algae at or below its water solubility level.
No effects at saturation.

1,2-Benzenedicarboxylic acid, benzyl C7 – 9 branched and linear alkyl esters (CASRN 68515-40-2)
Algae (*Pseudokirchneriella subcapitata*) were exposed to 1,2-benzenedicarboxylic acid, benzyl C7 – 9 branched and linear alkyl esters at 0, 3.125, 6.25, 12.5, 25.0, 50.0 or 100% saturation under static conditions for 7 days. Measured concentrations were < 0.10, 0.10, < 0.10, 0.10, 0.10, 0.20 or 0.33 mg/L. 1,2-Benzenedicarboxylic acid, benzyl C7 – 9 branched and linear alkyl esters was not toxic to algae at or below its water solubility level.
No effects at saturation

1,2-Benzenedicarboxylic acid, diundecyl ester (CASRN 3648-20-2)
Algae (*Pseudokirchneriella subcapitata*) were exposed to 1,2-benzenedicarboxylic acid, diundecyl ester as a WAF at measured concentrations of 0 or 2.1 mg/L. The calculated water solubility value for 1,2-benzenedicarboxylic acid, diundecyl ester ranges from 0.16×10^{-6} to 4.41×10^{-6} mg/L. 1,2-Benzenedicarboxylic acid, diundecyl ester was not toxic to algae at or below its water solubility level.
No effects at saturation.

1,2-Benzenedicarboxylic acid, di-C11 – 14-branched alkyl esters, C13 rich (CASRN 68515-47-9)
Algae (*Pseudokirchneriella subcapitata*) were exposed to 1,2-benzenedicarboxylic acid di-C11 – 14-branched alkyl esters, C13 rich as a WAF at measured concentrations of 0 or 0.6 mg/L under static conditions for 8 days. The calculated water solubility value for 1,2-benzenedicarboxylic acid di-C11 – 14-branched alkyl esters, C13 rich ranges from 2×10^{-8} to 7×10^{-8} mg/L. 1,2-Benzenedicarboxylic acid di-C11 – 14-branched alkyl esters, C13 rich was not toxic to algae at or below its water solubility level.
No effects at saturation.

1,2-Benzenedicarboxylic acid, di-C8 – C10 branched alkyl esters, C9 rich (CASRN 68515-48-0, supporting chemical)
Algae (*Pseudokirchneriella subcapitata*) were exposed to 1,2-benzenedicarboxylic acid, di-C8 – C10 branched alkyl esters, C9 rich as a WAF at measured concentrations of 0 or 1.8 mg/L under static conditions for 5 days. The calculated water solubility value for 1,2-benzenedicarboxylic acid, di-C8 – C10 branched alkyl esters, C9 rich ranges from 0.000308 to 0.00061 mg/L. 1,2-Benzenedicarboxylic acid, di-C8 – C10 branched alkyl esters, C9 rich was not toxic to algae at or below its water solubility level.
No effects at saturation.

1,2-Benzenedicarboxylic acid, di-C9, C10 and C-11 branched alkyl ester, C10 rich (CASRN 68515-49-1, supporting chemical)
Algae (*Pseudokirchneriella subcapitata*) were exposed to 1,2-benzenedicarboxylic acid, di-C8 – C10 branched alkyl esters, C9 rich as WAF at measured concentrations of < 0.10 and 0.8 mg/L under static conditions for 8 days. The dose concentration exceeded the calculated water solubility, which is 0.00004 mg/L. 1,2-Benzenedicarboxylic acid, di-C8 – C10 branched alkyl esters, C9 rich was not toxic to algae below its water solubility level.
8-d EC_{50} > 0.8 mg/L ~ No effect at satuation.

1,2-Benzenedicarboxylic acid, benzyl 3-hydroxy-1-isopropyl-2,2-dimethylpropyl ester isobutyrate (CASRN 16883-83-3)
Algae (*Pseudokirchneriella subcapitata*) were exposed to 1,2-benzenedicarboxylic acid, benzyl 3-hydroxy-1-isopropyl-2,2-dimethylpropyl ester isobutyrate at nominal concentrations of 0, 360, 600 and 1000 mg/L under static conditions for 96 hours. Measured concentrations were not reported. All test concentrations far exceeded the calculated water solubility, which is 0.00147 mg/L. The chlorophyll concentration and cell number were reduced at a nominal concentration of ≥ 360 mg/L.
No effects at saturation.

Chronic Toxicity to Fish

Subcategory I: Low Molecular Weight Phthalate Esters

1,2-Benzenedicarboxylic acid, dimethyl ester (CASRN 131-11-3)
Rainbow trout (*Oncorhynchus mykiss*) were exposed to 1,2-benzenedicarboxylic acid, dimethyl ester under flow-through conditions for 60 days. Test concentrations were not provided.
NOEC = 11 mg/L

Subcategory II: Transitional Phthalate Esters

1,2-Benzenedicarboxylic acid, dihexyl ester, branched and linear (CASRN 68515-50-4)
Rainbow trout (*Oncorhynchus mykiss*) were exposed to 1,2-benzenedicarboxylic acid, dihexyl ester, branched and linear at measured concentrations of 0.014, 0.029, 0.058, 0.10 and 0.22 mg/L under flow-through conditions for 111 days. The maximum concentration exceeded the calculated water solubility, which ranges from 0.023 to 0.159 mg/L. Egg hatchability/survival, fry survival and growth were not affected.
No effects at saturation.

1,2-Benzenedicarboxylic acid, butyl phenylmethyl ester (CASRN 85-68-7, supporting chemical)
Rainbow trout (*Oncorhynchus mykiss*) were exposed to 1,2-benzenedicarboxylic acid, butyl phenylmethyl ester at concentrations ranging from 0 to 0.2 mg/L under flow-through conditions for 109 days. Measured concentrations not specified. There was no effect of exposure on egg hatchability, fry survival or growth at any concentration.
NOEC = 0.2 mg/L

Subcategory III: High Molecular Weight Phthalate Esters

1,2-Benzenedicarboxylic acid (C7, C11) ester, branched and linear (CASRN 111381-90-9)
Rainbow trout (*Oncorhynchus mykiss*) were exposed to 1,2-benzenedicarboxylic acid (C7, C11) ester, branched and linear with acetone as a carrier solvent at measured concentrations of 0, 0.024, 0.044, 0.081, 0.18 and 0.41 mg/L under flow-through conditions for 120 days. Measured concentrations were 0, 0.024, 0.044, 0.081, 0.18 and 0.41 mg/L. The calculated water solubility value for 1,2-benzenedicarboxylic acid (C7, C11) ester, branched and linear ranges from 0.00002 to 0.00031 mg/L. Egg hatchability/survival, fry survival and growth were not affected.
No effects at saturation.

1,2-Benzenedicarboxylic acid, di-C8 – C10 branched alkyl esters, C9 rich (CASRN 68515-48-0, supporting chemical)
Medaka fish (*Oryzias latipes*) were exposed to 1,2-benzenedicarboxylic acid di-C8 – C10 branched alkyl esters, C9 rich at nominal concentrations of 0 or 20 μg/g feed for 284 days. No effects were observed on survival, growth, fecundity, development, sex ratio, gonadal-somatic index, histology, testosterone metabolism, ethoxyresorufin-O-deethylase (EROD) activity or vitellogenin production. Other study details not provided. The NOEC was estimated by assuming a body weight of 20 g and a daily food ingestion rate of 5% of wet body weight per day (body weight not provided in the summary). This study does not provide adequate data to properly evaluate the toxicity of 1,2-benzenedicarboxylic acid, di-C8 – C10 branched alkyl esters, C9 rich (CASRN 68515-48-0).
Inadequate Study

1,2-Benzenedicarboxylic acid, di-C9, C10 and C-11 branched alkyl ester, C10 rich (CASRN 68515-49-1, supporting chemical)
Medaka fish (*Oryzias latipes*) were exposed to 1,2-benzenedicarboxylic acid , di-C9, C10 and C-11 branched alkyl ester, C10 rich in the diet at a nominal concentration of 20 µg/g feed for 284 days. The measured concentration ranged from 19.2 to 22.7 µg/g. No effects were observed on survival, growth, fecundity, development, sex ratio, gonadal-somatic index, histology, testosterone metabolism, EROD activity or vitellogenin production. This study does not provide adequate data to properly evaluate the toxicity of 1,2-benzenedicarboxylic acid, di-C9, C10 and C-11 branched alkyl ester, C10 rich (CASRN 68515-49-1). **Inadequate Study**

Chronic Toxicity to Invertebrates

Subcategory I: Low Molecular Weight Phthalate Esters

1,2-Benzenedicarboxylic acid, dimethyl ester (CASRN 131-11-3)
Daphnia magna were exposed to 1,2-benzenedicarboxylic acid, dimethyl ester at measured concentrations of 0, 1.9, 5.7, 9.6, 23 and 54 mg/L under static renewal conditions for 21 days. Survival was lower than controls at 23 and 54 mg/L. Reproduction was not affected.
21-d LOEC = 23 mg/L

1,2-Benzenedicarboxylic acid, diethyl ester (CASRN 84-66-2)
Daphnia magna were exposed to 1,2-benzenedicarboxylic acid, diethyl ester at measured concentrations of 0, 5.8, 16, 25, 59 or 130 mg/L under static renewal conditions for 21 days. Survival and reproduction were lower than controls at 59 and 130 mg/L**.**
21-d LOEC = 59 mg/L

Subcategory II: Transitional Phthalate Esters

1,2-Benzenedicarboxylic acid, butyl phenylmethyl ester (CASRN 85-68-7, supporting chemical)
Daphnia magna were exposed to 1,2-benzenedicarboxylic acid, butyl phenylmethyl ester at measured concentrations of 0.073, 0.23, 0.28, 1.4 and 2.4 mg/L under static conditions for 21 days. Survival and reproduction were reduced at ≥ 1.4 mg/L.
LOEC = 1.4 mg/L
NOEC = 0.28 mg/L

1,2-Benzenedicarboxylic acid, di-C6 – 8 branched alkyl ester, C7 rich (CASRN 71888-89-6)
Daphnia magna were exposed to 1,2-benzenedicarboxylic acid, di-C6 – 8 branched alkyl ester, C7 rich at nominal concentrations of 0 or 1.0 mg/L with a castor oil 40-ethoxylate dispersant under static renewal conditions for 21 days. At the nominal concentration of 1.0 mg/L, the measured concentration was 0.92 mg/L. This concentration exceeded the calculated water solubility value for 1,2-benzenedicarboxylic acid di-C6 – 8 branched alkyl ester, C7 rich, which ranges from 0.00245 to 0.017 mg/L. Mortality, growth and reproduction rate were not affected.
No effects at saturation.

Subcategory III: High Molecular Weight Phthalate Esters

1,2-Benzenedicarboxylic acid, diundecyl ester (CASRN 3648-20-2)
(1) *Daphnia magna* were exposed to 1,2-benzenedicarboxylic acid, diundecyl ester at measured concentrations of 0 or 0.9 mg/L with a castor oil 40-ethoxylate dispersant under static conditions for 21 days. The test concentration exceeded the calculated water solubility value for 1,2-benzenedicarboxylic acid, diundecyl ester, which ranges from 0.16×10^{-6} to 4.41×10^{-6} mg/L. Survival, reproduction and parent length were not affected.
No effects at saturation.
(2) *Daphnia magna* were exposed to 1,2-benzenedicarboxylic acid, diundecyl ester at measured concentrations 0.004, 0.008, 0.014, 0.028, and 0.059 mg/L under static conditions for 21 days. All doses exceeded the calculated water solubility value, which ranges from 0.16×10^{-6} to 4.41×10^{-6} mg/L. Survival and reproduction were not affected.
No effects at saturation.

1,2-Benzenedicarboxylic acid, di-C11 – 14-branched alkyl esters, C13 rich (CASRN 68515-47-9)
Daphnia magna were exposed to 1,2-benzenedicarboxylic acid, di-C11 – 14-branched alkyl esters, C13 rich at nominal concentrations of 0 and 1 mg/L with a castor oil 40-ethoxylate dispersant under static conditions for 21 days. At the nominal concentration of 1.0 mg/L, the measured concentration was 0.9 mg/L. This concentration exceeded the calculated water solubility, which ranges from 2×10^{-8} to 7×10^{-8} mg/L. Survival, growth and reproduction were not affected.
No effects at saturation.

1,2-Benzenedicarboxylic acid, di-C7 – 9-branched and linear alkyl esters (CASRN 68515-41-3, supporting chemical)
Daphnia magna were exposed to 1,2-benzenedicarboxylic acid, di-C7 – 9-branched and linear alkyl esters at nominal concentrations of 0 or 1 mg/L with a castor oil 40-ethoxylate dispersant under static-renewal conditions for 21 days. The mean measured concentration over the test period was 0.82 mg/L. The test concentration exceeded the calculated water solubility, which is 0.000206 mg/L. Survival, reproduction, and growth were not affected.
No effects at saturation.

1,2-Benzenedicarboxylic acid, di-C8 – C10 branched alkyl esters, C9 rich (CASRN 68515-48-0, supporting chemical)
Daphnia magna were exposed to 1,2-benzenedicarboxylic acid, di-C8 – C10 branched alkyl esters, C9 rich at nominal concentrations of 0 or 1 mg/L with a castor oil 40-ethoxylate dispersant under static conditions for 21 days. Mean measured concentration over the test period was 1.05 mg/L. The test concentration exceeded the calculated water solubility, which ranges from 0.000308 to 0.00061 mg/L. Survival, growth, and reproduction were not affected.
No effects at saturation.

1,2-Benzenedicarboxylic acid, di-C9, C10 and C-11 branched alkyl ester, C10 rich (CASRN 68515-49-1, supporting chemical)
Daphnia magna were exposed to 1,2-benzenedicarboxylic acid, di-C9, C10 and C-11 branched alkyl ester, C10 rich at nominal concentrations of 0 or 1 mg/L with a castor oil 40-ethoxylate dispersant under static conditions for 21 days. The measured test concentration was 1 mg/L. The test concentration exceeded the calculated water solubility, which is 0.00004 mg/L. Survival, growth and reproduction were not affected.

No effects at saturation.

Conclusions:

Subcategory I: Low Molecular Weight Phthalate Esters

The 96-hr LC_{50} of CASRN 131-11-3 for fish is 56 mg/L. The 48-hr EC_{50} of CASRN 131-11-3 for aquatic invertebrates is 45.9 mg/L. The 6-d EC_{50} of CASRN 131-11-3 for aquatic plants is 142 mg/L (growth). The 60-d NOEC of CASRN 131-11-3 for fish is 11 mg/L. The 21-d LOEC of CASRN 131-11-3 to aquatic invertebrates is 23 mg/L.

The 96-hr LC_{50} of CASRN 84-66-2 for fish is 12 mg/L. The 48-hr EC_{50} of CASRN 84-66-2 for aquatic invertebrates is 86 mg/L. The 8-d EC_{50} of CASRN 84-66-2 for aquatic plants is 16 mg/L (growth). The 21-d LOEC of CASRN 84-66-2 is 59 mg/L.

Subcategory II: Transitional Phthalate Esters

There are no acute toxicity effects of CASRN's 68515-50-4 and 71888-89-6 for fish at the water solubility limit. However, the 96-hr LC_{50} of the supporting chemical, CASRN 85-68-7, for fish is 0.82 mg/L. There are no chronic effects of CASRN 68515-50-4 for fish at the water solubility limit.

The 48-hr LC_{50} of CASRN 68515-50-4 for aquatic invertebrates is $\geq$ 0.18 mg/L. There are no acute toxicity effects of CASRN 85-68-7 for aquatic invertebrates at the water solubility limit. There are no chronic effects of CASRN 7188-89-6 for aquatic invertebrates at the water solubility limit. The LOEC of the supporting chemical CASRN 85-68-7, for aquatic invertebrate is 1.4 mg/L.

The 7-d EC_{50} of CASRN 68515-50-4 for aquatic plants is > 0.33 mg/L (biomass), and the 5-d NOEC or LOEC of the supporting chemical, CASRN 85-68-7, for aquatic plants is 0.21 mg/L (biomass).

Subcategory III: High Molecular Weight Phthalate Esters

There are no acute toxicity effects reported for CASRN's 111381-90-9, 27554-26-3, 68648-93-1, 68515-40-2, 3648-20-2, 68515-47-9, and 16883-83-3 for fish at the water solubility limit. There are no chronic effects of CASRN 111381-90-9 to fish at the water solubility limit.

There are no acute toxicity effects of CASRN's 111381-90-9, 27554-26-3, 68648-93-1, 68515-40-2, 3648-20-2 and 68515-47-9 for aquatic invertebrates at the water solubility limit. However, the acute 48-hr LC_{50} of CASRN 16883-83-3 for aquatic invertebrates is 7.5 mg/L. There are no chronic effects of CASRNs 68515-47-9 and 3648-20-2 to aquatic invertebrates at the water solubility limit.

There are no acute toxicity effects reported for CASRN's 111381-90-9, 27554-26-3, 68648-93-1, 68515-40-2, 3648-20-2, 68515-47-9 and 16883-83-3 for aquatic plants at the water solubility limit.

Table 5a. Summary of Environmental Effects – Aquatic Toxicity Data						
	Subcategory I: Low Molecular Weight Phthalate Esters		Subcategory II: Transitional Phthalate Esters Subcategory			
Endpoints	**1,2-Benzene-dicarboxylic acid, dimethyl ester (131-11-3)**	**1,2-Benzene-dicarboxylic acid, diethyl ester (84-66-2)**	**1,2-Benzene-dicarboxylic acid, dihexyl ester, branched and linear (68515-50-4)**	**1,2-Benzene-dicarboxylic acid, diheptyl ester, branched and linear (68515-44-6)**	**1,2-Benzene-dicarboxylic acid, butyl phenylmethyl ester (85-68-7, supporting chemical)**	**1,2-Benzene-dicarboxylic acid, di-C6 – 8 branched alkyl ester, C7 rich (71888-89-6)**
Fish 96-h LC_{50} (mg/L)	**56 (m)**	**12 (m)**	**NES**	No Data NES (RA)	**0.82 (m)**	**NES**
Aquatic Invertebrates 48-h EC_{50} (mg/L)	**45.9 (m)**	**86 (m)**	**≥ 0.18* (m)**	No Data ≥ 0.18 (RA)	**NES**	No Data ≥ 0.18 (RA)
Aquatic Plants 72-h EC_{50} (mg/L)	**142 (6-d) (m)**	**16 (8-d) (m)**	**> 0.33 (7-d) (m)**	No Data > 0.21 (RA)	**0.21 (5-d) (m)**	No Data > 0.21 (RA)
Chronic Toxicity to Fish 21-d NOEC (mg/L)	**11 (60-d) (m)**	No Data 11 (RA)	**NES**	No Data NES (RA)	**0.2 (109-d) (m)**	No Data NES (RA)
Chronic Toxicity to Invertebrates 21-d LOEC (mg/L)	**23 (m)**	**59 (m)**	No Data NES (RA)	No Data NES (RA)	**1.4 (m)**	**NES**

NES = no effects at saturation (water solubility limit); **(m) = measured data (i.e., derived from testing;** (RA) = Read Across; – indicates that endpoint was not evaluated for this substance. * = carrier solvent was used in the experiment.

Table 5b. Summary of Environmental Effects – Aquatic Toxicity Data

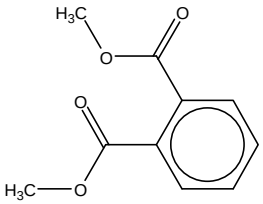
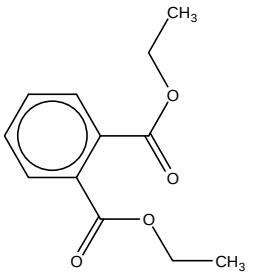
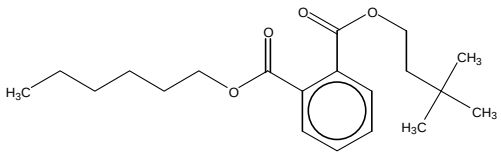
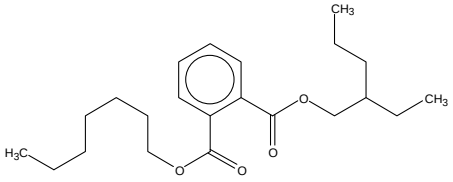
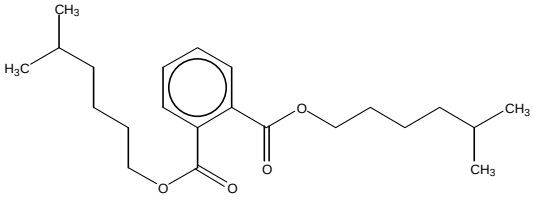
	Subcategory III: High Molecular Weight Phthalate Esters						
Endpoints	**1,2-Benzenedicarboxylic acid (C7, C9) ester, branched and linear (111381-89-6)**	**1,2-Benzene-dicarboxylic acid (C7, C11) ester, branched and linear (111381-90-9)**	**1,2-Benzene-dicarboxylic acid, diisooctyl ester (27554-26-3)**	**1,2-Benzene-dicarboxylic acid, mixed decyl and hexyl and octyl diesters (68648-93-1)**	**1,2-Benzene-dicarboxylic acid, dioctyl ester (117-84-0)**	**1,2-Benzene-dicarboxylic acid, benzyl C7– 9 branched and linear alkyl esters (68515-40-2)**	**1,2-Benzene-dicarboxylic acid, dinonyl ester, branched and linear (68515-45-7)**
Fish 96-h LC_{50} (mg/L)	No Data NES (RA)	**NES**	**NES***	**NES**	No Data NES (RA)	**NES**	No Data NES (RA)
Aquatic Invertebrates 48-h EC_{50} (mg/L)	No Data NES (RA)	**NES**	**NES**	**NES**	No Data NES (RA)	**NES***	No Data NES (RA)
Aquatic Plants 72-h EC_{50} (mg/L)	No Data NES (RA)	**NES (7-d)**	**NES (6-d)**	**NES (6-d)**	No Data NES (RA)	No Data NES (RA)	No Data NES (RA)
Chronic Toxicity to Fish 21-d NOEC (mg/L)	No Data NES (RA)	**NES (120 d)**	No Data NES (RA)	No Data NES (RA)	No Data NES (RA)	No Data NES (RA)	No Data NES (RA)
Chronic Toxicity to Invertebrates 21-d LOEC (mg/L)	No Data NES (RA)	No Data NES (RA)	No Data NES (RA)	No Data NES (RA)	No Data NES (RA)	No Data NES (RA)	No Data NES (RA)

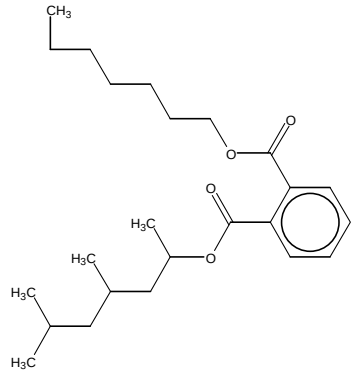
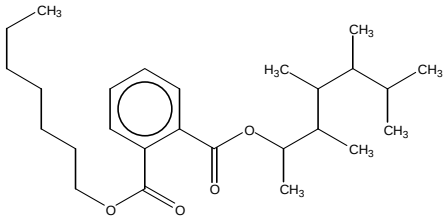
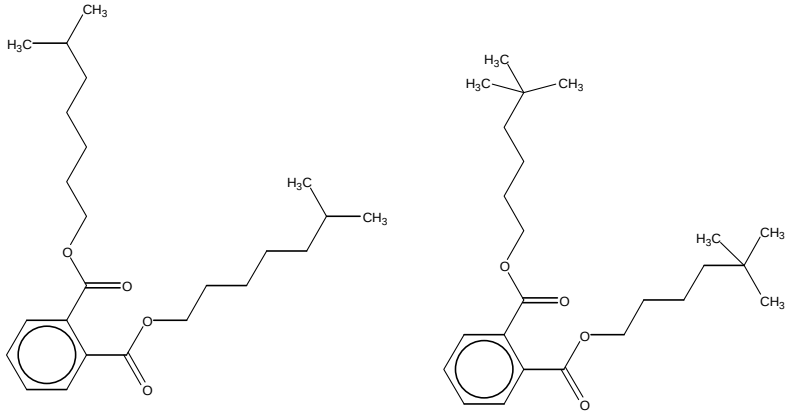
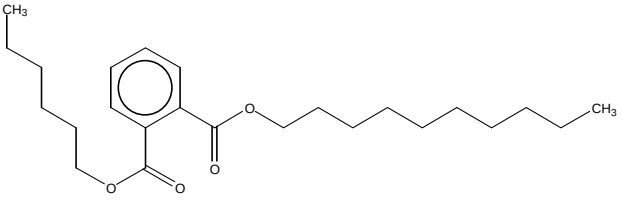
NES = no effects at saturation (water solubility limit); **(m) = measured data (i.e., derived from testing;** (RA) = Read Across; – indicates that endpoint was not evaluated for this substance. * = carrier solvent was used in the experiment.

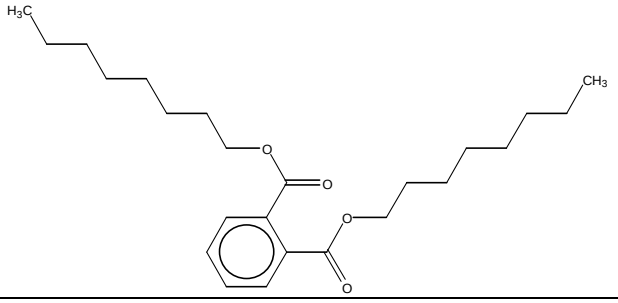
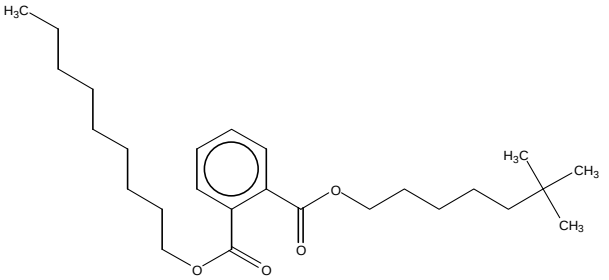
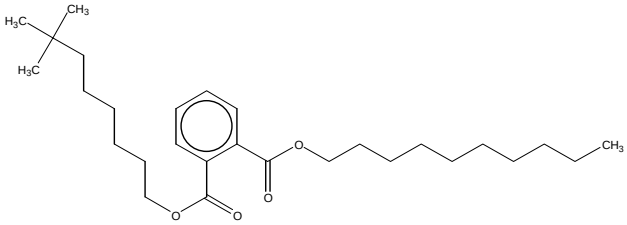
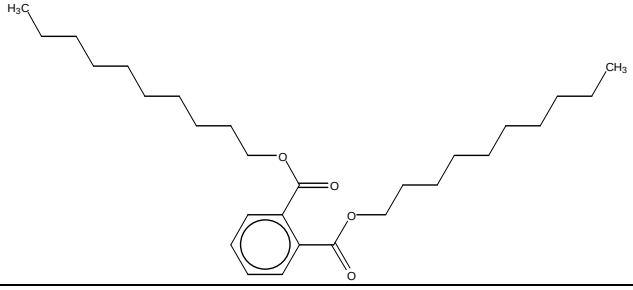
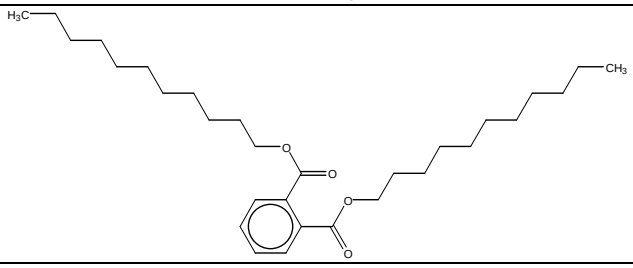
Table 5c. Summary of Environmental Effects – Aquatic Toxicity Data							
Subcategory III: High Molecular Weight Phthalate Esters							
Endpoints	**1,2-Benzene-dicarboxylic acid, di-C9 – 11-branched and linear alkyl esters (68515-43-5)**	**1,2-Benzenedicarboxylic acid, didecyl ester (84-77-5)**	**1,2-Benzenedicarboxylic acid, diundecyl ester (3648-20-2)**	**1,2-Benzenedicarboxylic acid, di (C11) ester, branched and linear (85507-79-5)**	**1,2-Benzenedicarboxylic acid, di(C11)ester, branched and linear (111381-91-0)**	**1,2-Benzenedicarboxylic acid, di-C11 – 14-branched alkyl esters, C13 rich (68515-47-9)**	**1,2-Benzenedicarboxylic acid, benzyl 3-hydroxy-1-isopropyl-2,2-dimethylpropyl ester isobutyrate (16883-83-3)**
Fish 96-h LC_{50} (mg/L)	No Data NES (RA)	No Data NES (RA)	**NES**	No Data NES (RA)	No Data NES (RA)	**NES***	**NES**
Aquatic Invertebrates 48-h EC_{50} (mg/L)	No Data NES (RA)	No Data NES (RA)	**NES**	No Data NES (RA)	No Data NES (RA)	**NES**	**7.5 (m)***
Aquatic Plants 72-h EC_{50} (mg/L)	No Data NES (RA)	No Data NES (RA)	**NES (8-d)**	No Data NES (RA)	No Data NES (RA)	**NES**	**NES**
Chronic Toxicity to Fish 21-d NOEC (mg/L)	No Data NES (RA)	No Data NES (RA)	No Data NES (RA)	No Data NES (RA)	No Data NES (RA)	No Data NES (RA)	No Data NES (RA)
Chronic Toxicity to Invertebrates 21-d LOEC (mg/L)	No Data NES (RA)	No Data NES (RA)	**NES**	No Data NES (RA)	No Data NES (RA)	**NES**	No Data NES (RA)

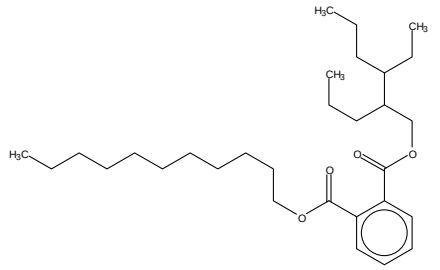
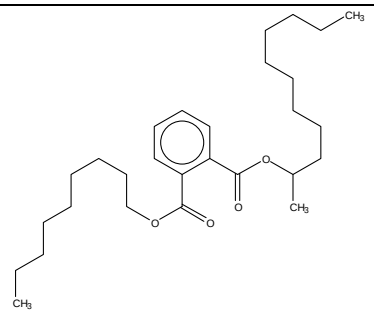
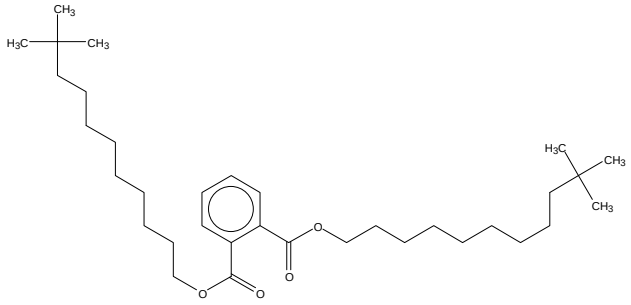
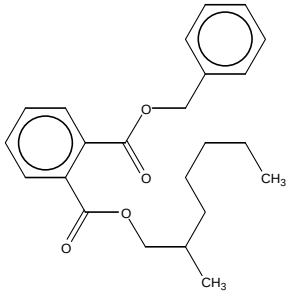
NES = no effects at saturation (water solubility limit); **(m) = measured data (i.e., derived from testing;** (RA) = Read Across; – indicates that endpoint was not evaluated for this substance. * = carrier solvent was used in the experiment.

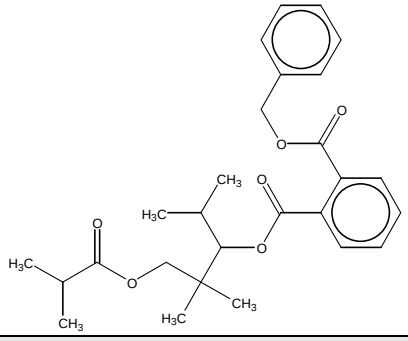
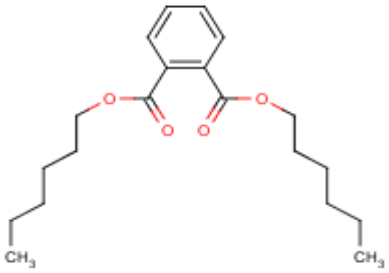
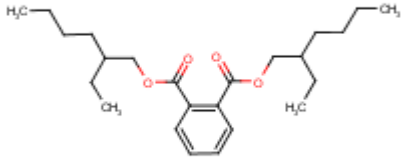
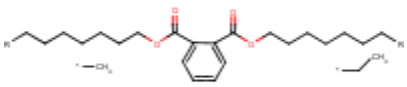
Appendix A

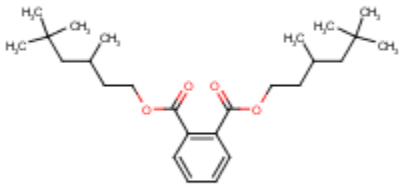
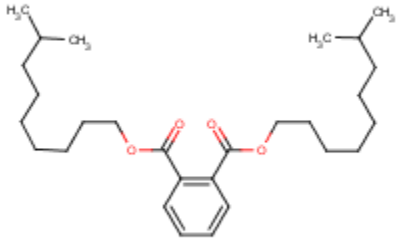
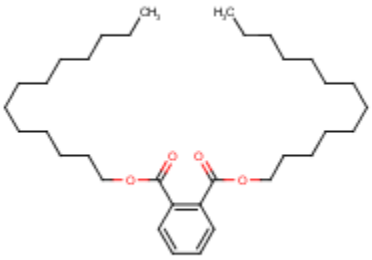
Phthalate Esters Category Members		
CASRN	**Chemical Name**	**Structure**
SPONSORED CHEMICALS		
131-11-3	**Dimethyl phthalate (DMP) [CA Index Name: 1,2-benzenedicarboxylic acid, dimethyl ester]**	
84-66-2	**Diethyl phthalate (DEP) [CA Index Name: 1,2-benzenedicarboxylic acid, diethyl ester]**	
68515-50-4	**Dihexyl phthalate, mixed isomers (DHP) [CA Index Name: 1,2-benzenedicarboxylic acid, dihexyl ester, branched and linear]**	 Representative Structure
68515-44-6	**Diheptyl phthalate, branched and linear isomers (DinHP) [CA Index Name: 1,2-benzenedicarboxylic acid, diheptyl ester, branched and linear]**	 Representative Structure
71888-89-6	**C_7 rich di-C_{6-8} –branched alkyl phthalates (DIHP) [CA Index Name: 1,2-benzenedicarboxylic acid, di-C_{6-8} branched alkyl ester, C_7 rich]**	 Representative Structure

Phthalate Esters Category Members		
CASRN	**Chemical Name**	**Structure**
111381-89-6	**Di (heptyl, nonyl) phthalate, branched and linear isomers (Din79P)** **[CA Index Name: 1,2-benzenedicarboxylic acid, heptyl nonyl ester, branched and linear]**	 Representative Structure
111381-90-9	**Di (heptyl, undecyl) phthalate (branched and linear isomers) (711P)** **[CA Index Name: 1,2-benzenedicarboxylic acid, heptyl undecyl ester, branched and linear]**	 Representative Structure
27554-26-3	**Diisooctyl phthalate (DIOP)** **[CA Index Name: 1,2-benzenedicarboxylic acid, diisooctyl ester]**	 Representative Structure
68648-93-1	**Mixed hexyl, octyl, decyl phthalates (610P)** **[CA Index Name: 1,2-benzenedicarboxylic acid, mixed decyl, hexyl, and octyl diesters]**	 Representative Structure

Phthalate Esters Category Members		
CASRN	**Chemical Name**	**Structure**
117-84-0	**Dioctyl phthalate (DnOP) [CA Index Name: 1,2-benzenedicarboxylic acid, dioctyl ester]**	
68515-45-7	**Dinonyl phthalate, branched and linear isomers (DNP) [CA Index Name: 1,2-benzenedicarboxylic acid, dinonyl ester, branched and linear]**	 Representative Structure
68515-43-5	**Di-C_{9-11} branched and linear alkyl phthalates (911P) [CA Index Name: 1,2-benzenedicarboxylic acid, di-C_{9-11} branched and linear alkyl esters]**	 Representative Structure
84-77-5	**Didecyl phthalate (DDP) [CA Index Name: 1,2-benzenedicarboxylic acid, didecyl ester]**	
3648-20-2	**Diundecyl phthalate (DUP) [CA Index Name: 1,2-benzenedicarboxylic acid, diundecyl ester]**	

Phthalate Esters Category Members		
CASRN	**Chemical Name**	**Structure**
85507-79-5	**1,2-benzenedicarboxylic acid, di (C_{11}) ester, branched and linear (DIUP) [CA Index Name: 1,2-Benzenedicarboxylic acid, diundecyl ester, branched and linear]**	 Representative Structure
111381-91-0	**1,2-benzenedicarboxylic acid, (C_9, C_{11}) ester, branched and linear (Din911P) [CA Index Name: 1,2-benzenedicarboxylic acid, nonyl undecyl ester, branched and linear]**	 Representative Structure
68515-47-9	**Ditridecyl phthalate (mixed isomers) (DTDP) [CA Index Name: 1,2-benzenedicarboxylic acid, di-C_{11-14} branched alkyl esters, C_{13} rich]**	 Representative Structure
68515-40-2	**Benzyl C_{7-9}-branched and linear alkyl phthalates (B79P) [CA Index Name: 1,2-benzenedicarboxylic acid, benzyl C_{7-9} branched and linear alkyl esters]**	 Representative Structure

Phthalate Esters Category Members		
CASRN	**Chemical Name**	**Structure**
16883-83-3	**1,2-benzenedicarboxylic acid, benzyl 3-hydroxy-1-isopropyl-2,2-dimethylpropyl ester isobutyrate (B84P) [CA Index Name: 1,2-benzenedicarboxylic acid, 2,2-dimethyl-1-(1-methylethyl)-3-(2-methyl-1-oxopropoxy) propyl phenylmethyl ester]**	
SUPPORTING CHEMICALS		
84-75-3	**Di-n-hexyl phthalate (DnHP) [CA Index Name: 1,2-benzenedicarboxylic acid, dihexyl ester]**	
117-81-7	**Diethylhexyl phthalate (DEHP) [CA Index Name: 1,2-benzenedicarboxylic acid, bis(2-ethylhexyl) ester]**	
68515-41-3	**Di-C_{7-9}-branched and linear alkyl phthalates (in79P) [CA Index Name: 1,2-benzenedicarboxylic acid, di-C_{7-9} branched and linear alkyl esters]**	

Phthalate Esters Category Members		
CASRN	**Chemical Name**	**Structure**
68515-48-0	**Diisononyl phthalate (DINP) [CA Index Name: 1,2-benzenedicarboxylic acid, diisononyl ester]**	
68515-49-1	**Diisodecyl phthalate (DIDP) [CA Index Name: 1,2-benzenedicarboxylic acid, diisodecyl ester]**	
119-06-2	**Ditridecyl phthalate (DTP) [CA Index Name: 1,2-benzenedicarboxylic acid, ditridecyl ester]**	
85-68-7	**Butyl benzyl phthalate (BBP) [CA Index Name: 1,2-benzenedicarboxylic acid, butyl phenylmethyl ester]**