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**HIGH PRODUCTION VOLUME (HPV)
CHEMICAL CHALLENGE PROGRAM**

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TEST PLAN

**FOR THE POLYOL ESTERS CATEGORY OF THE
ALIPHATIC ESTERS CHEMICALS**

Prepared by:

American Chemistry Council's
Aliphatic Esters Panel

August 24, 2004

POLYOL ESTERS HPV Test Plan

EXECUTIVE SUMMARY

The American Chemistry Council's (ACC) Aliphatic Esters Panel (Panel) hereby submits a revised test plan for the "polyol esters" category of the "aliphatic esters" chemicals, under the High Production Volume (HPV) Chemical Challenge Program. The Panel has used existing available public and company data in conjunction with scientific judgment/analysis to characterize the Screening Information Data Set (SIDS) of human health, environmental fate and effects, and physicochemical property endpoints for the polyol esters category.

This test plan addresses sixteen HPV polyol esters chemicals listed in Table 1A. The distinguishing feature of this category is that they represent structurally related polyol esters in which the fatty acids were linked to one or more of the multiple hydroxyl groups present in the polyol (alcohol portion of ester). The polyol is either trimethylolpropane (TMP), pentaerythritol (PE) or dipentaerythritol (diPE). The fatty acids range from C5-C18 in carbon number and include many natural fatty acids such as oleic, stearic and linoleic acids. The HPV polyol esters cover the C24-C77 carbon number range, depending on the extent of esterification of the polyol (e.g., monoesters, di-, tri-, tetraesters as well as hexaesters for dipentaerythritol). The polyol esters are used as synthetic lubricants, hydraulic fluids, and cosmetic ingredients, and in high temperature applications (e.g., transformer coolants, oven chain oils, high temperature greases).

The chemical and structural similarities of the polyol esters listed in Table 1A justify grouping these sixteen HPV chemicals together under the polyol esters category of the aliphatic esters. They have close commonalities in their physicochemical properties, chemical characteristics and biological/toxicological activities as a result of the structural polyol ester similarities in their molecules. Grouping these polyol esters together also represents a rational structural approach which will: (1) systematically compare existing data; (2) justify read-across assessments for structurally related or analogous polyol esters, and (3) develop a stepwise strategy test plan for the polyol esters substances based on their ester group type. The polyol esters as an ester group type are structurally differentiated from other aliphatic ester types such as the diacid esters, glycol esters and sorbitan esters.

Published information also is available for four structurally analogous surrogate polyol esters, which provides useful supplementary data to help toxicity data bridging for the HPV polyol esters. The four structurally analogous surrogate polyol esters are: (1) TMP ester of heptanoic and octanoic acid (CAS 189120-64-7); (2) hexanedioic acid, mixed esters with C9-C11 alcohols and TMP (CAS 180788-27-6); (3) hexanedioic acid, mixed esters with heptanoic, octanoic and decanoic acid and PE (CAS 68130-55-2); and (4) pentaerythritol esters of isooctanoic and C8-10 fatty acids (CAS Number not assigned yet).

Measured physicochemical property data are available for various HPV and surrogate polyol esters. In the course of preparing this Test Plan, computer estimation models were used to calculate physicochemical property and environmental fate data for the polyol esters. The calculated data were obtained using the EPIWIN and EQC (Level III) models that EPA has cited for use in the HPV Chemical Challenge Program. Use of the calculated and experimental values for HPV substances and for the surrogate polyol esters provides the information on the physicochemical and environmental fate properties of the chemicals in the polyol esters category to satisfy HPV pro-

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gram requirements. No additional testing for physicochemical and environmental fate properties is proposed.

Aquatic toxicity and biodegradation data exist for both the HPV polyol esters and the structurally analogous surrogate polyol esters to sufficiently allow for read-across assessments for the HPV substances and assist data bridging. No further aquatic toxicity and biodegradation testing is proposed for the polyol esters category of the aliphatic esters.

There are existing toxicity data for the HPV and structurally related surrogate polyol esters to sufficiently make hazard assessments for mammalian health effects (SIDS data endpoints) for the HPV polyol esters substances. The structurally analogous surrogate polyol ester substances include two TMP esters and two PE esters. Given the similar chemical and structural features between the HPV and surrogate polyol esters, the Panel was able to use the available existing data to make read-across assessments on potential toxicity and for toxicity data bridging for the HPV substances. No additional mammalian toxicity testing is proposed for substances in the polyol esters category. This resourceful use of existing data will help minimize the use of animals for testing while assessing the potential hazards in the polyol esters category of the aliphatic esters.

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The American Chemistry Council's Aliphatic Esters Panel includes the following member companies:

LIST OF MEMBER COMPANIES

Arizona Chemical Company

Cognis Corporation

ExxonMobil Chemical Company

Hercules Inc.

Inolex Chemical Company

Kaufman Holdings Corporation

Quaker Chemical Company

Reichhold, Inc.

Stepan Company

Uniqema

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Part I. HPV Substances in the Polyol Esters Category Test Plan

Part II. Surrogate Polyol Esters

TEST PLAN FOR THE POLYOL ESTERS CATEGORY OF THE ALIPHATIC ESTERS

1.0 INTRODUCTION

The American Chemistry Council's (ACC) Aliphatic Esters Panel (Panel) has committed voluntarily to develop a Screening Information Data Set (SIDS) (i.e., physicochemical data, environmental fate and effects, and human health effects) for the polyol esters category of aliphatic esters chemicals, listed under the High Production Volume (HPV) Chemical Challenge Program. This test plan sets forth how the Aliphatic Esters Panel intends to address the testing information for the sixteen polyol esters listed in Table 1A (organized by CAS Numbers in ascending order). The chemical structures of the polyol esters are given in Figure 1.

The Panel added three chemicals to the original polyol esters group of chemicals: Pentaerythritol tetrastearate (CAS 115-83-3), Fatty acids, tall-oil, tetraesters with pentaerythritol (CAS 68334-18-9), and Linseed oil, ester with pentaerythritol (CAS 68648-28-2). The other chemicals in this test plan were originally part of a larger test plan submitted on December 20, 2001. As a result of comments, the Panel has revised its original test plan for these chemicals, and the revised approach follows below.

The test plan identifies the CAS Numbers used to characterize the SIDS endpoints for the polyol esters in this category, describes the chemical and structural features/similarities of the polyol esters, identifies existing data of adequate quality for substances in the polyol esters category and provides the Panel's rationale for applying the available SIDS data to characterize the hazards of the category members. The primary objective of this effort is to identify and characterize the physicochemical properties, mammalian health and environmental fate and effects for the polyol esters category of the aliphatic esters consistent with the HPV Program.

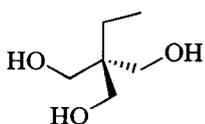
Developing a data matrix with reliable studies and applying justifiable read-across assessments will help provide a sufficiently robust data set to characterize the endpoints in the HPV Chemical Challenge Program. This approach to the resourceful use of existing data will help minimize the use of animals for testing while assessing the potential hazards in the polyol esters category of the aliphatic esters.

Table 1A. List of Individual Substances in the HPV Polyol Esters Category
(by ascending CAS Numbers and designated TSCA HPV chemical name)

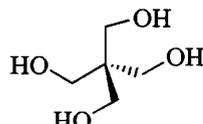
Chemical Name (designated TSCA HPV chemical name)	CAS Number
Pentaerythritol, tetrastearate	115-83-3
Nonanoic acid, triester with 2-ethyl-2-(hydroxymethyl)-1,3-propanediol	126-57-8
Decanoic acid, ester with 2-ethyl-2-(hydroxymethyl)-1,3-propanediol octanoate	11138-60-6
Nonanoic acid, neopentetetrayl ester	14450-05-6
9-Octadecenoic acid (Z)-, 2-ethyl-2-[[1-(1-oxo-9-octadecenyl)oxy]methyl]-1,3-propanediyl ester, (Z)-	57675-44-2
Carboxylic acids, C5-9, hexaesters with dipentaerythritol	67762-52-1
Carboxylic acids, C5-9, tetraesters with pentaerythritol	67762-53-2
Fatty acids, C14-18 and C16-18 unsatd, triesters with trimethylolpropane	68002-79-9
Decanoic acid, mixed esters with heptanoic acid, isovaleric acid, octanoic acid and pentaerythritol	68130-51-8
Decanoic acid, mixed esters with heptanoic acid, octanoic acid and trimethylolpropane	68130-53-0
Fatty acids, tall oil, tetra esters with pentaerythritol	68334-18-9
Fatty acids, C5-10, esters with pentaerythritol	68424-31-7
Fatty acids, C5-10, mixed esters with pentaerythritol and valeric acid	68424-34-0
Linseed oil, ester with pentaerythritol	68648-28-2
9-Octadecenoic acid (Z)-, ester with 2-ethyl-2-(hydroxymethyl)-1,3-propanediol	70024-57-6
Fatty acids, C5-10, esters with dipentaerythritol	70983-72-1

2.0 DESCRIPTION OF THE POLYOL ESTERS CATEGORY

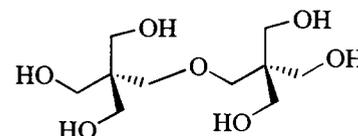
Sixteen CAS Numbers are used to describe the polyol esters in this HPV category of the aliphatic esters (Table 1A). The HPV polyol esters are comprised of esters of monoacids, mainly fatty acids, and trihydroxy or polyhydroxy alcohols or polyols such as trimethylolpropane (TMP) [or 2-ethyl-2-(hydroxymethyl)-1,3-propanediol], pentaerythritol (PE) and dipentaerythritol (diPE) (see structures below).



Trimethylolpropane (TMP) or
2-ethyl-2-(hydroxymethyl)-1,3-propanediol.



Pentaerythritol (PE)



Dipentaerythritol (diPE)

The polyol esters are unique in their chemical characteristics since they lack β -tertiary hydrogen atoms, thus leading to stability against oxidation and elimination. The fatty acids often range from

C5-C10 to as high as C18 (e.g., oleic, stearic, isostearic, linoleic acids) in carbon number and many are derived from naturally occurring sources (e.g., oleic, stearic acids, tall oil fatty acids, linseed oil fatty acids). Polyol esters may have multiple ester linkages and may include mixed esters derived from different carbon-length fatty acid mixtures.

The lack of β -tertiary hydrogen atoms in the structure of the polyol esters makes them characteristically and chemically stable against oxidation and elimination in comparison to other ester classes or groups. For these reasons, trimethylolpropane (TMP) and pentaerythritol (PE) esters with fatty acids of C5 to C10 carbon-chain length have applications as synthetic lubricants for passenger car motor oil and military and civilian jet engines. TMP and PE esters of C18 acids (e.g., isostearic and oleic acids) also have found use in synthetic lubricant applications, including refrigeration lubricants and hydraulic fluids. Because of their higher thermal stability characteristics, they find use in a variety of high temperature applications such as industrial oven chain oils, high temperature greases, fire resistant transformer coolants and turbine engines (Randles, 1999; Eisenhard, 1999). Polyol esters that are extensively esterified also have greater polarity, less volatility and enhanced lubricity characteristics.

Metabolism of the HPV polyol esters in animals would be expected to occur initially via enzymatic hydrolysis leading to the corresponding free fatty acids and free polyol alcohols. Therefore, PE and diPE esters are capable of being enzymatically hydrolyzed to generate pentaerythritol or dipentaerythritol, and the corresponding fatty acids which are comprised of oleic, linoleic and stearic acids (natural fatty acids) or fatty acids in the C5-10 carbon-length. Similarly, TMP esters can undergo enzymatic metabolism to yield trimethylolpropane (2-ethyl-2-hydroxymethyl-1,3-propanediol) and fatty acid constituents. Multiple-linked polyol esters may be subject to slower rates of enzymatic hydrolysis due to possible steric hindrance but nevertheless would be expected to be subsequently metabolized over a period of time. The free polyols and free fatty acids can be further metabolized or conjugated (e.g., glucuronides, sulfates, etc.) to polar products that are excreted in the urine [Bisesi (2001); Cragg (2001a,b); Bevan (2001b); Thurman (1992)]. Pentaerythritol, dipentaerythritol and trimethylolpropane have been reported to have low degrees of toxicity [BIBRA (1987); UNEP (2003); Proctor and Hughes (1996)]. The free fatty acids, including the natural occurring ones such as stearic, oleic and linoleic acids, have low degrees of toxicity [Cragg (2001a,b); Elder (1986, 1987); Chow (1999)].

Metabolic hydrolytic reactions of esters have been extensively reviewed in the literature [Testa and Mayer (2003); Bisesi (2001); Buchwald (2001); Parkinson (2001); Heyman (1982)]. It is beyond the scope of this test plan to discuss or review this topic in more detail except to mention its contribution in the general metabolism scheme for ester linkages.

Organization of the Sixteen HPV Polyol Esters According to Parent Polyol

Due to the large number of substances in this category, it is useful to organize the sixteen HPV polyol esters on the basis of the parent polyol rather than in the order of their CAS numbers given in Table 1A. Hence, Table 1B organizes the sixteen HPV polyol esters according to the parent polyol (i.e., TMP, PE, diPE) and to the fatty acid carbon-number range (within each parent polyol ester series).

Table 1B. Organization of 16 HPV Polyol Esters according to Parent Polyol
[e.g., arranged according to trimethylolpropane (TMP), pentaerythritol (PE) and dipentaerythritol (diPE)]

Individual Polyol Ester (organized according to Parent Polyol: TMP, PE , diPE) Chemical Name (designated TSCA HPV names)	CAS Number	Carbon Number in Fatty Acids	Carbon Number in Polyol	Total Carbons in Polyol Ester	MW
TMP Esters (Trimethylolpropane Esters)					
Decanoic acid, mixed esters with heptanoic acid, octanoic acid and trimethylolpropane	68130-53-0	C7,8,10	C6	C31	513
Decanoic acid, ester with 2-ethyl-2-(hydroxymethyl)-1,3-propanediol octanoate	11138-60-6	C8,10	C6	C24	415
Nonanoic acid, triester with 2-ethyl-2-(hydroxymethyl)-1,3-propanediol	126-57-8	C9	C6	C33	555
Fatty acids, C14-18 and C16-18 unsatd, triesters with trimethylolpropane	68002-79-9	C14,18,18	C6	C56	875
9-Octadecenoic acid (Z)-, ester with 2-ethyl-2-(hydroxymethyl)-1,3-propanediol	70024-57-6	C18	C6	C24	417
9-Octadecenoic acid (Z)-, 2-ethyl-2-[[[(1-oxo-9-octadecenyl)oxy]methyl]-1,3-propanediyl ester, (Z)-	57675-44-2	C18	C6	C60	928
PE Esters (Pentaerythritol Esters)					
Carboxylic acids, C5-9, tetraesters with pentaerythritol	67762-53-2	C5-9	C5	C33	529
Decanoic acid, mixed esters with heptanoic acid, isovaleric acid, octanoic acid and pentaerythritol	68130-51-8	C5,7,8,10	C5	C37	641
Fatty acids, C5-10, esters with pentaerythritol	68424-31-7	C5-10	C5	C35	613
Fatty acids, C5-10, mixed esters with pentaerythritol and valeric acid	68424-34-0	C5-10	C5	C35	613
Nonanoic acid, neopentetetrayl ester	14450-05-6	C9	C5	C41	697
Pentaerythritol, tetrastearate	115-83-3	C18	C5	C77	1202
Linseed oil, ester with pentaerythritol	68648-28-2	C18	C5	C77	1188
Fatty acids, tall oil, tetra esters with pentaerythritol	68334-18-9	C18	C5	C77	1190
diPE Esters (Dipentaerythritol Esters)					
Fatty acids, C5-10, esters with dipentaerythritol	70983-72-1	C5-10	C10	C60	927
Carboxylic acids, C5-9, hexaesters with dipentaerythritol	67762-52-1	C5-9	C10	C60	955

The arrangement of the HPV substances based on parent polyol will be useful in comparing and visualizing chemical/structural similarities among the analogous series of polyol esters in this HPV category and will provide a rational and systematic basis for using the existing read-across data to assess structurally analogous or homologous polyol esters.

As will be discussed in Section 4, in addition to the existing available data for the sixteen HPV polyol esters, there are significant amounts of relevant published or unpublished toxicity data that also exist for four structurally homologous or analogous polyol esters (denoted as "surrogate polyol esters") which provide useful read-across information.

The four relevant surrogate polyol esters are:

- TMP ester of heptanoic and octanoic acid (CAS 189120-64-7)
- Hexanedioic acid, mixed esters with C9-C11 alcohols and TMP (CAS 180788-27-6),
- Hexanedioic acid, mixed esters with heptanoic, octanoic and decanoic acid and PE (CAS 68130-55-2)
- Pentaerythritol esters of isooctanoic and C8-10 fatty acids (No CAS Number has been assigned yet)

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Incorporation of these four surrogate polyol esters into Table 1B (based on parent polyol) leads to Table 1C below which should be useful in the overall HPV data review and test plan evaluation and which should provide reasonable justification (based on structural, carbon number or MW similarities, etc.) to support read-across assessments.

Table 1C. Organization of the 16 HPV Polyol Esters and the 4 Surrogate* Polyol Esters according to the Parent Polyol in the HPV Data Assessment and Testing Rationale

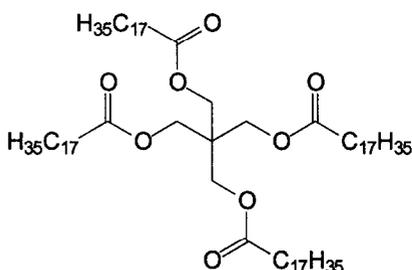
Individual Polyol Ester (organized according to Parent Polyol: TMP, PE, diPE) Chemical Name (designated TSCA HPV names)	CAS Number	Carbon Number in Fatty Acids	Carbon Number in Polyol	Total Carbons in Polyol Ester	MW
TMP Esters (Trimethylolpropane Esters)					
Decanoic acid, mixed esters with heptanoic acid, octanoic acid and trimethylolpropane	68130-53-0	C7,8,10	C6	C31	513
Trimethylolpropane ester of heptanoic and octanoic acid *	189120-64-7	C7,8	C6	C29	499
Hexanedioic acid, mixed esters with C10-rich, C9-11 isoalcohols and trimethylolpropane *	180788-27-6	C6	C6	C55	954
Decanoic acid, ester with 2-ethyl-2-(hydroxymethyl)-1,3-propanediol octanoate	11138-60-6	C8,9	C6	C24	415
Nonanoic acid, triester with 2-ethyl-2-(hydroxymethyl)-1,3-propanediol	126-57-8	C9	C6	C33	555
Fatty acids, C14-18 and C16-18 unsatd, triesters with trimethylolpropane	68002-79-9	C14,18,18	C6	C56	875
9-Octadecenoic acid (Z)-, ester with 2-ethyl-2-(hydroxymethyl)-1,3-propanediol	70024-57-6	C18	C6	C24	417
9-Octadecenoic acid (Z)-, 2-ethyl-2-[[[(1-oxo-9-octadecenyl)oxy]methyl]-1,3-propanediyl ester, (Z)-	57675-44-2	C18	C6	C60	928
PE Esters (Pentaerythritol Esters)					
Carboxylic acids, C5-9, tetraesters with pentaerythritol	67762-53-2	C5-9	C5	C33	529
Decanoic acid, mixed esters with heptanoic acid, isovaleric acid, octanoic acid and pentaerythritol	68130-51-8	C5,7,8,10	C5	C37	641
Fatty acids, C5-10, esters with pentaerythritol	68424-31-7	C5-10	C5	C35	613
Fatty acids, C5-10, mixed esters with pentaerythritol and valeric acid	68424-34-0	C5-10	C5	C35	613
Hexanedioic acid, mixed esters with heptanoic, octanoic and decanoic acid and pentaerythritol *	68130-55-2	C6,7,8,10	C5	C37	672
Nonanoic acid, neopentetetrayl ester	14450-05-6	C9	C5	C41	697
Pentaerythritol esters of isooctanoic and C8-10 fatty acids *	Has not been assigned	C8-10	C5	C41	698
Pentaerythritol, tetrastearate	115-83-3	C18	C5	C77	1202
Linseed oil, ester with pentaerythritol	68648-28-2	C18	C5	C77	1188
Fatty acids, tall oil, tetra esters with pentaerythritol	68334-18-9	C18	C5	C77	1190
diPE Esters (Dipentaerythritol Esters)					
Fatty acids, C5-10, esters with dipentaerythritol	70983-72-1	C5-10	C10	C60	927
Carboxylic acids, C5-9, hexaesters with dipentaerythritol	67762-52-1	C5-9	C10	C60	955

* These four surrogate polyol esters (highlighted or shaded) are not part of the HPV polyol esters category test plan. They are included in this matrix table since existing toxicity data for these materials can be used for read-across assessment or for toxicity data bridging for the HPV substances in the polyol esters category, based on their chemical /structural similarities.

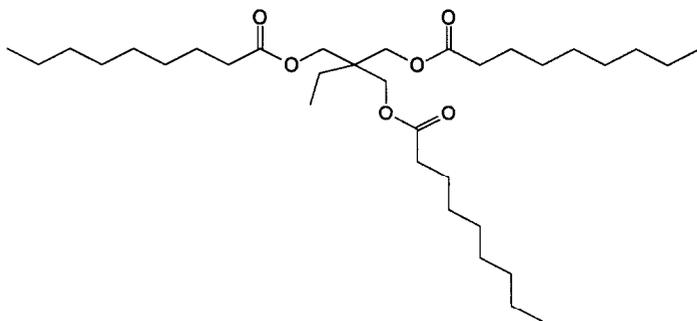
Figure 1. Chemical Structure of the Polyol Esters Listed in Table 1A

The structures of the HPV polyol esters are given in the order listed in Table 1A, which is organized according to ascending CAS Numbers. The chemical structure depicted for each HPV substance is consistent with the designated CAS Number and is considered representative of the commercial product evaluated.

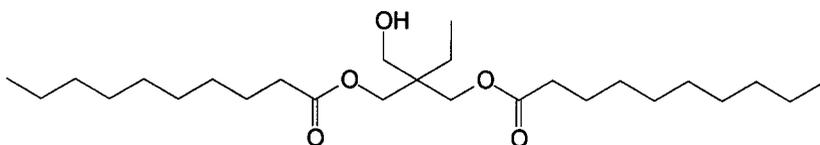
Pentaerythritol, tetrastearate (CAS 115-83-3)



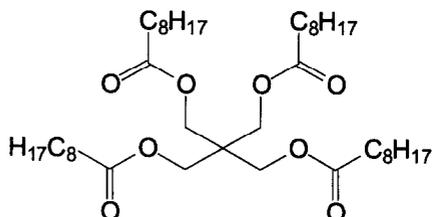
Nonanoic acid, triester with 2-ethyl-2-(hydroxymethyl)-1,3-propanediol (CAS 126-57-8)



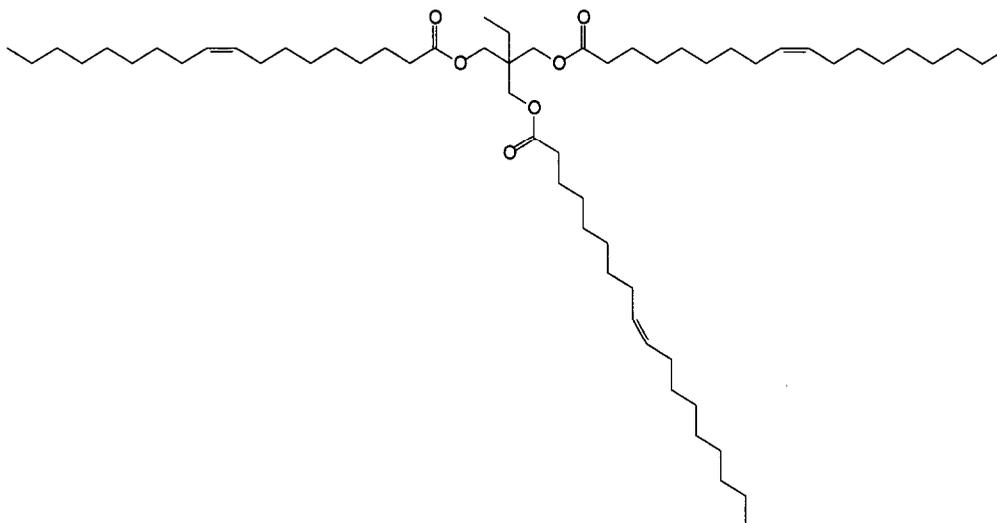
Decanoic acid, ester with 2-ethyl-2-(hydroxymethyl)-1,3-propanediol octanoate (CAS 11138-60-6)



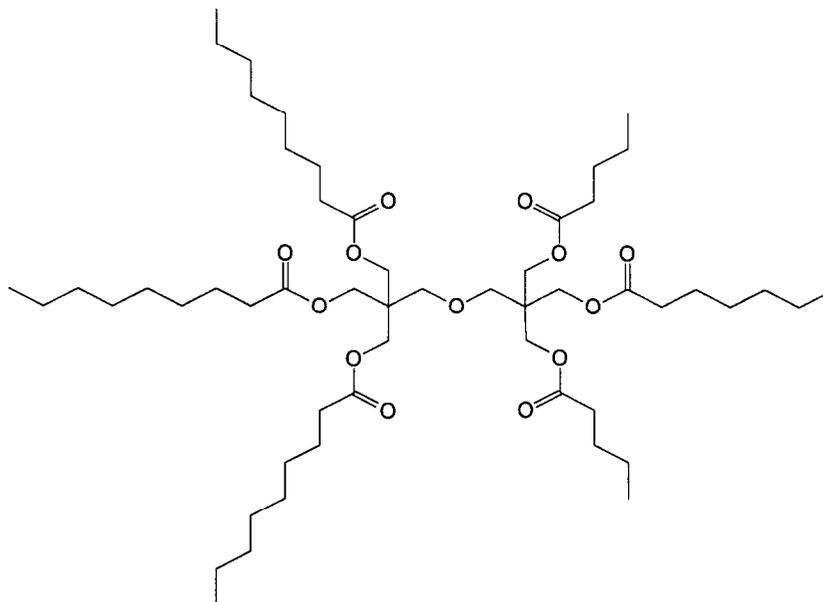
Nonanoic acid, neopentanetetrayl ester (CAS 14450-05-6)



9-Octadecenoic acid (Z)-, 2-ethyl-2-[[[(1-oxo-9-octadecenyl)oxy]methyl]-1,3-propanediyl ester, (Z)- (CAS 57675-44-2)

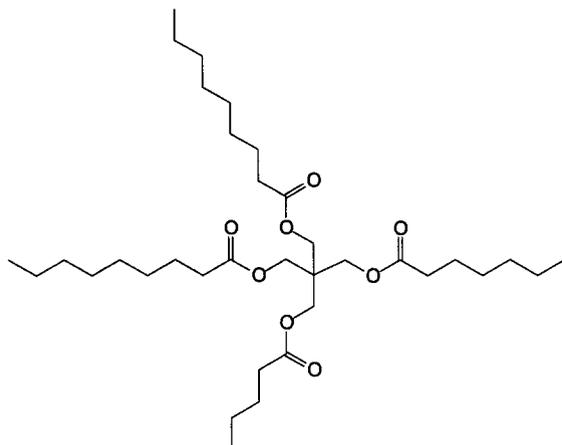


Carboxylic acids, C5-9, hexaesters with dipentaerythritol (CAS 67762-52-1)

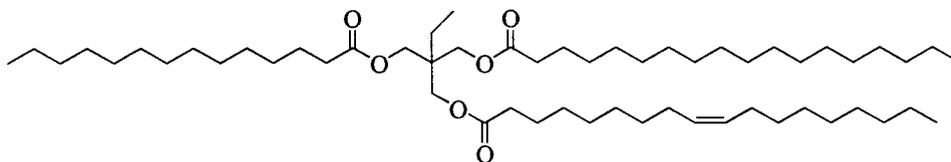


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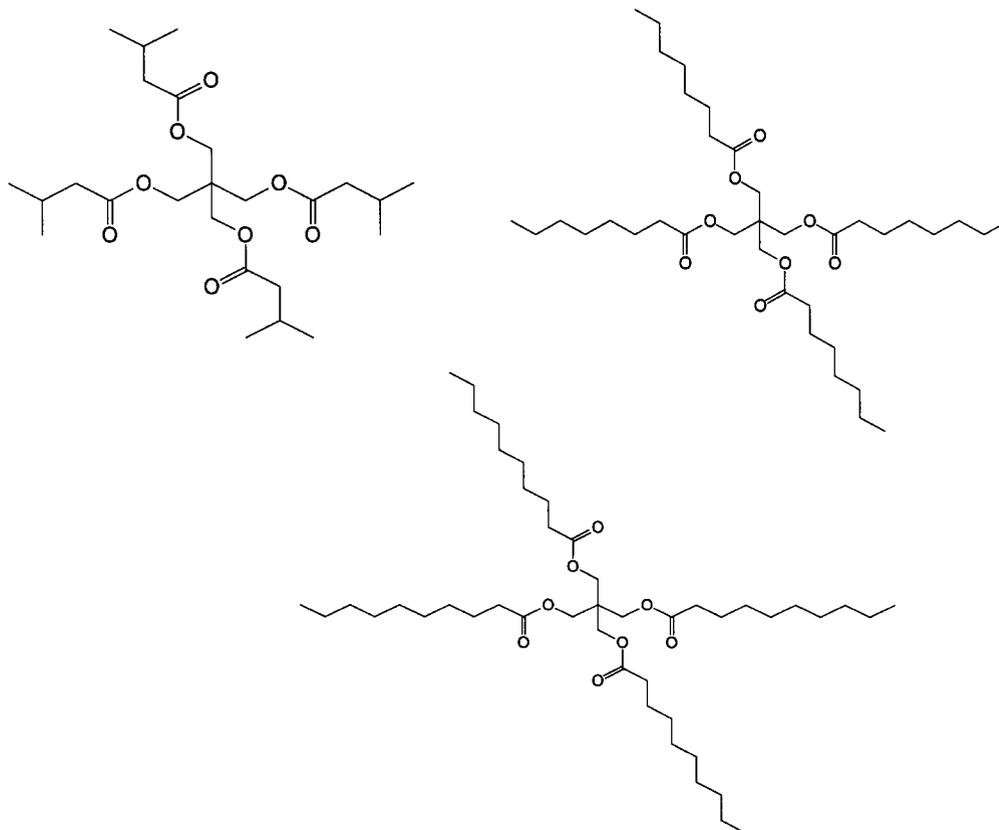
Carboxylic acids, C5-9, tetraesters with pentaerythritol (CAS 67762-53-2)



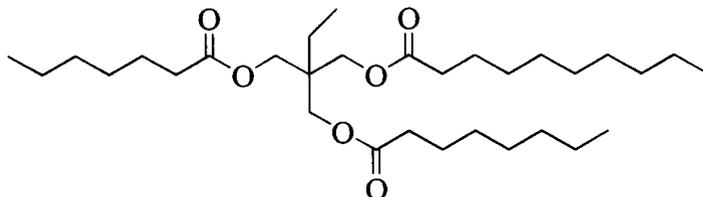
Fatty acids, C14-18 and C16-18 unsatd, triesters with trimethylolpropane (CAS 68002-79-9)



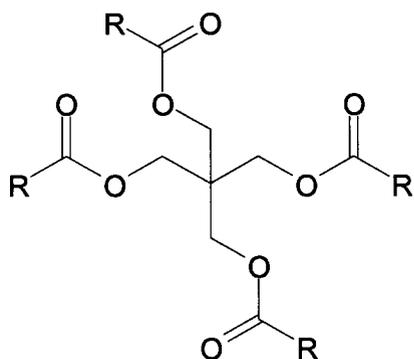
Decanoic acid, mixed esters with heptanoic acid, isovaleric acid, octanoic acid and pentaerythritol (CAS 68130-51-8)



Decanoic acid, mixed esters with heptanoic acid, octanoic acid and trimethylolpropane
(CAS 68130-53-0)

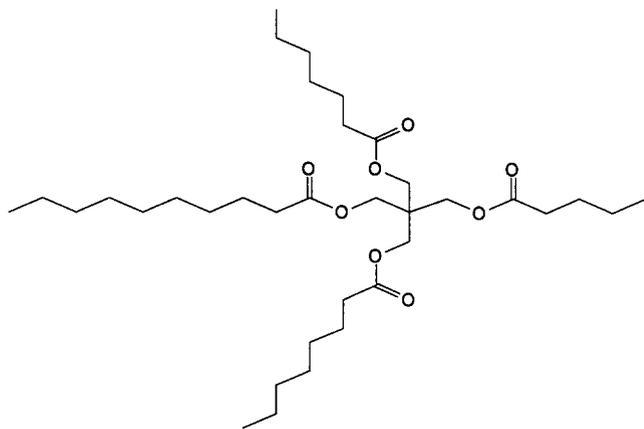


Fatty acids, tall oil, tetra esters with pentaerythritol (CAS 68334-18-9)



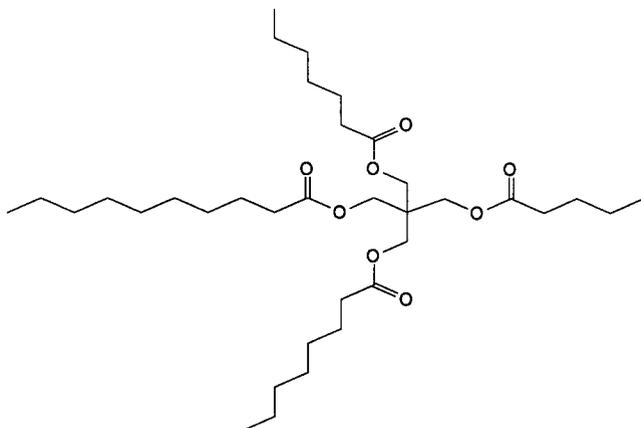
R = predominantly (70-90%) a mixture of
 $\text{---(CH}_2\text{)}_7\text{CH=CHCH}_2\text{CH=CH(CH}_2\text{)}_4\text{CH}_3$ and
 $\text{---(CH}_2\text{)}_7\text{CH=CH(CH}_2\text{)}_7\text{CH}_3$

Fatty acids, C5-10, esters with pentaerythritol (CAS 68424-31-7)

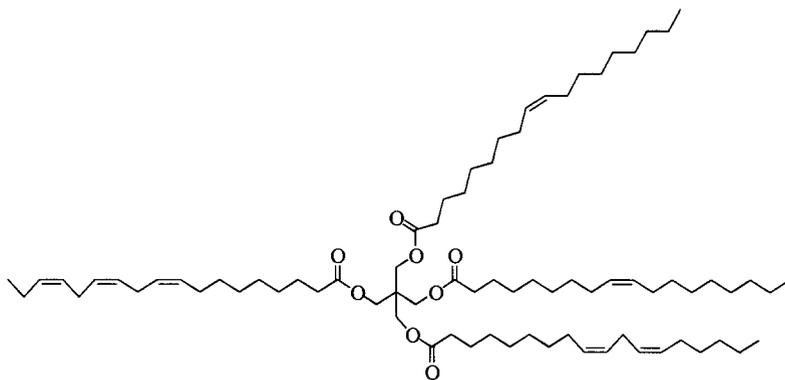


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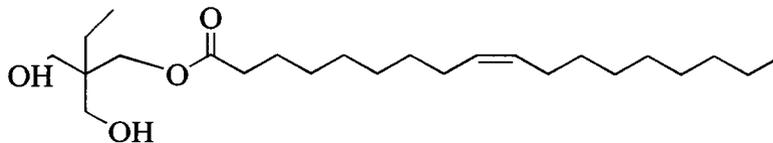
Fatty acids, C5-10, mixed esters with pentaerythritol and valeric acid (CAS 68424-34-0)



Linseed oil, ester with pentaerythritol (CAS 68648-28-2)



9-Octadecenoic acid (Z)-, ester with 2-ethyl-2-(hydroxymethyl)-1,3-propanediol (CAS 70024-57-6)



Fatty acids, C5-10, esters with dipentaerythritol (CAS 70983-72-1)

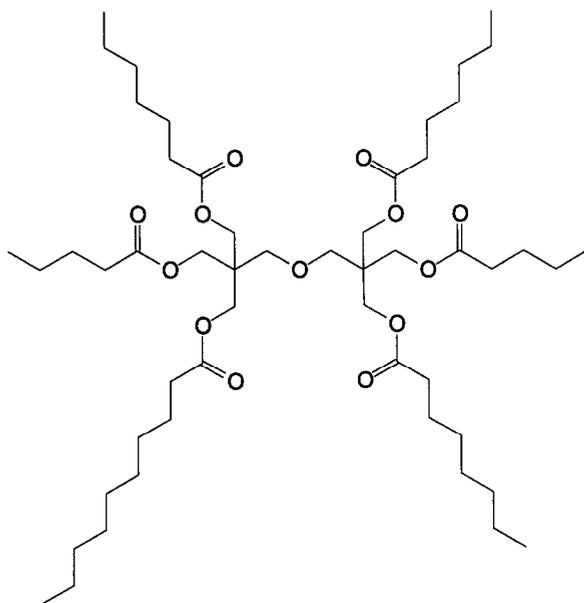
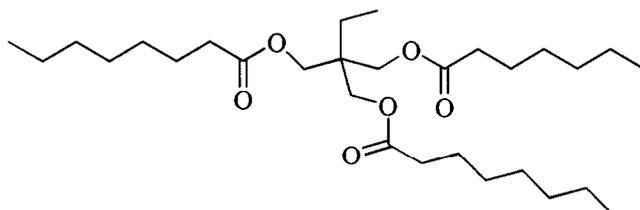
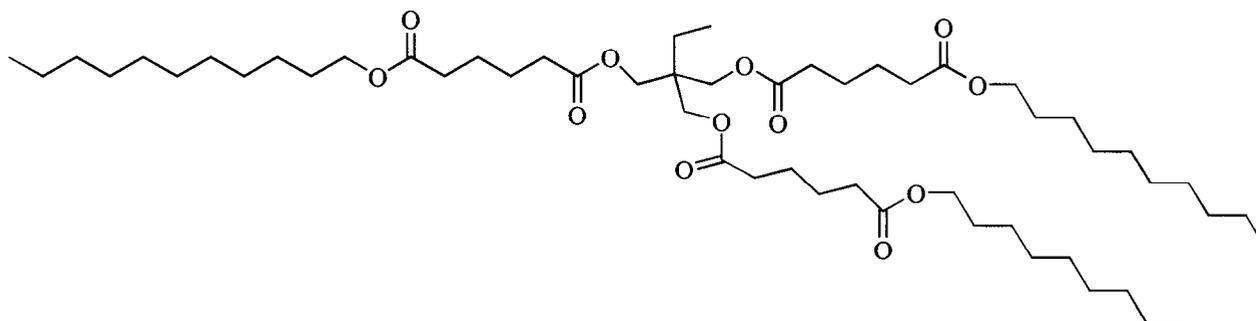


Figure 2. Chemical Structure of Surrogate Polyol Esters

Trimethylolpropane esters of heptanoic and octanoic acid (CAS 189120-64-7)

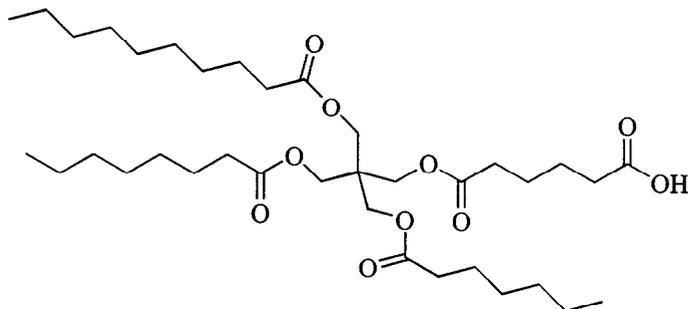


Hexanedioic acid, mixed esters with C9-C11 alcohols and trimethylolpropane (CAS 180788-27-6)

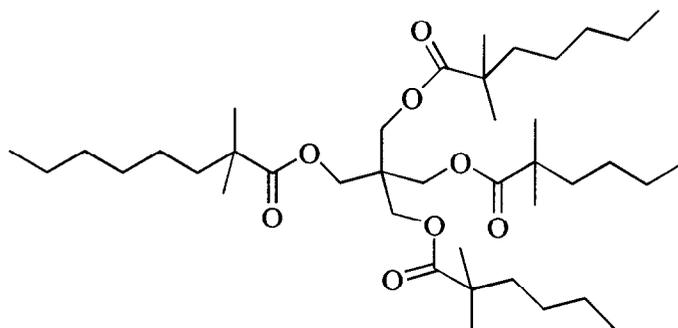


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Hexanedioic acid, mixed esters with heptanoic, octanoic and decanoic acid and pentaerythritol
(CAS 68130-55-2)



Pentaerythritol esters of isooctanoic and C8-10 fatty acids (CAS Number not assigned yet)



3.0 DESCRIPTION OF AVAILABLE PUBLIC AND COMPANY DATA

A review of the literature and Panel member company data was conducted on the physicochemical properties, mammalian toxicity endpoints, and environmental fate and effects for the sixteen polyol esters using CAS numbers and chemical names. Searches included the following sources: MEDLINE, RTECS and TOXLINE databases; the TSCATS database for relevant unpublished studies on these chemicals; and standard handbooks and databases (e.g., Sax, CRC Handbook on Chemistry and Physics, IUCLID, Merck Index, and other references) for physicochemical properties.

The reports were selected for review based on the following criteria: relevant SIDS endpoint, relevant CAS number, final report of company study (TSCATS), peer-reviewed journal, or comprehensive reviews.

3.1 Physicochemical Properties Data

Physicochemical data [i.e., melting point, boiling point, vapor pressure, water solubility and octanol-water partition coefficient] for the HPV polyol esters and the surrogate polyol esters were obtained from the searches and sources described above. In addition to available experimental and measured data, calculated physicochemical values were also incorporated into a summary table for all these physical and chemical properties. There are a number of reasons for this approach:

- The EPA guidance (www.epa.gov/chmrtk/robsumgd.htm) allows inclusion of calculated values in the robust summaries for physicochemical elements.
- A complete set of physical property data was a prerequisite to calculate fugacity or the chemical distribution in the environment (see below).
- Physicochemical properties had yet to be developed for some of the polyol esters.

The physicochemical properties were also modeled using the Syracuse Research Corp./EPA computer program EPIWIN, a modeling package that includes a number of algorithms developed for the EPA [EPIWIN (1999); US EPA (1999b)]. EPIWIN is the program used and advocated by the EPA. Because the model is a structure-property model, a specific discrete structure is required. EPIWIN contains a CAS number database, which contains the structures for a large number of chemicals. For mixtures, a single representative structure is contained in the database, and in this test plan, these surrogate chemical structures were accepted for further modeling.

3.2 Environmental Fate and Biodegradability Data

Environmental fate data including biodegradability, photodegradation, stability in water (i.e., hydrolysis) and fugacity (chemical distribution in the environment) data were primarily obtained through the literature, from unpublished company data, or from modeling [e.g., EPIWIN, EQC (Level III) - Mackay *et al.* (1996)]. When relevant studies (particularly biodegradability endpoints) were identified, the study reports were reviewed, robust summaries were prepared and the reliability of the data was assessed. The method of Klimisch *et al.* (1997) was utilized to evaluate the data quality and reliability of the studies.

3.3 Aquatic Toxicity Data

Existing data for aquatic toxicity studies (e.g., fish, invertebrate and algae) for the HPV and surrogate polyol esters were obtained primarily from the literature or from unpublished studies. When relevant studies were identified, the study reports were reviewed, robust summaries were prepared and the reliability of the data was assessed. The method of Klimisch *et al.* (1997) was utilized to evaluate the data quality and reliability of the aquatic toxicity studies.

3.4 Mammalian Toxicity Data

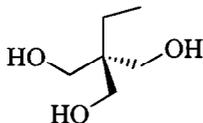
The existing data for the mammalian toxicity endpoints for the HPV polyol esters and the surrogate polyol esters were reviewed using the literature searches to identify the most relevant studies for the substances in the polyol esters category. For the HPV polyol esters that contained relevant data, the available studies were reviewed using the criteria outlined in the EPA's methods for determining the data quality and adequacy of the existing data and the reliability ranking method of Klimisch *et al.* (1997). Relevant studies that were available for the mammalian toxicity endpoints are summarized in the HPV test plan and presented in greater detail in the robust summaries in the Appendix.

Studies that were selected for the robust summaries generally represented those identified as the most relevant or reliable data for a particular SIDS endpoint. Published studies from the general literature as well as from a number of unpublished company reports were obtained and summarized. Some of the reported studies (particularly older acute data) could not be summarized because of limited experimental details to assess their quality (i.e., not assignable, Klimisch reliability code 4) or only were reported as LD₅₀ values from secondary sources. These studies were included in the summary data table and may be included in the robust summaries with reference to the secondary literature source.

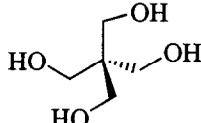
4.0 EVALUATION OF EXISTING DATA

The sixteen HPV substances in Table 1A were grouped together under the polyol esters category of aliphatic esters because they form a series of structurally related or analogous esters comprised of TMP esters, PE esters or diPE esters. The presence of a trihydroxy or "polyol" alcohol functionality was a distinguishing chemical /structural feature of the HPV polyol esters. Hence, these HPV substances are structurally related polyol esters derived from fatty acids, ranging from C5-C18 in carbon number which include many natural fatty acids (e.g., oleic, stearic acid, linseed oil and tall oil fatty acids). The polyol portion of the HPV substances consisted of either:

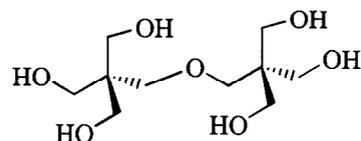
- 1) Trimethylolpropane (TMP)
- 2) Pentaerythritol (PE)
- 3) Dipentaerythritol (diPE)



Trimethylolpropane (TMP) or
2-ethyl-2-(hydroxymethyl)-1,3-propanediol.



Pentaerythritol (PE)



Dipentaerythritol (diPE)

Since multiple hydroxy groups are present in the parent polyol molecules (see structures above of TMP, PE and diPE), the HPV polyol esters may have multiple ester linkages and may include mixed esters having different carbon-length fatty acids.

Four surrogate polyol esters, which are not on the HPV list, were also reviewed because they are chemically similar or structurally analogous and provide useful data for bridging the toxicity of HPV substances in this category.

The four surrogate polyol esters are:

- Trimethylolpropane ester of heptanoic and octanoic acids (CAS 189120-64-7).
- Hexanedioic acid, mixed esters with C9-C11 alcohols and trimethylolpropane (CAS 180788-27-6).
- Hexanedioic acid, mixed esters with heptanoic, octanoic and decanoic acid and pentaerythritol (CAS 68130-55-2).
- Pentaerythritol esters of isooctanoic and C8-10 fatty acids (CAS Number not assigned yet).

The existing data, located in the literature search and Panel member company search, for the HPV polyol esters and for the surrogate polyol esters have been reviewed. Discussion will be provided in this section regarding the available data for SIDS toxicity endpoints, an assessment and summary of the data, and comments on HPV test plan as to whether the existing data are adequate for that purpose and whether further testing is proposed. The order of discussion of endpoints will be: (1) physicochemical properties; (2) environmental fate and biodegradability; (3) aquatic toxicity; and (4) mammalian health effects.

4.1 Physicochemical Properties Data

Summary of Physicochemical Properties Data

The physicochemical properties for the HPV polyol esters and surrogate polyol esters are summarized in Table 2. EPIWIN was used to calculate the physicochemical properties for the sixteen HPV polyol esters as well as for the four surrogate polyol esters. The experimental data and calculated (EPIWIN) data for the physicochemical properties of the polyol esters are summarized in Table 2.

Data Assessment and Test Plan for Physicochemical Properties

The HPV polyol esters covered the carbon-number range from C24 to C77. This reflects the range of fatty acids [C5 to C18], the polyol (TMP, PE or diPE) and the degree of esterification [e.g., monoester to hexaesters] in the substances. The chain-length of the fatty acids in the polyol esters as well as the degree of esterification (e.g., monoester *versus* triester for the TMP series, monoester *versus* tetraester for the PE series) would be expected to influence water solubility, boiling point, lipophilicity and vapor pressure as observed from the calculated values in Table 2. The predicted boiling point and partition coefficient were predicted to be much higher for the HPV substance TMP trioleate (i.e., CAS 57675-44-2) than the corresponding TMP monooleate (i.e., CAS 70024-57-6). Also the vapor pressure and water solubility of the TMP trioleate would be expected to be much lower than the corresponding TMP monooleate which were consistent with the predicted values (Table 2). Relative comparison of the C5-9 esters of PE and diPE (CAS 67762-53-2 and CAS 67762-52-1, respectively) indicated that the dipentaerythritol hexaester had a higher boiling point and partition coefficient and a lower vapor pressure and water solubility than those of the corresponding pentaerythritol tetraester.

In general, the polyol esters have molecular weights of greater than 400, have high boiling points greater than >400°C and are expected to be relatively non-volatile, lipophilic (log P > 7) and water-insoluble.

Based on the summarized data in Table 2, for purposes of the HPV Program there are sufficient physicochemical data to characterize the substances in the polyol esters category and no additional testing is proposed.

4.2 Environmental Fate and Biodegradability Data

Summary of Environmental Fate and Biodegradability Data

The environmental fate and biodegradability data relevant to the polyol esters category are summarized in Table 2 and Table 3, respectively. Biodegradation testing has been carried out for six HPV polyol esters and for four surrogate polyol esters. The reported biodegradability data covered the C24 to C60 range for the polyol esters (Table 3).

Other environmental fate endpoints such as photodegradation, stability in water (hydrolysis), and chemical distribution (transport) in the environment (fugacity modeling) have been calculated for the polyol esters using EPIWIN. Calculated hydrolysis half-lives and atmospheric photodegradation rates for the polyol esters using EPIWIN are summarized in Table 2.

Chemical distribution of the polyol esters in the environment has been determined using the EQC (Level III) fugacity-based multimedia model [Mackay *et al.* (1996)]. The calculated values for the transport (or distribution) in the soil, air, water and sediment environmental compartments are summarized in Table 2.

Data Assessment and Test Plan for Environmental Fate and Biodegradability

Biodegradability results have been reported for six of the sixteen HPV polyol esters as well as for all four surrogate HPV polyol esters (see Table 3). The tested polyol esters showed considerable or extensive biodegradation in the standard 28-day test and these findings indicate that polyol esters are capable of undergoing biodegradation which likely involve initial microbial or enzymatic metabolic ester cleavage, leading to the corresponding fatty acids and polyol alcohols. Interestingly, the biodegradability findings observed for many of the polyol esters [especially trimethylolpropane esters containing oleic acid as well as C5-C10 carboxylic acids] indicate that enzymatic cleavage of the ester linkage(s) must be occurring extensively and rapidly, in order to achieve the level of biodegradation observed. This would be consistent with the fact that natural fatty acids such as oleic acid, resulting from enzymatic cleavage of the parent polyol esters, are rapidly biodegraded (Verschuere, 1996; Swisher, 1987). In addition, the results are also consistent with the fact the free pentaerythritol can undergo extensive biodegradation (84% biodegradation in 28 days) (Birch *et al.* 1991).

Thus, there is sufficient biodegradability information available from HPV and surrogate substances (C24-C60 range covered) to provide useful data for read-across for the polyol esters, based on the chemical similarities of the polyol fatty acid esters. The existing biodegradability data is considered adequate to address the biodegradability potential of the structurally related HPV polyol esters substances and, therefore, no further biodegradation testing is proposed.

In addition, hydrolysis half-lives and atmospheric photodegradation rates were calculated by EPIWIN. Environmental distribution was determined using the EQC (Level III) model (Mackay, *et al.* 1996). The distribution between the environmental compartments for polyol esters in this category appears to be influenced by lipophilicity or water solubility. For lipophilic polyol esters that have calculated $\log Pow \geq 7$ and $>C24$, the EQC (Level III) model predicted a predominant chemical distribution in the sediment and soil compartment (see Table 2). Based on the calculated data for these environmental fate endpoints in Table 2, for purposes of the HPV Program sufficient data exist and no additional testing is proposed for the substances in the polyol esters category.

4.3 Aquatic Toxicity Data

Summary of Aquatic Toxicity Data

Twenty-five acute aquatic toxicity studies (e.g., fish, invertebrates, algae) relevant to the polyol esters category are summarized in Table 3. Aquatic toxicity testing have been reported for seven HPV polyol esters and for four structurally analogous surrogate polyol esters (see Table 3). The ACC Aliphatic Esters Panel believes that the existing acute aquatic toxicity data for the HPV substances and the surrogates tested, collectively, provide sufficient information to help assess the potential aquatic toxicity for the substances in the polyol esters category or to reasonably justify read-across assessments for bridging toxicity data based on the structural and chemical similarities of the polyol (fatty acid) esters.

Data Assessment and Test Plan for Aquatic Toxicity

Seven HPV polyol esters and four structurally analogous surrogate polyol esters have been adequately tested for acute toxicity in aquatic organisms (see Table 3 and robust summaries). The acute aquatic studies followed generally accepted test guidelines in which water accommodated fractions (WAFs) were often generated for poorly water-soluble lubricant or petroleum test materials at nominal loading rates and then evaluated for toxicity. However, the ACC Panel believes that in cases where the LC₅₀ or EC₅₀ values (based on nominal loading rates to generate the WAFs or water test solutions) clearly exceed the water solubility of the polyol ester and appear exceeding improbable (e.g., >1000 mg/L or >5000 mg/L), it would be more appropriate to note that the toxicity endpoint (LC₅₀ or EC₅₀ value) greatly exceeded the maximum water solubility limit (WSL) of the test material. For very water insoluble test materials, the existing data suggest that aquatic toxicity would not be expected at the maximum water solubility limit (WSL) or at water saturated levels, typical of WAF solutions generated from high nominal loading rate concentrations. In several studies, measured concentrations in collected water samples indicated low but detectable presence of the test substances (albeit high nominal loading rates). At these water saturated limits or at concentrations close to the maximum water solubility limit (WSL), there was no reported toxicity to aquatic organisms (see Robust Summaries in Appendix).

The data for a majority of the polyol esters indicated a low degree of acute toxicity in aquatic species. The actual LL₅₀ or EL₅₀ values reported were much higher than their calculated maximum water solubility limit (see robust summaries and Tables 2 and 3). The low degree of observed acute aquatic toxicity is likely to be attributable to the very low water solubility of the polyol esters. In addition, there are published data which indicate that the constituent free parent polyols (i.e., trimethylolpropane, pentaerythritol and dipentaerythritol) that are generated from enzymatic ester hydrolysis have low degrees of aquatic toxicity [see SIDS documents for the TMP, PE and diPE (UNEP, 2003)].

Overall, there are adequate aquatic toxicity data in fish, daphnids and algae to cover the TMP, PE and diPE polyol esters in the C24 to C60 range. The available data (Table 3) indicate that acute aquatic toxicity would not be expected at the water solubility limits (WSL) of the polyol esters. Because of the structural similarities between the polyol esters and because of their very limited water solubility (especially those esters >C60 and the C77 polyol esters), the existing data should be adequate to address the aquatic toxicity potential of the members of the polyol esters category and, therefore, no additional aquatic toxicity testing is proposed.

4.4 Mammalian Toxicity Data

A) Acute Mammalian Toxicity

Summary of Available Acute Oral Toxicity Data

Acute oral toxicity data relevant to the polyol esters category are summarized in Table 3 and have been reported for nine of the sixteen HPV polyol esters and for all of the four structurally analogous surrogate polyol esters. There were no deaths when the HPV polyol esters and the surrogate polyol esters were administered at doses of >2000 mg/kg. Overall, the acute oral LD₅₀ for these substances was greater than the 2000 mg/kg, indicating a very low order of toxicity for the polyol esters.

Data Assessment and Test Plan for Acute Mammalian Toxicity

Adequate acute oral toxicity studies have been conducted for nine HPV polyol esters and four structurally analogous surrogate polyol esters. The data consistently demonstrate a very low order of acute oral toxicity for the polyol esters in the C24-C77 carbon number range. The similarity in the low order of toxicity for these substances is consistent with the structural similarities among the polyol fatty acid esters and supports the scientific justification for toxicity data bridging. No additional acute toxicity testing is proposed for substances in the polyol esters category.

B) Mutagenicity and Genotoxicity

Summary of Mutagenicity and Genotoxicity Data

The mutagenicity and genotoxicity data for the HPV substances in the polyol esters category and structurally analogous surrogate polyol esters are summarized in Table 3. Bacterial gene mutation (Ames) assays, *in vitro* chromosomal aberration assays and *in vivo* micronucleus assays have been conducted for these substances. Neither mutagenicity nor clastogenicity were exhibited by any of these polyol esters in the cited *in vitro* tests, with or without metabolic activation. The HPV and surrogate polyol esters tested did not produce any increase in micronuclei formation and did not induce cytotoxicity in the bone marrow of rodents in any of the *in vivo* micronucleus assay studies.

Bacterial Gene Mutation (Ames) Assay

Five HPV polyol esters [i.e., CAS 11138-60-6; CAS 126-57-8; CAS 67762-53-2; CAS 67762-52-1; CAS 68648-28-2] have been adequately tested in bacterial reverse mutation (Ames) tests. All five tested HPV substances were negative for mutagenic activity, with and without metabolic activation. The four surrogate polyol esters have also been evaluated for mutagenicity and were found to be negative in bacterial reverse mutation assay, with and without metabolic activation (Table 3).

In vitro Chromosomal Aberration Assay

Two HPV polyol ester substances [i.e., CAS 11138-60-6 and CAS 68648-28-2] and four surrogate polyol esters [i.e., CAS 189120-64-7; CAS 180788-27-6; CAS 68130-55-2; PE esters with isooctanoic and C8-10 fatty acids] have been adequately tested for chromosomal aberrations in the Chinese hamster ovary (CHO) cell assay. These polyol ester substances tested did not cause chromosomal aberrations, with and without metabolic activation.

In vivo Mammalian Micronucleus Assay

The HPV polyol ester, carboxylic acids C5-9, tetraesters with pentaerythritol [CAS 67762-53-2], was negative in the micronucleus test in the rat (*in vivo*). In addition, three surrogate polyol esters [i.e., CAS 189120-64-7; CAS 180788-27-6; PE esters with isooctanoic and C8-10 fatty acids] have been evaluated in the *in vivo* mouse micronucleus test and have all been demonstrated to be negative. These three surrogate polyol esters did not produce any increase in micronuclei formation and did not induce cytotoxicity in the bone marrow of CD-1 mice administered two or three single oral doses (500, 1000 or 2000 mg/kg) of the test substance.

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Data Assessment and Test Plan for Mutagenicity and Genotoxicity

Five HPV polyol esters and four surrogate polyol esters have been adequately tested for gene mutations in bacterial cells, with and without metabolic activation. Although only five HPV polyol esters (which covered the C24 to C60 carbon-number range) and four surrogate substances have been tested for mutagenicity, these tested substances were shown to be not mutagenic. Collectively, these nine tested substances can be used to bracket the mutagenicity potential of the polyol esters category. Three HPV polyol esters [i.e., CAS 11138-60-6; CAS 67762-53-2; CAS 68648-28-2] along with the four surrogate polyol esters (structural analogs which covered the C29 to C55 carbon-number range) have been tested and the data are useful for bracketing the genotoxicity of the polyol esters category. The data consistently demonstrated no evidence of mutagenicity or genotoxicity regardless of metabolic activation of polyol esters. This suggests that members of the polyol esters category and related structural analogs lack genotoxicity due to their functional similarity in chemical structures and supports reasonable justification for bridging data within this HPV Challenge Program.

By bridging these data, members of the polyol esters category have been evaluated adequately for genotoxicity for purposes of the HPV Program, and no additional testing is proposed.

C) Repeated-Dose Toxicity

Summary of Repeated-Dose Toxicity Data

Adequate data on repeated dose toxicity are available for two HPV polyol esters [CAS 11138-60-6 and CAS 67762-53-2] and four structurally analogous surrogate polyol esters.

Repeated-Dose Dermal Toxicity

The HPV substance, TMP ester (C8, C10 acid) [CAS 11138-60-6], was evaluated for repeated dose toxicity in a 28-day dermal study at dose levels of 0, 125, 500, and 2000 mg/kg/day (administered 5-days a week). The effects noted as a result of treatment (viz., decrease in body weight and serum protein values) were slight and of little toxicological concern. There was no evidence of microscopic changes noted in the histopathological evaluation; therefore, the NOAEL for TMP ester (C8, C10 acid) [CAS 11138-60-6] was 2000 mg/kg/day. The HPV substance, PE tetraester (C5-9 acid) [CAS 67762-53-2], was also evaluated for repeated dose toxicity in a 13-week dermal study at dose levels of 0, 800, and 2000 mg/kg/day (administered 5-days a week). The effects noted as a result of treatment (viz., slight decrease in body weight of male rats) were slight and not considered to represent toxicity. There was no evidence of microscopic changes noted during histopathology. The NOAEL for PE tetraester [CAS 67762-53-2] in this 13-week dermal toxicity study was 2000 mg/kg/day.

A surrogate polyol ester, hexanedioic acid, mixed esters with decanoic acid, heptanoic acid, octanoic acid and PE [CAS 68130-55-2], was also evaluated for repeated dose toxicity in a 28-day dermal toxicity study. CAS 68130-55-2 was applied to the skin of groups of 20 (male and female) rats for five days a week for four (4) weeks at dose levels of 0, 125, 500 and 2000 mg/kg/day. Treated animals exhibited no signs indicative of systemic toxicity. No visible signs of irritation were observed at treatment sites. Microscopically, treated skin (viz., greater than or equal to 500 mg/kg/day) exhibited a dose-related increased incidence and severity of hyperplasia and hyperkeratosis of the epidermis and sebaceous gland hyperplasia. These effects were reversible. None of the minor changes in hematology and serum chemistry parame-

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ters were considered biologically significant. High dose females (2000 mg/kg/day) exhibited a significant increase in relative adrenal and brain weights when compared to the controls. These differences were attributed to the lower final body weight of the female animals. The NOAEL in this study for systemic toxicity was established as 500 mg /kg/day and 125 mg/kg/day for skin irritation.

Results from these studies showed a low order of repeated-dose dermal toxicity are summarized in Table 3.

Repeated-Dose Oral Toxicity

Adequate available data for repeated-dose oral toxicity was not located for any of the HPV polyol esters. However, three 28-day oral toxicity studies in rats exist for the following structurally related surrogate polyol esters: CAS 189120-64-7; CAS 180788-27-6; and PE esters of isooctanoic and C8-10 fatty acids (CAS Number has not been assigned).

The surrogate polyol ester [CAS 189120-64-7] (which is TMP ester of heptanoic and octanoic acid), was also well tolerated by rats in a 28-day oral toxicity study. This material did not produce signs of overt systemic toxicity at any dose levels tested (i.e., 100, 300, and 1000 mg/kg/day). There were no treatment-related clinical in-life, functional observation battery, or gross post-mortem findings. There were no treatment-related mortality, and no adverse effects on body weight, food consumption, clinical laboratory parameters, or organ weights. However, there were increased numbers of hyaline droplets in the proximal cortical tubular epithelium of the 300 and 1000 mg/kg/day in male rats. Based on these findings (hyaline droplets), the NOAEL for this surrogate polyol ester [CAS 189120-64-7] was reported to be 100 mg/kg/day for male rats. However, hyaline droplet formation in the male rat kidneys has been subsequently shown to be a very gender- and species-specific condition (i.e., occurring only in male rats) for various chemicals including lipophilic esters and has been shown to have little toxicological relevance to humans.

In the repeated oral toxicity study of the surrogate polyol ester, [CAS 180788-27-6], groups of 10 (male and female) rats were administered by gavage (7-days a week) with dose levels of 0, 100, 300, and 1000 mg/kg/day. Overall, CAS 180788-27-6 did not cause chemical specific signs of systemic toxicity at any dose level tested. The kidney hyaline droplet formation in male rats only and the adaptive changes in the liver were not considered toxicologically significant and were not considered in the estimation of the NOAEL. Therefore, the NOAEL for CAS 180788-27-6 was established at 1000 mg/kg/day under the conditions of this study. As pointed out previously (see CAS 189120-64-7 above), the renal hyaline droplet formation is considered to be a gender- and species-specific biological response (male rats only) and considered not to be relevant to humans.

In the repeated dose toxicity study of PE esters of isooctanoic and C8-10 fatty acids [CAS Number not assigned], groups of 10 (male and female) rats were administered by gavage (7-days a week) with dose levels of 0, 100, 500, and 1000 mg/kg/day. Overall, PE esters of isooctanoic and C8-10 fatty acids, did not cause chemical specific signs of systemic toxicity at any dose level tested. On the basis of these results, the NOAEL for PE esters of isooctanoic and C8-10 fatty acids was established at 1000 mg/kg/day under the conditions of this study.

Results from these studies showed a low order of repeated-dose oral toxicity and are summarized in Table 3.

Data Assessment and Test Plan for Repeated-Dose Toxicity

A total of six repeated-dose toxicity studies using two different routes of administration have been reported for two HPV substances [decanoic acid, ester with 2-ethyl-2-(hydroxy methyl)-1,3-propanediol octanoate (CAS 11138-60-6), and carboxylic acid, C5-9, tetraester with pentaerythritol)(CAS 67762-53-2] and for four surrogate structurally related polyol esters (see Table 3). The results from these repeated dose toxicity studies suggest that polyol esters exhibit a low order of oral and dermal toxicity following repeated application. This may be attributable to similarities in their chemical structures, physicochemical properties, and common metabolic pathways (i.e., esters can be enzymatically hydrolyzed to the corresponding polyol and the corresponding fatty acids) which would support scientific justification for using the matrix set of toxicity information for bridging data gaps within the polyol ester category. Hence, by bridging these data, the polyol esters have been evaluated adequately for repeated exposure toxicity, and no additional testing is proposed.

D) Reproductive/Developmental Toxicity

Summary of Reproductive/Developmental Toxicity Data

Data for reproductive and developmental toxicity are available for two HPV polyol esters [CAS 11138-60-6 and 67762-53-2] and one structurally analogous surrogate polyol ester [i.e., PE esters of isooctanoic and C8-10 fatty acids, CAS Number not assigned yet].

Toxicity to reproduction

No adequate, available reproductive toxicity studies have been located for these polyol esters. However, there have been no adverse effects observed histopathologically for reproductive tissues (ovaries and testes) in the repeated dose toxicity studies in rats with the two HPV polyol esters, CAS 11138-60-6 and CAS 67762-53-2. In addition, two structurally analogous surrogate polyol esters [i.e., CAS 180788-27-6 and PE esters of isooctanoic and C8-10 fatty acids (CAS Number not yet assigned)] have been reported not to adversely affect female and male reproductive organs.

Since metabolism of the polyol esters can occur, leading to the generation of the corresponding fatty acids and the polyol alcohol (such as pentaerythritol, trimethylolpropane, and dipentaerythritol), the issue of whether these metabolites may pose any potential reproductive toxicity concerns is important to address. However, the polyol alcohols such as pentaerythritol, trimethylolpropane, and dipentaerythritol, would be expected to undergo further metabolism, conjugation and excretion in the urine. Available evidence indicates that these ester hydrolysates (i.e., hydrolysis products), primarily fatty acids (e.g., heptanoic, octanoic, and decanoic acids; see Cragg, 2001a) and secondarily the polyol alcohols should exhibit a low order of reproductive toxicity [see SIDS for TMP, PE and diPE (UNEP 2003)]. Thus, it can be concluded that this group of high molecular weight polyol esters would not be expected to produce reproductive effects in rodents and no further testing of substances is proposed.

Developmental Toxicity

Two HPV listed substances, decanoic acid, ester with 2-ethyl-2-(hydroxy methyl)-1,3-propanediol octanoate [CAS 11138-60-6] (which is a TMP ester with C8, C10 acids) and the carboxylic acids, C5-9, tetraesters with pentaerythritol [CAS 67762-53-2] (which is a PE tetraester with C5-9 acids) were evaluated for developmental toxicity. In addition, a structurally analogous surrogate polyol ester, PE esters of isooctanoic and C8-10 fatty acids [CAS Number not yet assigned] (PE mixed esters; C8-10 acids) was evaluated for developmental toxicity.

The HPV substance, TMP ester with C8, C10 acids [CAS 11138-60-6], was evaluated for developmental toxicological effects following dermal administration in rats at dose levels of 0, 200, 600, and 2000 mg/kg/day (administered on gestation days 6-15). As evaluated in this study, dermal application of this test article at a dosage of 2000 mg/kg/day was not selectively toxic to the development of the offspring (i.e., no adverse effects on embryo-fetal number, viability, external and visceral defects, body weight or morphology). The NOAEL for the HPV TMP ester [CAS 11138-60-6] in this developmental toxicity screening study in rats was 2000 mg/kg/day.

The HPV substance, PE tetraester (C5-9 acid) [CAS 67762-53-2], was also evaluated for developmental effects in a dermal developmental toxicity screening study in rats at dose levels of 0, 800, and 2000 mg/kg/day (administered daily on gestation days 0-19). The effects noted as a result of treatment was slight skin irritation (erythema and flaking) at the site of application. Neither maternal parameters nor reproductive parameters (number of implants, resorptions, or viable fetuses) were adversely affected at either of the dose levels tested. No evidence of teratogenicity was observed during external examination of the fetuses from pregnant dams. Mean fetal body weights and crown-rump distances were similar in all of the experimental groups. Dermal administration of CAS 67762-53-2 did not adversely affect *in utero* survival and developmental of concepti. The NOAEL for the PE tetraester [CAS 67762-53-2] in this developmental toxicity screening study in rats was 2000 mg/kg/day.

The surrogate polyol ester, pentaerythritol esters of isooctanoic and C8-10 fatty acids [CAS Number not yet assigned] (PE mixed esters; C8-10 acids), was also evaluated for developmental effects in an oral developmental toxicity screening study in rats at dose levels of 0, 100, 500, and 1000 mg/kg/day (administered daily on gestation days 6-15). There was no evidence of maternal toxicity observed at any dose level tested. In the fetuses, there was no evidence of growth retardation or increased fetal death in the treated groups compared to controls. Additionally, there were no biologically significant differences in total or individual variations or malformations (external, visceral, or skeletal) in the treated groups when compared with controls on either a per fetus or per litter basis. Pentaerythritol esters of isooctanoic and C8-10 fatty acids, was not considered embryotoxic nor teratogenic under the conditions of this test. The NOAEL for pentaerythritol esters of isooctanoic and C8-10 fatty acids (CAS Number not yet assigned) was established at 1000 mg/kg/day.

No other adequate, available developmental toxicity studies have been located for HPV polyol esters. Since metabolism of the polyol esters can occur, leading to the generation of the corresponding fatty acids and the polyol alcohol (such as pentaerythritol, trimethylolpropane, and dipentaerythritol), the issue of whether these metabolites may pose any potential developmental toxicity concerns is important to address. However, the polyol alcohols such as pentaerythritol, trimethylolpropane, and dipentaerythritol, would be expected to undergo further metabolism, conjugation and excretion in the urine. Available evidence indicates that these ester hydrolysates, primarily

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fatty acids (e.g., heptanoic, octanoic, and decanoic acids; see Cragg, 2001a) and secondarily the free polyol alcohols should exhibit a low order of developmental toxicity [see OECD SIDS dossiers for toxicity reviews of TMP, PE and diPE (UNEP, 2003)]. Thus, it can be concluded that this group of high molecular weight polyol esters should not cause fetal toxicity and developmental anomalies in rodents and no further testing of substances is proposed.

Data Assessment and Test Plan for Reproductive/Developmental Toxicity

Data were available on the reproductive toxicity for members of the HPV polyol esters category [viz., two subchronic studies indicating no adverse effects to reproductive organs for two HPV substances (CAS 11138-60-6 and CAS 67762-53-2); and two subchronic studies of surrogate substances (CAS 180788-27-6 and PE esters of isooctanoic and C8-10 fatty acids) indicating no adverse effects to reproductive organs] and developmental toxicity [viz., CAS 11138-60-6; CAS 67762-53-2; and one surrogate substance (pentaerythritol esters of isooctanoic and C8-10 fatty acids)]. In addition, the ester hydrolysates of their primary fatty acids and polyol alcohols exhibit a low order of reproductive and developmental toxicity. It is unlikely that the polyol esters would cause reproductive and developmental effects based on their structural characteristics and *in vivo* metabolic processes. Based on the available reproductive/developmental toxicity data, no additional reproductive/developmental toxicity testing is proposed for the HPV polyol esters.

5.0 TEST PLAN SUMMARY

The American Chemistry Council's Aliphatic Esters Panel believes that sufficient health effects and toxicity data exist for the polyol esters category of the aliphatic esters (taking into account data available for structurally related and analogous surrogate polyol esters) to substantially characterize the mammalian health effects, aquatic toxicity and biodegradation endpoints for the members of this category under the HPV program (Table 4). No additional toxicity tests are proposed for the polyol esters category of the aliphatic esters.

Table 4. Assessment Plan for Substances in the Polyol Esters Category under the HPV Program

Polyol Ester Name (Type Ester; Fatty Acids) CAS Number	Mammalian Health Effects						Ecotoxicity-Biodegradation			
	Acute	Repeat dose	Genetic tox (mutation)	Genetic tox (chrom ab)	Reprod Tox	Develop Tox	Acute fish	Acute daphnia	Algal	Biodeg
Decanoic acid, mixed esters with heptanoic acid, octanoic acid and trimethylolpropane (TMP Ester; C7, 8, 10 Acid) CAS 68130-53-0	R	R	R	R	R	R	R	R	R	R
Trimethylolpropane esters of heptanoic and octanoic acid (TMP Ester; C7, 8 acid)* CAS 189120-64-7	√	√	√	√	-	-	√	√	√	√
Hexanedioic acid, mixed esters with C10-rich, C9-11 isoalcohols and TMP (TMP+C10+iso-C9-11 Alcohols, Mixed Ester, with C6-dioic acid)* CAS 180788-27-6	√	√	√	√	√	-	√	√	√	√
Decanoic acid, ester with 2-ethyl-2-(hydroxymethyl)-1,3-propanediol octanoate (TMP Ester; C8, C10 acids) CAS 11138-60-6	√	√	√	√	√	√	√	√	√	√
Nonanoic acid, triester with 2-ethyl-2-(hydroxymethyl)-1,3-propanediol (TMP Triester; C9 acid) CAS 126-57-8	√	R	√	R	R	R	√	√	√	√
Fatty acids, C14-18 and C16-18 unsatd, triesters with trimethylolpropane (TMP Triester; C14-18 satd, C16-18 unsatd acid) CAS 68002-79-9	R	R	R	R	R	R	R	R	R	R
9-Octadecenoic acid (Z)-, ester with 2-ethyl-2-(hydroxymethyl)-1,3-propanediol (TMP monoester; oleic C18 acid) CAS 70024-57-6	√	R	R	R	R	R	√	R	R	√
9-Octadecenoic acid (Z)-, 2-ethyl-2-[(1-oxo-9-octadecenyl)oxy]methyl]-1,3-propanediyl esterZ (TMP Triester; oleic C18 acid) CAS 57675-44-2	R	R	R	R	R	R	√	R	R	√
Carboxylic acids, C5-9, tetraesters with pentaerythritol (PE tetra ester; C5-9 acids) CAS 67762-53-2	√	√	√	√	√	√	√	R	R	√
Decanoic acid, mixed esters with heptanoic acid, isovaleric acid, octanoic acid and pentaerythritol (PE mixed esters; C7-8, 10 acids) CAS 68130-51-8	R	R	R	R	R	R	R	R	R	R
Fatty acids, C5-10, esters with pentaerythritol (PE esters, C5-10 acids) CAS 68424-31-7	√	R	R	R	R	R	R	R	√	R
Fatty acids, C5-10, mixed esters with pentaerythritol and valeric acid (PE esters, C5-10 acids) CAS 68424-34-0	√	R	R	R	R	R	R	R	R	R

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Hexanedioic acid mixed esters with decanoic acid, heptanoic acid, octanoic acid and PE (PE Mixed Ester; C6,7,8,10 acids)* CAS 68130-55-2	√	√	√	√	-	-	√	√	√	√
Nonanoic acid, neopentetetrayl ester (PE Tetraester; C9 acids) CAS 14450-05-6	R	R	R	R	R	R	R	R	R	R
Pentaerythritol esters with isooctanoic and C8-10 fatty acids (PE Ester; C8-10 acids)* CAS Number has not been assigned	√	√	√	√	√	√	√	√	√	√
Pentaerythritol, tetrastearate (PE Tetraester; C18 acids) CAS 115-83-3	R	R	R	R	R	R	R	R	R	R
Linseed oil, ester with pentaerythritol (PE ester; oleic, linoleic, linolenic C18 acids) CAS 68648-28-2	√	R	√	√	R	R	R	R	R	R
Fatty acids, tall oil, tetra esters with pentaerythritol (PE tetraester; oleic, linoleic, C18 acids) CAS 68334-18-9	R	R	R	R	R	R	R	R	R	R
Fatty acids, C5-10, esters with dipentaerythritol DiPE hexaester; C5-10 acids CAS 70983-72-1	√	R	R	R	R	R	R	R	√	R
Fatty acids, C5-10, esters with dipentaerythritol DiPE hexaester; C5-9 acids CAS 67762-52-1	√	R	√	R	R	R	√	R	R	√

* Shaded (highlighted) areas denote surrogate polyol ester substances - their data are included in table to help bridge data for structurally analogous HPV polyol esters.

Abbreviations in table:

√ = adequate existing data available,

R = read-across data from structurally analogous polyol esters

-- denotes that no data for specific toxicity endpoint heading has been located for this surrogate polyol ester

Adequate experimental and calculated data for physicochemical properties (i.e., melting point, boiling point, vapor pressure, water solubility and octanol-water partition coefficient) exist for the polyol esters and surrogates in this category. No further testing is proposed for these endpoints for the polyol esters category of the aliphatic esters.

In addition, there are adequate calculated and experimental data for environmental fate endpoints such as photodegradation, hydrolysis, biodegradability (see below) and chemical distribution in the environment (via fugacity modeling) for the polyol esters in this category. No further testing is proposed for these endpoints for the polyol esters category.

Aquatic toxicity and biodegradation data exist for both the HPV polyol esters and the structurally analogous surrogate polyol esters to sufficiently allow for read-across assessments for the HPV substances and for bridging data. No further aquatic toxicity and biodegradation testing is proposed for polyol esters category of the aliphatic esters.

There were existing toxicity data for the HPV and structurally related surrogate polyol esters to sufficiently make hazard assessments for mammalian health effects (SIDS data endpoints) for the HPV polyol esters substances. Given the similar chemical and structural features between the HPV and surrogate polyol esters, it was justifiable to utilize the available existing data to make read-across assessments on potential toxicity and to bridge toxicity data for the HPV substances. No additional mammalian toxicity testing is proposed for substances in the polyol esters category.

Robust summaries of existing health effects, environmental fate and effects, and physicochemical properties data are attached in the Appendix. Summaries of other environmental fate endpoints are also included. Existing data for the HPV and structurally analogous surrogate polyol esters are

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either included in robust summaries or are referenced in the Appendix when they have been reviewed or summarized elsewhere (such as existing SIDS, HPV test plans, other peer reviews) in the literature/public domain. This test plan is expected to provide adequate information to substantially characterize the mammalian health effects, physicochemical properties and environmental fate and effects (including aquatic toxicity, biodegradability) endpoints for the polyol esters category of the aliphatic esters under the HPV Chemical Challenge Program.

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Table 2. Summary Table of Physicochemical Properties and Environmental Fate Data for the Polyol Esters

Total Carbon Number in Ester	MW	CAS Number	Chemical Name	MP* (°C)	BP** (°C)	Vapor Pressure (mm Hg@25°C)	Octanol-Water Partition Coefficient (log Pow)	Water Solubility (mg/L @25°C)	Photo-degradation Half-life (days)	Hydrolysis Half-life (yrs)	Chemical Distribution (Transport) within Environmental Compartments- Fugacity Model c			
											Soil %	Air %	Water %	Sediment %
31	513	68130-53-0	Decanoic acid, mixed esters with heptanoic acid, octanoic acid and trimethylolpropane (TMP Ester; C7, 8, 10 Acid)	148 c	505 c	1.14 E-09 c	10.68 c	4.52 E-07 c	0.31 c	0.89 c	32.9 c	0.7 c	10.5 c	55.8 c
29	499	189120-64-7	Trimethylolpropane esters of heptanoic and octanoic acid (TMP Ester; C7 Acid)	< .25 157 c	>310 489 c	3.5 E-06 Pa 25C 2.3 E-09 c	> 7 10.15 c	< 0.1 1.57 E-06 c	0.39 c	3.5 c	31.9 c	0.4 c	6.9 c	60.8 c
55	954	180788-27-6	Hexanedioic acid, mixed esters with C10-rich, C9-11 isoalcohols and Trimethylolpropane (TMP Ester; C6 Acid + C9-11 Alcohol Ester; C6 Acid)	350 c	>250 830 c	1.7 E-05 Pa 25C 9.34 E-21 c	>6 17.24 c	0.41 1.27 E-15 c	0.19 c	1.2 c	29.5 c	0.1 c	3.4 c	67.1 c
24	415	11138-60-6	Decanoic acid, ester with 2-ethyl-2-(hydroxymethyl)-1,3-propanediol octanoate (TMP Ester; C8, C10 Acid)	116 c	>300 448 c	< 13 Pa 25C 8.7 E-10 c	>2.7 7.67 c	0.48 0.0023 c	0.40 c	7.3 c	34.7 c	0.3 c	6.8 c	58.2 c
33	555	126-57-8	Nonanoic acid, triester with 2-ethyl-2-(hydroxymethyl)-1,3-propanediol (TMP Triester; C9 Acid)	-61 Pour pt 193 c	>300 535 c	21 Pa 25C 5.86 E-11 c	>2.8 12.11 c	8.4 1.44 E-08 c	0.32 c	7.8 c	31.3 c	0.4 c	6.9 c	61.4 c
56	875	68002-79-9	Fatty acids, C14-18 and C16-18 unsatd, triesters with trimethylolpropane (TMP Triester; C14-18 satd, C16-18 unsatd Acid)	350 c	806 c	4.4 E-20 c	23.19 c	3.6 E-20 c	0.05 c	4.2 c	27.8 c	0.03 c	3.5 c	68.7 c
24	417	70024-57-6	9-Octadecenoic acid (Z)-, ester with 2-ethyl-2-(hydroxymethyl)-1,3-propanediol (TMP Monoester; Oleic C18 Acid)	228 c	532 c	3.82 E-14 c	6.93 c	0.00728 c	0.19 c	---	31.6 c	0.3 c	8.0 c	60.2 c
60	928	57675-44-2	9-Octadecenoic acid (Z)-, 2-ethyl-2-[(1-oxo-9-octadecenyl)oxy]methyl]-1,3-propanediyl ester, (Z)- (TMP Triester; Oleic C18 Acid)	350 c	859 c	1.47 E-21 c	24.73 c	7.8 E-22 c	0.02 c	2.2 c	27.4 c	0.01 c	3.5 c	69.1 c
33	529	67762-53-2	Carboxylic acids, C5-9, tetraesters with pentaerythritol (PE Tetraester; C5-9 Acids)	209 c	522 c	2.83 E-10 c	11.41 c	8.4 E-08 c	0.11 c	---	29.5 c	0.2 c	7.1 c	63.2 c
37	641	68130-51-8	Decanoic acid, mixed esters with heptanoic acid, isovaleric acid, octanoic acid and pentaerythritol (PE Mixed Ester; C7, 8 Acids)	242 c	601 c	3.12 E-13 c	12.56 c	1.62 E-09 c	0.29 c	3.9 c	31.2 c	0.4 c	6.9 c	61.5 c
35	613	68424-31-7	Fatty acids, C5-10, esters with pentaerythritol (PE Ester; C5-10 Acids)	233 c	585 c	1.4 E-10 c	11.7 c	1.5 E-08 c	---	---	34 c	0.7 c	11 c	55 c
35	613	68424-34-0	Fatty acids, C5-10, mixed esters with pentaerythritol and valeric acid (PE Ester; C5-10 Acids)	233 c	585 c	1.4 E-10 c	11.7 c	1.5 E-08 c	---	---	34 c	0.7 c	11 c	55 c

Highlighted row denotes substance that was not on the HPV list for the Polyol Esters category but that was included in table to facilitate group evaluation or for bridging purposes due to their chemical/structural similarities as polyol esters.

c = calculated data using EPWIN; all other values in table are derived from measurements or data obtained from company reports, documents, MSDS, reference handbooks, secondary literature sources.

* = Note: Mixtures are expected to have melting points below those of pure components. Modeled data may not accurately reflect melting points for these substances.

** = Some boiling points may have been determined under reduced pressure and some values may have been extrapolated to one atmosphere.

Table 2. (Cont'd) Summary Table of Physicochemical Properties and Environmental Fate Data for the Polyol Esters

Total Carbon Number in Ester	MW	CAS Number	Chemical Name	MP* (°C)	BP** (°C)	Vapor Pressure (mm Hg@25°C)	Octanol-Water Partition Coefficient (log Pow)	Water Solubility (mg/L @25°C)	Photo-degradation Half-life (days)	Hydrolysis Half-life (yrs)	Chemical Distribution (Transport) within Environmental Compartments- Fugacity Model c			
											Soil %	Air %	Water %	Sediment %
37	672	68130-55-2	Hexanedioic acid mixed esters with decanoic acid, heptanoic acid, octanoic acid and PE (PE Mixed Esters; C6,7,8,10 acids)	278 c	640 c	1.06 E-14 c	10.1 c	3.53 E-07	0.30 c	3.1 c	41.6 c	0.04 c	9.3 c	49.1 c
41	697	14450-05-6	Nonanoic acid, neopentetetrayl ester (PE Tetraester; C9 Acid)	279 c	654 c	4.13 E-15 c	14.6 c	1.25 E-11 c	0.25 c	5.8 c	30.8 c	0.3 c	7.0 c	61.9 c
41	698	None assigned yet	Pentaerythritol esters of isooctanoic and C8-10 fatty acids (PE Mixed Esters; C8-10 Acids)	< -40 Pour pt 227 c	>300 569 c	4.0 E-06 Pa 25C 3.17 E-12 c	> 8 11.3 c	0.06 4.21 E-10c	0.37 c	2.8 c	30.8 c	0.16 c	3.3 c	65.7 c
77	1202	115-83-3	Pentaerythritol, tetrastearate (PE Tetraester; C18 Acid)	350 c	1072 c	1.5 E-27 c	32.3 c	3.62 E-30 c	0.12 c	5.8 c	29.4 c	0.04 c	2.4 c	68.2 c
77	1188	68648-28-2	Linseed oil, ester with pentaerythritol (PE Ester; oleic, linoleic, linolenic C18 acids)	350 c	1097 c	2.87 E-28 c	30.8 c	8.75 E-29 c	0.01 c	1.6 c	27.9 c	0.0 c	2.4 c	69.7 c
77	1190	68334-18-9	Fatty acids, tall oil, tetra esters with pentaerythritol (PE Tetraester; oleic and linoleic C18 acids)	350c	1094 c	3.63 E-28 c	31.0 c	5.55 E-29 c	0.01 c	1.6 c	27.9 c	0.0 c	2.4 c	69.6 c
60	927	70983-72-1	Fatty acids, C5-10, esters with dipentaerythritol (DiPE hexaester; C5-10 Acids)	350 c	835 c	9.3 E-19 c	15.8 c	3.6 E-14 c	---	---	34 c	0.4 c	11 c	55 c
60	955	67762-52-1	Carboxylic acids, C5-9, hexaesters with dipentaerythritol (DiPE hexaesters; C5-C9 Acids)	350 c	858 c	2.1 E-19 c	16.7 c	3.4 E-15 c	---	---	32 c	0.4 c	11 c	57 c

Highlighted row denotes substance that was not on the HPV list for the Polyol Esters category but that was included in table to facilitate group evaluation or for bridging purposes due to their chemical/structural similarities as polyol esters.

c = calculated data using EPWIN; all other values in table are derived from measurements or data obtained from company reports, documents, MSDS, reference handbooks, secondary literature sources.

* = Note: Mixtures are expected to have melting points below those of pure components. Modeled data may not accurately reflect melting points for these substances.

** = Some boiling points may have been determined under reduced pressure and some values may have been extrapolated to one atmosphere.

Table 3. Summary Table of Mammalian Health Effects, Ecotoxicity and Biodegradation Data for the Polyol Esters

Total Carbon Number in Ester	MW	CAS Number	Chemical Name	Mammalian Health Effects					Ecotoxicity and Biodegradation					
				Acute Oral LD50	Repeated Dose Toxicity	Genetic Tox (Point/Gene Mutation)	Genetic Tox (Chrom. Aber.)	Reproductive Toxicity	Developmental Toxicity/ Teratogenicity	Acute Fish LCS0 or LLS0	Daphnia ECS0 or EL50	Algal ECS0 or EL50	Biodegradation %	
31	513	68130-53-0	Decanoic acid, mixed esters with heptanoic acid, octanoic acid and trimethylolpropane (TMP Ester; C7, 8, 10 Acid)											
29	499	189120-64-7	Trimethylolpropane esters of heptanoic and octanoic acid (TMP Esters; C7,8 acids)	> 2000 mg/kg (rat)	28-Day oral toxicity (rat) NOAEL 100 mg/kg/day	Negative (Ames)	Negative (Chrom. Aber. CHO cell assay; BM Micronucl.)			>1000 mg/L Aq. toxicity not expected at WSL*	>1000 mg/L Aq. toxicity not expected at WSL*	>1000 mg/L Aq. toxicity not expected at WSL*	Not Readily Biodeg. 68.56% in 28 days OECD 301F	
55	954	180788-27-6	Hexanedioic acid, mixed esters with C10-rich, C9-11 isooalcohols and TMP (TMP +other alcohols Mixed Esters; C6 dioic acids) - TMP Ester C6-dioic acid	> 2000 mg/kg (rat)	28-Day oral toxicity (rat) well tolerated at 1000 mg/kg/day	Negative (Ames)	Negative (Chrom. Aber. CHO cell assay; BM Micronucl.)	28-Day repeated dose oral toxicity study has not been shown to adversely affect male and female reproductive organs. Testis/ovaries were examined microscopically.		> 2 mg/L Aq. toxicity not expected at WSL*	>1000 mg/L Aq. toxicity not expected at WSL*	>1000 mg/L Aq. toxicity not expected at WSL*	Not Readily Biodeg. 65.24% in 28 days OECD 301F	
24	415	11138-60-6	Decanoic acid, ester with 2-ethyl-2-(hydroxymethyl)-1,3-propanediol octanoate (TMP Ester; C8, C10 Acid)	> 5000 mg/kg (rat)	28-day Dermal (rat) NOAEL 2000 mg/kg/day	Negative (Ames)	Negative Chrom. Aber.	Repeated dose dermal toxicity study (2000 mg/kg/d) did not show any histopathology in male or female reprod tissues.	Embryo/fetotoxicity/teratogenicity NOAEL > 2000 mg/kg. No adverse effects on embryo-fetal number, viability, external and visceral defects, sex ratio, body wt., morphology.	>1035 mg/L Aq. toxicity not expected at WSL*	>2370 mg/L Aq. toxicity not expected at WSL*	>1018 mg/L Aq. toxicity not expected at WSL*	Not Readily Biodeg. 64-76% in 28 days	
33	555	126-57-8	Nonanoic acid, triester with 2-ethyl-2-(hydroxymethyl)-1,3-propanediol (TMP Triester; C9 Acid)	>2000 mg/kg >5000 mg/kg (rat)		Negative (Ames)				>1000 mg/L Aq. toxicity not expected at WSL*	>9.3 mg/L Aq. toxicity not expected at WSL*	>4.4 mg/L Aq. toxicity not expected at WSL*	Not Readily Biodeg. 43-54% in 29 days	
56	875	68002-79-9	Fatty acids, C14-18 and C16-18 unsatd, triesters with trimethylolpropane (TMP Triester; C14-18 satd, C16-18 unsatd Acid)											
24	417	70024-57-6	9-Octadecenoic acid (Z)-, ester with 2-ethyl-2-(hydroxymethyl)-1,3-propanediol (TMP Monoester, Oleic C18 Acid)	> 10 ml/kg (rat)						~2000 mg/L Aq. toxicity not expected at WSL*			Readily Biodeg. 73% in 28 days OECD 301B	
60	928	57675-44-2	9-Octadecenoic acid (Z)-, 2-ethyl-2-[(1-oxo-9-octadecenyloxy)methyl]-1,3-propanediyl ester, (Z)- (TMP Triester; Oleic C18 Acid)							> 1056 mg/L Aq. toxicity not expected at WSL*			Readily Biodegrad. 80.7% in 28 days CO2 Evolution (also another study 85% in 28 days)	
33	529	67762-53-2	Carboxylic acids, C5-9, tetraesters with pentaerythritol (PE Tetraester; C5-9 Acids)	> 1940 mg/kg (rat)	13-Week Dermal Toxicity (rat) NOAEL 2000 mg/kg/day	Negative (Ames)	Negative (in vivo micronuclei assay, bone marrow and peripheral blood cells)	Repeated dose 13-wk dermal study showed no adverse effects on sperm morphology or reprod organs at 2000 mg/kg/d.	Dermal admin 2000 mg/kg/d on GD 0-19. No adverse effects on development or in utero survival in develop toxicity screening study (rats). NOAEL 2000 mg/kg for develop toxicity.	>5012 mg/L Aq. toxicity not expected at WSL*			Not Readily Biodeg. 47.1% in 28 days 85.9% in 86 days CO2 Evolution	
37	641	68130-51-8	Decanoic acid, mixed esters with heptanoic acid, isovaleric acid, octanoic acid and pentaerythritol (PE Mixed Ester; C7, 8 Acids)											

Highlighted row denotes read-across data from surrogate polyol esters that was included in Table in order to help facilitate category evaluation and for bridging purposes for HPV polyol esters due to their chemical/structural similarities.

* WSL = Water solubility limit or water saturation level. Aquatic toxicity not expected at maximum WSL (either calculated or measured) of test material based on findings at nominal loading rate or water accommodated fractions (WAF).

Table 3 (Cont'd) . Summary Table of Mammalian Health Effects, Ecotoxicity and Biodegradation Data for the Polyol Esters

Total Carbon Number in Ester	MW	CAS Number	Chemical Name	Mammalian Health Effects					Ecotoxicity and Biodegradation				
				Acute Oral LDS0	Repeated Dose Toxicity	Genetic Tox (Point/Gene Mutation)	Genetic Tox (Chrom. Aber.)	Reproductive Toxicity	Developmental Toxicity/ Teratogenicity	Acute Fish LCS0 or LLS0	Daphnia ECS0 or EL50	Algal ECS0 or EL50	Biodegradation %
35	613	68424-31-7	Fatty acids, C5-10, esters with pentaerythritol (PE Ester; C5-10 Acids)	> 5000 mg/kg (rat)								>4.4 mg/L Aq. toxicity not expected at WSL*	
35	613	68424-34-0	Fatty acids, C5-10, mixed esters with pentaerythritol and valeric acid (PE Ester; C5-10 Acids)	> 5000 mg/kg (rat)									
37	672	68130-55-2	Hexanoic acid mixed esters with decanoic acid, heptanoic acid, octanoic acid and PE (PE Mixed Esters; C6,7,8,10 acids)	> 2000 mg/kg (rat)	28-Day dermal toxicity (rat) NOAEL 500 mg/kg/day	Negative (Ames)	Negative (Chrom. Aber. CHO cell assay)			>5017 mg/L Aq. toxicity not expected at WSL*	>5076 mg/L Aq. toxicity not expected at WSL*	974 mg/L Aq. toxicity not expected at WSL*	Readily Biodeg. 84.2-85.4% in 28 days CO2 Evolution
41	697	14450-05-6	Nonanoic acid, neopentametrayl ester (PE Tetraester; C9 Acid)										
41	698	None assigned yet	Pentaerythritol esters of isooctanoic and C8-10 fatty acids (PE Mixed Esters; C8-10 Acids)	> 2000 mg/kg (rat)	28-Day oral toxicity (rat) NOAEL 1000 mg/kg/day	Negative (Ames)	Negative (Chrom. Aber. CHO cell assay; BM Micronucl.)	28-Day repeated dose oral toxicity studies (up to 1000 mg/kg/d) has not been shown to adversely affect male or female reproductive organs. Histomorphologic observations in testis and ovaries were normal.	No adverse effects on development or in utero survival in develop tox study (rats). Oral dose up to 1000 mg/kg/d (GD 6-15) to pregnant rats. NOAEL 1000 mg/kg	> 4.11 mg/L (measured) Aq. toxicity not expected at WSL*	>1000 mg/L Aq. toxicity not expected at WSL*	>1000 mg/L Aq. toxicity not expected at WSL*	Not Readily Biodeg. 65.0% in 28 days OECD 301B
77	1202	115-83-3	Pentaerythritol, tetraesterate (PE Tetraester; C18 Acid)										
77	1188	68648-28-2	Linseed oil, ester with pentaerythritol (PE Ester; oleic, linoleic, linolenic C18 acids)	> 2000 mg/kg (rat)		Negative (Ames)	Negative (Chrom. Aber. CHO cell assay)						
77	1190	68334-18-9	Fatty acids, tall oil, tetra esters with pentaerythritol (PE Tetraester; oleic and linoleic C18 acids)										
60	927	70983-72-1	Fatty acids, C5-10, esters with dipentaerythritol (DIPE hexaester; C5-10 Acids)	> 5000 mg/kg (rat)								>4.4 mg/L Aq. toxicity not expected at WSL*	
60	955	67762-52-1	Carboxylic acids, C5-9, hexaesters with dipentaerythritol (DIPE hexaesters; C5-C9 Acids)	> 1940 mg/kg (rat)		Negative (Ames)				>5012 mg/L Aq. toxicity not expected at WSL*			Not Readily Biodeg. 47.1% in 28 days 85.9% in 86 days CO2 Evolution

Highlighted row denotes read-across data from surrogate polyol esters that was included in Table in order to help facilitate category evaluation and for bridging purposes for HPV polyol esters due to their chemical/structural similarities.

* WSL = Water solubility limit or water saturation level. Aquatic toxicity not expected at maximum WSL (either calculated or measured) of test material based on findings at nominal loading rate or water accommodated fractions (WAF).