201-15013

Alkenes, C6-10, hydroformylation products, high-boiling

CAS Number 68526-82-9

A Chemical Mixture Also Know as:

- Alcohols, C7-11, distn. bottoms
- EP-290
- Oxo heavy ends

RECEIVED
OPPT CBIC
04 JAN -9 AM 10:46

U.S. EPA HPV Challenge Program Submission

December 29, 2003

Submitted by:

BASF Corporation
3000 Continental Drive
Mt. Olive, NJ 07828-1234

Prepared by:
Toxicology and Regulatory Affairs
1201 Anise Court
Freeburg IL 62243
618-539-5280

Table of Contents

Executive Overview 3
Testing Plan and Rationale 5
Testing Plan in Tabular Format 6
1.0 Introduction 7
1.1 Overview *7*
1.2 Methods for Data Review *7*
1.3 Substance Information for EP-290 ..... *8*
2.0 Chemistry 9
2.1 Production of EP-290 ..... *9*
2.2 Typical composition EP-290 ..... *11*
Table 1: Typical Composition of EP-290 ..... *12*
3.0 SIDS Data Set 12
3.1 Physicochemical Data *13*
Table 2: Physicochemical Summary Data for EP-290 ..... *13*
Table 3: Calculated Octanol-Water Partitions Coefficients for EP-290 ..... *14*
Table 4: Calculated and Experimental Vapor Pressures for Components *15*
Table 5: Calculated Water Solubilities for Components of EP-290 ..... *15*
3.2 Environmental Fate and Pathways 16
3.2.1 Biodegradation *16*
Table 6. Biodegradation Potential of EP-290 Components *16*
3.2.2 Photodegradation *18*
Table 7, Summary of Photodegradation Estimates *18*
3.2.3 Water Stability *19*
3.2.4 Environmental Distribution *20*
Table 8: Theoretical Distribution (Fugacity) of EP-290 in the environment *20*
3.3 Ecotoxicity *21*
Table 9: Aquatic Toxicity of EP-290. ..... *21*
3.4 Mammalian Toxicity 21
3.4.1 Metabolism 22
Figure 1. Oxidation of Linear and Branched Fatty Acids *23*
3.4.2 Acute Toxicity 23
3.4.2.1 Oral Exposure *23*
3.4.2.2 Inhalation Exposure *24*
3.4.2.3 Dermal Exposure *24*
3.5.0 Repeat Dose Toxicity 24
Oral Exposure *24*
3.6.0 Genetic Toxicity 25
Table 10. Genetic Toxicity of EP-290 Components *25*
3.7.0 Reproductive Toxicity 27
3.8.0 Developmental Toxicity 27
4.0 Conclusions 28
4.1 HPV Data Matrix 29
5.0 References 30

Executive Overview

The high-boiling fraction from the hydroformylation of C6-10 alkenes, CAS no. 68526-82-9, is known by several names in commerce including the more generic name "Oxo heavy ends", Alcohols, C7-11, distillation bottoms, and the BASF Trade name EP-290. The reaction conditions that prevail during hydroformylation are such that several byproducts are formed by dimerization, partial oxidation and condensation. The crude reaction product is fractionally distilled to remove the alcohols (C7, C9 and C11) that are the primary reaction products. What is left behind after removal of the alcohols by distillation is the "high-boiling" fraction, which has been assigned the CAS no 68525-82-9 and is designated EP-290 at BASF. Due to the variability of the mixture depending on feedstocks and reaction conditions, the information in this document is specific to material produced by BASF under their reaction conditions.

EP-290 has numerous industrial and commercial applications due to its chemical and solvent properties. Some of the applications are as an antifoamer/defoamer, a lubricant in textile manufacture, leather processing and in coal mining. This material is produced by BASF at one plant the United States. Occupational exposure in manufacture is limited by the low vapor pressure and use of essentially closed systems for production. Dermal exposure is considered the only relevant route of occupational exposure and this is limited by the use of personal protective equipment when handling the material outside of the closed manufacturing system.

EP-290 is colorless to straw colored clear liquid with a mild odor. It has a low volatility and is relatively insoluble in water but is miscible with most organic solvents. The composition of EP-290 is a critical aspect of this HPV hazard analysis; thus, the chemistry of formation of EP-290 and its typical composition is discussed in detail in this document. The main class of components is aliphatic alcohols, which can comprise up to about 70% of the mixture. Higher molecular weight alkenes are the next most abundant category of component and can comprise up to 25% of the mixture. Other identified components include carboxylic acids, esters, ethers and acetals.

As a chemical mixture, EP-290 does not have specific physicochemical properties; thus, experimental or calculated physiochemical properties for components are provided in the document. Generally, the

components are high boiling, have low vapor pressures, are relatively insoluble in water and have a broad range of octanol water partitions coefficients (log K_{ow} range of 3 to above 11).

Fate of EP-290 in the environment is a function of the individual components. Biodegradation is rapid for most of the components, but some only biodegrade slowly. No identified component, however, is sufficiently resistant to biodegradation that it would be considered persistent in the environment. Photodegradation of all known components will occur with a half-life of less than one day. Sediment and water are predicted to be the primary environmental sink for the majority of distribution.

Most of the known components of EP-290 are toxic to fish, invertebrates and aquatic plants with EC_{50} values of less than 1 mg/L. Toxicity to aquatic organisms, however, may be limited by the low solubility of the toxic components of this mixture.

Mammalian toxicity of the mixture has been determined to be low based on acute and subchronic studies of the actual mixture. This low toxicity for EP-290 is supported by experimental data on several components and the knowledge that most of the fatty acids, alcohols and esters in this mixture are readily metabolized as nutrients by the fatty acid oxidative pathways. The fact that these high-capacity mammalian pathways readily metabolize most of the components, suggests little potential for systemic toxicity in mammals.

Genotoxicity has been extensively investigated both *in vitro* and *in vivo* for representative compounds of all the known components of EP-290 and they universally have minimal potential for causing damage to the gene.

Reproductive and developmental toxicity has likewise been investigated for the major components of EP-290 and they show no potential for interference with reproduction or for causing developmental effects in multiple species.

It is concluded, on the basis of available knowledge of this material and its components, that the toxicological hazards of this material are sufficiently defined for the purposes of the U.S. EPA High Production Volume program and that additional studies are not indicated.

Testing Plan and Rationale

Testing Plan in Tabular Format

CAS # 68526-82-9 EP-290	Information Available?	OECD Study ?	GLP Study?	Supporting Information?	Estimation Method?	Acceptable?	Testing Recommended?	
HPV Endpoint								
Physical Chemical								
Melting Point	Y	N	N	N	N	Y	N	
Boiling Point	Y	N	N	Y	N	Y	N	
Vapor Pressure	Y	N	N	Y	Y	Y	N	
Partition Coefficient	Y	N	N	N	Y	Y	N	
Water Solubility	Y	N	N	Y	Y	Y	N	
Environmental & Fate								
Photo-Degradation	Y	N	N	N	Y	Y	N	
Water Stability	Y	N	N	Y	Y	Y	N	
Transport	Y	N	N	N	Y	Y	N	
Biodegradation	Y	N	N	Y	N	Y	N	
Ecotoxicity								
96-Hour Fish	Y	N	N	Y	N	Y	N	
48-Hour Invertebrate	Y	N	N	Y	N	Y	N	
96-Hour Algae	Y	N	N	Y	Y	Y	N	
Toxicity								
Acute	Y	N	N	N	Y	Y	N	
Repeated Dose	Y	N	N	N	Y	Y	N	
Genetic Toxicology *in vitro*	Y	YN	YN	Y	N	Y	N	
Genetic Toxicology *in vivo*	Y	N	YN	Y	N	Y	N	
Reproductive	Y	N	YN	N	N	Y	N	
Developmental	Y	N	YN	N	N	Y	N	

1.0 Introduction

1.1 Overview

BASF Corporation hereby submits for review and public comment the Test Plan and Robust Summaries for CAS no. 68526-82-9 Alkenes, C6-10, hydroformylation products, high-boiling (herein known as EP-290), under the United States Environmental Protection Agency's (U.S. EPA) High Production Volume (HPV) Chemical Challenge Program. This document addresses a single HPV sponsored material; however, data from structurally related chemicals have been used to support the dataset for EP-290 through a read across approach. Data read across can occur when physicochemical and toxicological data from one chemical are used for another chemical, and is done only when the two chemicals are deemed sufficiently similar in structure that they are likely to have similar chemical and toxicological properties. The use of structural analogs is consistent with EPA guidance for use of structure-activity relationships (SAR) in the HPV Chemical Challenge Program (EPA, 1999).

The purpose of this plan is to develop physicochemical data, environmental fate and effects data, and mammalian health effects data for EP-290 consistent with the Screening Information Data Set (SIDS). Therefore, this plan summarizes the existing SIDS data for EP-290 makes recommendations for testing to fill any data gaps in the SIDS endpoints.

1.2 Methods for Data Review

A review of the scientific literature and BASF Corporation's company data was conducted on the physicochemical properties, environmental fate and effects, and mammalian toxicity endpoints for EP-290 and structurally related materials. Searches were conducted using CAS numbers and chemical names from various sources including the following databases: STN, CIS, EFDB, TOXLINE, ECOTOX, MEDLINE, and CHEMID. Standard handbooks and databases (e.g., CRC Handbook on Chemicals, IUCLID, Merck Index, etc.) were consulted for physicochemical properties of individual components of this mixture.

In accordance with U.S. EPA guidance, in those instances where measured physicochemical parameters and environmental fate data were not available, these properties were estimated using EPIWIN (version 3.05) modeling. EPIWIN is an acronym for the Estimation Programs Interface for Microsoft Windows (June 1998), and is a package of computer programs developed by the U.S. EPA Office of Pollution Prevention and Toxics (OPPTS) that uses computational methods and structure-activity relationships (SAR) in estimating chemical properties, environmental fate and aquatic toxicity of organic chemicals. Due to the inherent limitations of SAR approaches, EPIWIN modeling may produce non-realistic estimates; therefore, EPIWIN data are evaluated for reasonableness prior to use.
Lastly, robust summaries were prepared for studies as to provide a detailed summary of the test methods and results. Though several studies may have been evaluated for a particular SIDS endpoint, robust summaries were prepared only for the critical studies that represented the best available data. Selection of the critical study was

based on a review of all studies using the ranking system developed by Klimisch et al (1), as well as the criteria outlined in the U.S. EPA's methods for determining the adequacy of existing data.

1.3 Substance Information for EP-290

The high-boiling fraction from the hydroformylation of C6-10 alkenes, CAS no. 68526-82-9, is known by several names in commerce including the more generic name "Oxo heavy ends", Alcohols, C7-11, distn. bottoms and the more specific name EP-290 used by BASF to designate this product. The objective of the hydroformylation reaction is to prepare alcohols with a one-carbon longer chain length from alkenes and carbon monoxide under reductive conditions using a catalyst. The chemistry is not highly specific and several products are formed by dimerization, partial oxidation and condensation. The crude reaction product is fractionally distilled to remove the alcohols (C7, C9 and C11) that are the primary desired products of the reaction. What is left behind after removal of the C7 to C11 alcohols by distillation is the "high-boiling" fraction, which has been assigned the CAS no 68525-82-9 and is designated EP-290 at BASF.

This material has numerous industrial applications due to its chemical and solvent properties. Some of the applications are as an antifoamer/defoamer, a lubricant in textile manufacture, leather processing and in coal mining. Estimated production of EP-290 by BASF in the United States is in the range of 10 to 20 million pounds. The material is produced by BASF at one United States plant. Occupational exposure in manufacture is limited by the low vapor pressure and use of essentially closed systems for production. Dermal exposure is considered the only relevant route of occupational exposure and this is limited by the use of personal protective equipment when handling the material outside of the closed manufacturing system.

EP-290 is colorless to straw colored clear liquid with a mild odor (2). It has a low volatility and is relatively insoluble in water but is miscible with most organic solvents (2). The composition of EP-290 is a critical aspect of this HPV hazard analysis; thus, the chemistry of formation of EP-290 and its typical composition is discussed in detail below in the "chemistry" section of this document.

Several physicochemical, fate and toxicity studies have been conducted with EP-290 itself. These studies are briefly reviewed in this testing rationale document, which also describes how these studies meet the SIDS end-points of the USEPA HPV program. Robust summaries have been prepared for key studies; supporting studies are referenced in these summaries or given as shorter summaries using the IUCLID format. Where specific studies on EP-290 have not been conducted, data from studies of the major components or other surrogates are provided to fill the HPV endpoints without specific data. In some cases where calculated data are acceptable, a calculation based on the major components has been utilized.

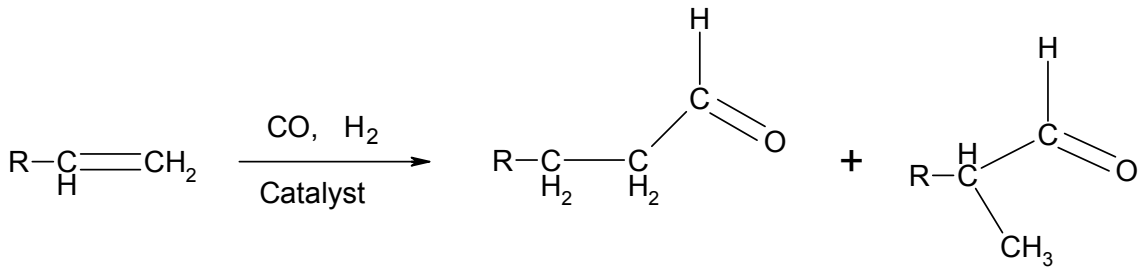
2.0 Chemistry

EP-290 (CAS RN 68526-82-9) is a mixture of variable composition derived from the hydroformylation of C6-10 alkenes. To understand how this material relates to other mixtures that have relevant data and to understand the scope of various components, it is necessary to appreciate the process and variables that contribute to the production of this mixture.

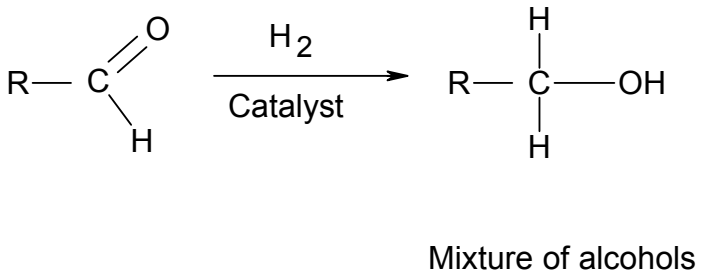
2.1 Production of EP-290

EP-290 is a residue remaining from the distillation of aliphatic alcohols from a hydroformylation reaction product. This reaction product containing the alcohols is produced by the hydroformylation of feedstock containing primarily C-6, C-8 and C-10 alkenes over a catalyst followed by reduction of the subsequent aldehydes. Although hydroformylation is the desired reaction, under these conditions a number of alternative reactions can occur. There are several variables that will alter the products of this reaction, including feedstock composition, activity of reaction catalyst, reaction time, reaction temperature, and distillation conditions.

The intended primary reaction of hydroformylation is an alcohol formed from an aldehyde, as shown in the following equations:

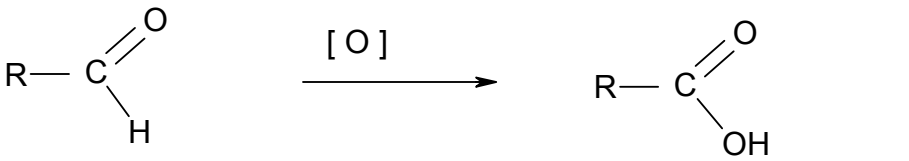


This aldehyde mixture is subsequently reduced under the reaction conditions to produce the desired alcohols.



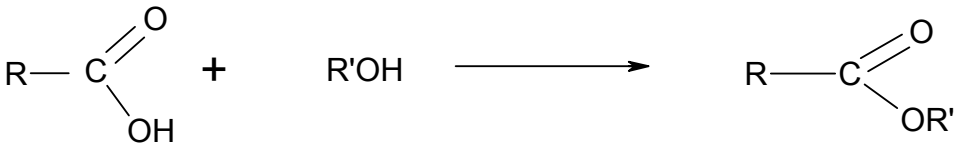
During the reactions and subsequent distillation steps several other reactions can occur to produce several related products. For example, formation of the mixed acetals occurs when aldehydes and alcohols combine.

Aldehydes are readily converted to the corresponding carboxylic acid by any oxidizing equivalents.



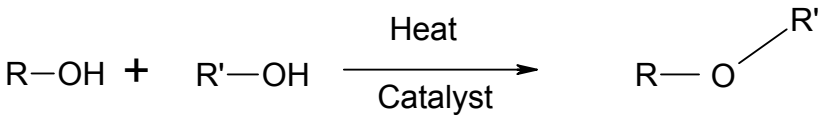
Alkyl Carboxylic Acids

The formed carboxylic acids will form esters in the presence of alcohols and dehydrating conditions (such as high temperature distillation).



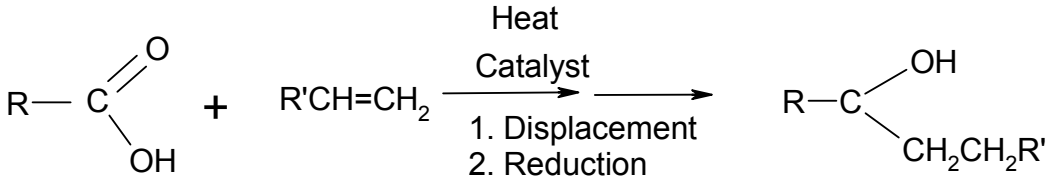
Alkyl Esters

Alcohols, under dehydrating conditions and particularly it the presence of acids will form ethers.



Alkyl Ethers

The formation of the higher chain length molecules may proceed by various mechanisms in the presence of catalyst. One postulated mechanism resulting in secondary alcohols is shown below.



Postulated mechanism of longer alkyl chain alcohol formation

Dimerization of alkenes (a well known reaction occurring in the presence of a transition-metal catalyst) in the C8 to C10 range give rise to the hexedecene, octadecene and eicosene that are observed in the distillation residue. These reactions combined together produce an initial product mixture rich in C7, C9 and C11 alcohols, which are mostly removed from the mixture by distillation, leaving the higher boiling components (distillation bottoms) behind. Originally, the distillation bottoms were disposed as a waste; however, due to pollution prevention efforts, several commercial applications were identified for this mixture. These applications are dependent on the overall physicochemical properties of the mixture and not upon its exact chemical composition.

In summary, the hydroformylation process results in the production of small quantities of undesired byproducts in addition to the desired alcohols. The chemistry described above accounts for the components of EP-290 and explains the variable nature of this mixture, with quantities of individual components given as ranges. Using this process and composition knowledge, it is possible to identify related substances that can be used in a “read across” approach to estimating the hazard of EP-290.

2.2 Typical composition EP-290

The feedstock that is most often used in the hydroformylation reaction that produces EP-290 is a mixture of approximately equal quantities of C6, C8 and C10 alkenes that are 20-30% branched. The primary products from the reaction (>90% yield) are the corresponding C7, C9 and C11 alcohols. These alcohols are distilled from the reaction mixture leaving the EP-290 as the residue from the distillation. The EP-290 fraction represents 5 to 10% of the total reaction product.

Other feedstocks that are employed to a lesser extent in the production of EP-290 are olefins enriched in C6 and C8, enriched in C8, or enriched in C10. The use of these alternative feedstocks is dependent on both the desired chain length and composition of the primary alcohol product and on the relative cost of the feedstock. This variability in the ratios of C6, C8 and C10 alkenes and the amount of branching in the alkene feedstock, is described in the TSCA Inventory Registration for the high-boiling fraction after removal of the alcohols using CAS RN 68526-82-9.

As indicated above, variation in the feedstock composition, reaction time and catalyst activity may result in variations in the composition of EP-290. The typical composition is shown below in Table 1. The main class of components is aliphatic alcohols, which can comprise up to about 70% of the mixture. Higher molecular weight alkenes are the next most abundant category of component and can comprise up to 25% of the mixture.

Typical composition EP-290	
Component	**Weight %**
Acetals	2.0- 4.0
2-Butyl-1-octanol	4.0- 6.5
Nonanol	0.8- 2.0
Decanol*	9.0-12.0
Dodecanol*	4.0- 5.5
Alcohols, C_{13}-C_{20}	32.0-38.0
Alcohols, C_{21} and higher	10.0-12.0
Ethers, C_{18}-C_{22}	5.0-7.0
Esters, C_{23} and higher	4.0-5.0
Carboxylic acids	1.0-4.0
Hexedecene	5.5-7.5
Octadecene	9.0-11.0
Eicosene	5.0-7.0

* Decanol and dodecanol have been identified in the material but may actually represent some quantity of undecanol (C11) based on the feedstock and reaction chemistry.

Table 1: Typical Composition of EP-290

3.0 SIDS Data Set

Most of the studies conducted on EP-290 product were conducted for Monsanto Company on CAS RN 68526-82-9, which was referred to by Monsanto as “Heavy Oxo Ends”. BASF purchased the Monsanto hydroformylation business and produces EP-290 using the same equipment and procedure that was used to produce Heavy Oxo Ends. The Heavy Oxo Ends are considered to have the same composition as the current EP-290 as the equipment, feedstock, process and specifications are essentially equivalent.

3.1 Physicochemical Data

Physicochemical data for EP-290 are available from manufacturer's information and from EPIWIN estimates and are summarized in Table 2.

Melting Point	ca. –44˚ C (3)
Boiling Point	130° - 273° C @ 13 hPa (3)
Vapor Pressure	< 0.1 hPa @ 20˚ C
Partition Coefficient	Log $K_{o/w}$ = 3.1 – 12.0 ()
Water Solubility	Very low, max ca 0.01%

Table 2: Physicochemical Summary Data for EP-290

These properties are mainly taken from the Technical Specification for the product. Notice that the boiling point is given as a wide range, which is typical of a material that undergoes fractional distillation as it boils.

A single octanol-water partition coefficient is not applicable to this mixture since it has a variety of components with varying hydrophobicities. The range given in the table, 3.1 to 12.0, is the range of Ko/w values calculated for the identified components of EP-290 using EPIWIN. To understand the potential distribution and bioaccumulative properties of EP-290, individual components must be taken into consideration. Table 3 contains the EPIWIN estimated log Ko/w for several representative components. Because the isomeric make up of the components is not defined, various arbitrarily selected isomeric structures were also evaluated to ascertain the log Ko/w of some potential isomers. It can be seen by examination of the table that isomers have only a minor effect on Ko/w as compared to the number of carbons in the representative alcohols. Thus, identification of isomers is not considered to be important in the calculation of most physical properties for EP-290. In addition, the calculations indicate that the range of Log Ko/w values for individual components is expected to vary from about 3 to greater than 11.

Component	SMILES	log K_{ow}
C9 Alcohols	CCCCCCCCCO	3.2965
	CCCCCCC(C)CO	3.2230
	CCC(CC)CCCCO	3.2230
	CCC(CC)CC(C)CO	3.1495
C11 Alcohols	CCCCCCCCCCCO	4.2787
	CCCCCCCCC(C)CO	4.2052
	CCC(CC)CCCCCCO	4.2052
	CCC(CC)CCCC(C)CO	4.1317
C13 Alcohols	CCCCCCCCCCCCCO	5.2609
	CCCCCCCCCCC(C)CO	5.1874
	CCCCC(CC)CCCCCCO	5.1874
	CCCCC(CC)CCCC(C)CO	5.1139
C20 Alcohols	CCCCCCCCCCCCCCCCCCCCCO	8.6986
	CCCCCCCCCCCCCCCCCCC(C)CO	8.6251
	CCCCC(CC)CCCCCCCCCCCCCCO	8.6251
	CCCCC(CC)CCCCCCCCCCC(C)CO	8.5516
C25 Alcohols	CCCCCCCCCCCCCCCCCCCCCCCCCCCCCO	11.1541
C18 Ether	CCCCCCCCCOCCCCCCCCC	7.9246
C22 Ether	CCCCCCCCCCCOCCCCCCCCCCC	9.8890
Hexedecene	CCCCCCCCCCCCCCC=C	8.0626
Eicosene	CCCCCCCCCCCCCCCCCC=C	9.0448
2-Butyl-1-octanol	CCCCCCC(CCCC)CO	4.6963
C22 Ester	CCCCCCCCCCC(=O)OCCCCCCCCCCC	9.7040
C28 Ester	CCCCCCCCCCCCC(=O)OCCCCCCCCCCCCC	11.6684

Table 3: Calculated Octanol-Water Partitions Coefficients for EP-290

Vapor pressure for EP-290 depends primarily on the vapor pressure of the most volatile component and, as the mixture evaporates and changes composition, the vapor pressure will decrease. To understand the vapor pressure behavior of EP-290, several representative individual components were examined for experimental VP data and calculated VP data using EPIWIN. The results of this are shown in Table 4. The vapor pressure of EP-290 will initially be in the range of approximately 0.03 hPa and as it evaporates the remaining components after loss of most of the mass could have a vapor pressure less than 0.0001 hPa.

Component	Vapor Pressure (mm Hg)		Higher VP (hPa)
	Exp*	Calc	
n-C9 alcohol	0.023	0.033	0.044
n-C11 alcohol	0.003	0.005	0.007
n-C13 alcohol	0.0004	0.0002	0.0003
n-C20 alcohol	0.00000005	0.0000001	0.00000013
C9 Diether (C18)	0.000053	0.0007	0.0009
1-Hexedecene (C16)	0.0026	0.0077	0.01
C11-C11 Ester (C22)		0.00019	0.003

Table 4: Calculated and Experimental Vapor Pressures for Components

Water solubility is dependent on the solubility of individual components, as shown in Table 5. The lower molecular weight alcohols (C9 to C11) in EP-290 are known or predicted to have water solubilities in the range of 20 to 160 mg/L. As the length of the carbon chain increases, the water solubility goes down rapidly to below 0.01 mg/L for the C20 alcohols, olefins, esters and ethers. Basically, the water solubility of EP-290 is dependent on the composition of the material and dependent on the partition coefficient of these limited water solubility between the water column and bulk EP-290. Thus, although some components have solubilities in excess of a few mg/L, they will tend to stay in the bulk organic phase rather than distribute readily to the water column.

Component	Water Sol (mg/L)	
	Exp*	Calc
n-C9 alcohol	140	157
n-C11 alcohol		43
n-C13 alcohol		4.5
n-C20 alcohol		0.002
C9 Diether (C18)		0.0031
1-Hexedecene (C16)		0.001
C11-C11 Ester (C22)		0.00004

Table 5: Calculated Water Solubilities for Components of EP-290

Recommendation: No additional physicochemical studies are recommended. The available data fill the HPV required data elements with sufficient precision to define the hazards of this material.

3.2 Environmental Fate and Pathways

3.2.1 Biodegradation

EP-290 is considered to be biodegradable based on information from materials representative of EP-290's components. The usual assumption when considering the biodegradability of a chemical mixture is that each component is independently metabolized by bacteria. Using this premise, the biodegradability of EP-290 can be assessed with confidence. Data for several representative materials are found in the literature and in previous U.S. EPA HPV submissions. Some of these data are summarized in Table 6.

Class	Test Substance	Test	% Deg	Ref
Alcohols	Olefin hydroformylation products C7-9 branched alcohols	OECD 301F	82%	4
	Olefin hydroformylation products C9-11 iso, C10 rich (68526-85-2) [rs]	OECD 301F	71%	5
	2-Ethylhexanol (C-8 branched)	Sturm (CO_2 evol)	55-68% (17days)	6
	Olefin hydroformylation products C11-14 iso, C13 rich (68526-86-3) [rs]	OECD 301F	58%	7
Acids	Dodecanoic acid (C-12) [rs]	Closed bottle	85%	8
	Dodecanedioic acid (C-12) [rs]	301-D	71%	9
Esters	2-Ethylhexyl laurate (C-20) [rs]	Closed bottle	95%	10
Olefins	Olefin hydroformylation products, Alkenes, C7-91, C8 Rich (68526-54-5)	OECD 301F	29%	11
	Olefin hydroformylation products, Alkenes, C9-11, C10 Rich (68526-56-7) [rs]	OECD 301F	21%	12
Ethers	Limited data indicate aliphatic ether linkage is moderately resistant to biodegradation.			13
[rs] indicates that a roust summary has been included in the Appendix				

Table 6. Biodegradation Potential of EP-290 Components

Examination of Table 6 reveals that the listed components vary in biodegradability from "readily biodegradable" to what could be called slow or difficult. The most important category for consideration of the biodegradability of EP-290 is the alcohols. Alcoholic products from hydroformylation reactions have been tested in guideline ready biodegradation tests. These are the "olefin hydroformylation products" listed in the table in the alcohols category. As these are actual hydroformylation products, the degree of branching should be representative of the alcohols (and alcoholic moieties of the esters, acetals and ethers).

The alcoholic components generally would be classed as "readily biodegradable" but the ease of biodegradation appears to increase with the shorter chain lengths.

The acetals in EP-290 are anticipated to be labile in water and hydrolyze to aldehydes and alcohols, which both proceed to carboxylic acids. The esters hydrolyze more slowly than the acetals abiotically, but bacterial esterases readily break the ester linkage giving an alcohol and a carboxylic acid; both of which are susceptible to rapid biodegradation. An example of a synthetic ester, 2-ethylhexyl laurate, is given in the table and is supplemented by a robust summary in the appendix. The degree of branching will influence the ease of biodegradation; the rate is expected to be fastest with straight chain esters and become progressively slower as the degree of branching increases

Biodegradability of the ethers is more difficult to predict, as there is a limited literature to draw from. Simple ethers show some resistance to biodegradation; however, given enough time and/or bacterial adaptation, complete degradation is likely.

The olefins, which are an important class of material in EP-290 are likewise biodegradable but not typically at a rate that would allow for categorization as readily biodegradable". As can be seen from the limited data in the table, longer chain olefins may be more resistant to biodegradation.

It can be predicted with confidence that when EP-290 is subjected to aerobic biodegradation conditions, the shorter strait chain alcohols, acids, acetals and esters will be rapidly mineralized. The longer chain and more branched alcohols, acids and esters will biodegrade completely but will require more time and would not be classified as readily biodegradable. Likewise, the olefins are expected to fully biodegrade but over a longer period of time.

It cannot be predicted with certainly if a particular batch of EP-290 with a particular bacterial inoculum would pass a ready biodegradation; however the information from existing data and this analysis is considered sufficient for the purposes of the HPV program as it provides a reasonable estimate of the biodegradability of the material. Actually, the existing data and analysis is of more value than another biodegradation screening assay as it addresses the potential for the release of individual components into the environment after limited bio-treatment.

3.2.2 Photodegradation

Photodegradation was estimated using version 1.90 of the Atmospheric Oxidation Program for Microsoft Windows (AOPWIN) that estimates the rate constant for the atmospheric, gas-phase reaction between photochemically produced hydroxyl radicals and organic chemicals. The estimated rate constant is used to calculate atmospheric half-lives for organic compounds based upon average atmospheric concentrations of hydroxyl radical. The approach used was to take the five most prevalent materials in the preparation and individually determine their reactivity with hydroxyl radical assuming each component will be unaffected by the others after vaporization into the troposphere. The program produced estimated rate constants ranging from 19.6 x 10^{-12} to 47.1 x 10^{-12} cm^3/molecule-sec. Using the default atmospheric hydroxyl radical concentration in APOWIN and the range of estimated rate constants of major components of EP-290 for reaction with hydroxyl radical, the estimated half-life of EP-290 vapor in air is approximately 2 to 8 hours. The full details of the calculations are given in the robust summaries and the table below provides a summary of the results.

EP-290 Component	C#	SMILES	Results of AOP v 1.09 Hydroxyl Radical Reaction Prediction	
			Rate Constant ($x10^{-12}$ cm^3/molec-sec)	Half-life (hrs)
Alcohols, C_{13}-C_{20}	C13	CCCCCCCCCCCCCO	19.6	6.5
	C20	CCCCCCCCCCCCCCCCCCCCCO	29.4	4.4
Octadecene	C18	CCCCCCCCCCCCCCCCC=C	47.1	2.7
Ethers, C_{18}-C_{22}	C20	CCCCCCCCCCOCCCCCCCCCC	41.6	3.1
Esters, C_{23} and higher	C28	CCCCCCCCCCCCC(=O)OCCCCCCCCCCCCC	31.7	4.1

Table 7, Summary of Photodegradation Estimates

As the calculations show, the primary reaction for this series of material is hydrogen abstraction and the rate increases linearly as the number of hydrogens increase. The ether moiety activates the adjacent hydrogen atoms toward radical abstraction while the ester is a deactivating influence. The olefin has the additional reaction possibility of the double bond with the hydroxyl radical, which gives it the highest predicted reaction rate constant on balance. In addition, the double bond allows the olefin to react with atmospheric ozone (estimated atmospheric half life of 23 hours), but this would not be expected to have a significant effect on its already short atmospheric half-life. None of the materials will absorb light above 290 nm; thus, direct photolysis in the troposphere will not be significant. In summary, all components are expected to have relatively short atmospheric half-lives reacting primarily with atmospheric hydroxyl radical.

3.2.3 Water Stability

The stability of EP-290 in water cannot be definitively determined because it is a variable chemical mixture with some components that are potentially hydrolysable. To develop an understanding of EP-290's water stability, two different conditions for its contact with water have to be considered: bulk phase contact and solution phase contact. In bulk phase contact the assumption is made that sufficient EP-290 is mixed with water such that distinct oil droplets or an oil layer exist. In this case, depending on the mixing conditions, hydrolysable components will only slowly partition from the bulk EP-290 into water due to the components' high K_{ow} values. Calculations could be conducted if relative volumes of organic phase and water phase were known, mixing conditions were established and other variables such as temperature were defined. Based on some preliminary calculations, the bulk phase EP-290 would remain stable at approximately the same relative composition for an extended period unless surfactants or cosolvents dispersed it.

Under solution phase conditions, essentially infinite dilution conditions are assumed which allow the stability of the individual components to be estimated based on their chemical properties. For EP-290 most of the components have no hydrolysable group are considered resistant to hydrolysis (14). These are:

- Aliphatic alcohols
- Aliphatic carboxylic acids
- Alkenes
- Aliphatic ethers

The following components have hydrolysable groups:

- Aliphatic acetals
- Aliphatic esters

The stability of the aliphatic esters has been estimated using the EPIWIN software (see robust summary in Appendix) and their estimated half-life at pH 7 is ca. 20 years. As the hydrolysis is faster in the presence of base and estimate for pH 8.0 was conducted and it predicts a half-life of about 2 years. In light of these long half-lives, EP-290 is considered hydrolytically stable.

Stability of acetals cannot be estimated using the EPIWIN software and no definitive information was located on the water stability of these long-chain acetals. As simple acetals are typically resistant to hydrolysis at neutral pH (15) and as the acetals are a minor component of EP-290, their contribution to the water stability of EP-290 is minimal. It can be concluded that the half-life of EP-290 in water is greater than one year.

3.2.4 Environmental Distribution

Theoretical Distribution (Fugacity) of EP-290 in the environment was estimated using the MacKay EQC level III model with standard defaults in EPIWIN v 3.05 using 100% release to water as the means of entry into the environment. The approach used was to take the five most prevalent materials in the preparation and individually determine their fugacity assuming that one component will not greatly affect the distribution of the other (assumption of infinite dilution). As the measured vapor pressure of EP-290 is a function of the partial pressures of each component, it is more appropriate to use the EPIWIN predicted vapor pressure for each component in the calculation. Likewise individual predicted values for log Kow, Koc, and half-lives were utilized. The biodegradation half-lives that were utilized were EPIWIN generated but were evaluated for consistency with the known biodegradability of the preparation and found to be representative.

The entire data set with the values utilized for all parameters is shown in the Robust Summery for distribution in the environment, and a summary table is shown below. The components evaluated are representative of the full spectrum of components contained in EP-290 and include alcohols, a higher olefin, an ether and an ester. The components distribute primarily to water and sediment and the ratio varies little except for the slightly more water soluble 13-carbon alcohol. This analysis provides a worst-case assessment since it does not incorporate the relatively short half-lives of the components due to biodegradation and indirect photolysis.

EP-290 Component	C#	SMILES	Distribution (Percent)			
			Air	Water	Soil	Sediment
Alcohols, C_{13}-C_{20}	C13	CCCCCCCCCCCCCO	0.61	50.6	0.04	48.8
	C20	CCCCCCCCCCCCCCCCCCCCCO	0.001	10.2	0.002	89.8
Octadecene	C18	CCCCCCCCCCCCCCCCCC=C	0.0002	10.1	0.000003	89.9
Ethers, C_{18}-C_{22}	C20	CCCCCCCCCCCOCCCCCCCCCC	0.0004	10.1	0.00002	89.9
Esters, C_{23} and higher	C28	CCCCCCCCCCCCCC(=O)OCCCCCCCCCCCCCC	0.000001	10.1	0.000004	89.9

Table 8: Theoretical Distribution (Fugacity) of EP-290 in the environment

Recommendation: No additional fate and pathway studies are recommended. The available data fill the HPV required data elements.

3.3 Ecotoxicity

Acute fish and daphnia studies on EP-290 have been conducted, and the results are shown in Table 9. The fish studies were conducted without a carrier solvent, while the daphnid studies used dimethylformamide to dissolve and disperse the test material. It was also reported in the fish tests that oil droplets of test material were on the surface of the water at all test concentrations suggesting that the EP-290 was above its solubility limit in water. Furthermore, the daphnid results may be influenced by the presence of dimethylformamide. Based on the empirical information, the measured toxicity is limited by the solubility of EP-290, particularly since it is unlikely that a dispersant such as dimethylformamide would be present in significant concentrations in the environment. The ECOSAR predictions, therefore, do not adequately represent the relevant toxicity of the component as they exist in the mixture EP-290.

Aquatic Toxicity of EP-290		
	Reported Values	ECOSAR Prediction
Rainbow trout, 48-hr LC_{50}	>1000 mg/L (16)	
Bluegill sunfish, 48-hr LC_{50}	>1000 mg/L (17)	
Daphnia, 48 hour EC_{50}	0.17 mg/L (18)	
Algae, 96 hour EC_{50}	No data	< 1 mg/L

* Estimated using ECOSAR with measured $K_{o/w}$ (19)

Table 9: Aquatic Toxicity of EP-290.

Recommendation: As evidenced by the different results in the fish and daphnid studies, the potential for environmental toxicity of EP-290 is probably more a function of the environmental conditions and the presence of co-solvents and dispersants (e.g. the daphnid result) or the presence of bulk-phase EP-290 (e.g. the fish result) No additional ecotoxicity studies are recommended as results under laboratory conditions may not be representative of actual toxicity. The available information fills the HPV required data elements.

3.4 Mammalian Toxicity

Several studies have been conducted on the components of EP-290, which generally indicate a low order of toxicity for these higher molecular weight alcohols, olefins, ethers and esters. Specific health effects information for EP-290 comes from studies on Heavy Oxo Ends (HOE), which is another name for the material defined by the CAS RN 68526-82-9. Studies that were conducted on HOE include, acute oral, acute dermal, acute inhalation, 14-day inhalation and 13-week inhalation toxicity studies.

3.4.1 Metabolism

Adsorption, distribution, metabolism and excretion are important components in developing an understanding of the potential health effects of a material and of extrapolating data between studies, between routes of administration and between compounds. In the case of EP-290, the mixture is too complex to fully characterize metabolically; however, some generalities are useful in understanding the interrelationships of the components and why data from the long chain alcohol components can be used to estimate the overall toxicity of EP-290.

Although there are marked differences in the structures and physicochemical properties of the components of EP-290, their mammalian toxicity potential is largely similar due to common metabolic pathways and common metabolites. The basic structure in the composition of this material is the aliphatic chain with an oxygen-containing group. The esters, for example, in the body will be subject to rapid carboxylesterase catalyzed hydrolysis to the corresponding alcohol and carboxylic acid. The alcohols are known to undergo oxidative metabolism to the corresponding carboxylic acid (fatty acid). As a wide variety of different chain length and configurations of fatty acids compose a significant portion of the mammalian diet, the body has developed effective metabolic pathways to convert these fatty acids into energy and building blocks for growth and maintenance of bodily function. Mitochondrial beta-oxidation, which removes two-carbon units from a fatty acid, is the best-known pathway for metabolism of fatty acids and is known to “detoxify” large quantities of dietary fatty acids daily. The branched fatty acids cannot undergo beta-oxidation, but as branched fatty acids are also a normal part of the mammalian diet, the body has developed an effective means to detoxify branched fatty acids, specifically peroxisomal alpha-oxidation. Likewise, higher olefinic compounds can be oxidized, initially to two aldehydes, which are readily converted into the carboxylic acids that form the common metabolic pathway for mammalian metabolism of EP-290.

Potential toxicity of the branched fatty acids is demonstrated from Refsum’s disease, a rare hereditary metabolic disease in which peroxisomal alpha-oxidation is lacking. In this autosomal recessive disorder, the clinical features include retinitis pigmentosa, blindness, anosmia, deafness, sensory neuropathy, ataxia and accumulation of phytanic acid in plasma- and lipid-containing tissues (20). Phytanic acid is a naturally occurring branched-chain fatty acid found in many foods and the daily intake is estimated at 50-100 mg (ibid.). Thus, with rare exception, humans are known to have the capability of effectively detoxifying both the linear and the branched chain fatty acids and using both of these types of materials as primary nutrients for energy production.

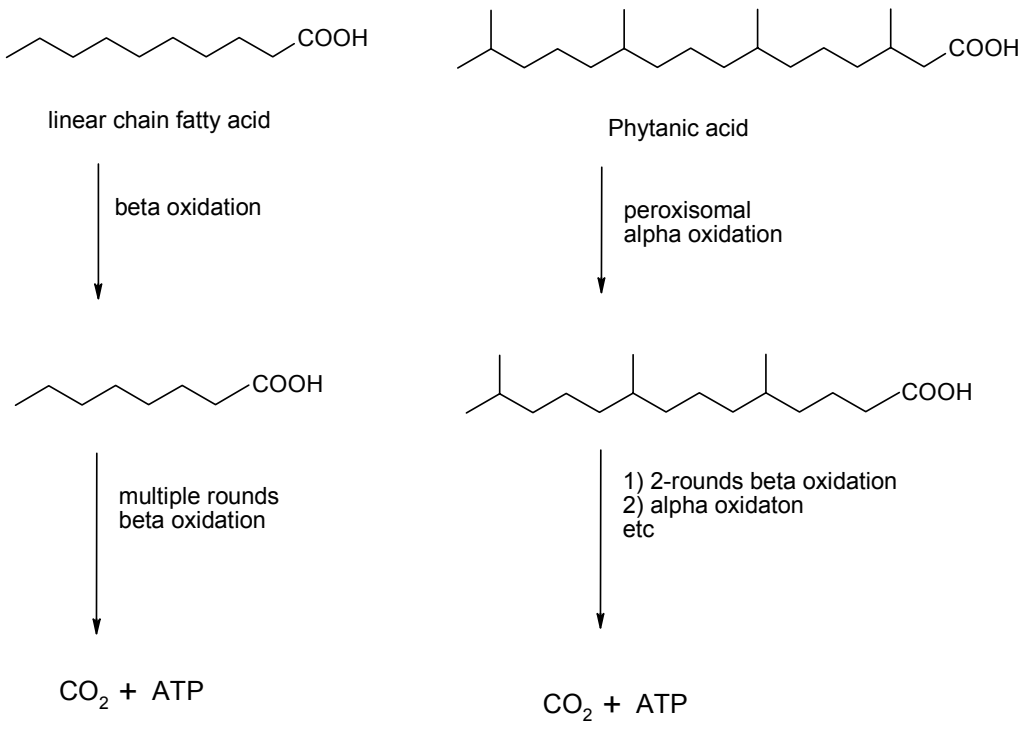


Figure 1. Oxidation of Linear and Branched Fatty Acids

In summary, virtually all of the chemical entities contained in EP-290 are metabolized initially into linear and branched chain fatty acids. These fatty acids are readily metabolized as nutrients by established mammalian biochemical pathways. Therefore, adverse effects from incidental systemic exposure to EP-290 are not anticipated and the use of surrogate data from the long chain alcohols is justified for estimation of potential EP-290 health effects.

3.4.2 Acute Toxicity

3.4.2.1 Oral Exposure

The oral LD_{50} of EP-290 (tested as HOE) was determined in Sprague-Dawley rats to be greater than 15,800 mg/kg (21). This study used incremental increasing doses of test material (similar to the current OECD Toxic Class protocol) to reduce animal usage and maximize the amount of data generated. The only limitation to this study is that the animals were only observed for seven days post dosing rather than the current 14-day observation period. The doses, however, were several times the maximum that would be used today and the animals recovered from the initial toxic signs by three of four days after dosing; therefore, this is considered an adequate study.

3.4.2.2 Inhalation Exposure

The four-hour LC50 for Heavy Oxo Ends was determined to be greater than 4.9 mg/L in a 1985 aerosol study conducted with analytical verification of concentrations and aerosol size determination (22). Exposure produced signs of respiratory, eye, and skin irritation at 4.9 and 1.1 mg/1. Clear body weight reduction occurred at the 4.9 mg/L with marginal reduction occurring at 1.1 mg/L. As the recommended (OECD 403) limit–dose for respirable materials is 5 mg/L this study is considered an adequate test of the acute inhalation toxicity of this material

3.4.2.3 Dermal Exposure

The dermal LD50 was also determined to be greater than 7940 mg/kg in rabbits in a study conducted with incrementally increasing doses and a limited number of test animals (23). In the dermal study, a 14-day post-dosing observation period was employed and the main limitation is that only four rabbits were treated; however, with the high doses, it is considered an adequate test of dermal toxicity.

Recommendation: No additional acute toxicity studies are recommended. The available data fill the HPV required endpoints for acute toxicity. Although the available studies do not meet all the requirements of the current OECD guidelines in all cases, the weight of evidence shows that the oral and inhalation toxicity is very low. Likewise, the limited study of dermal toxicity provides support for low hazard by this route. Conduct of additional studies would not add significantly to our understanding of this material's toxicity and it is recommended that no additional acute toxicity studies be conducted.

3.5.0 Repeat Dose Toxicity

Oral Exposure

A subchronic aerosol inhalation study of HOE was conducted in 1987 (24). Groups of 15 Sprague-Dawley rats of each sex were exposed to atmospheres containing the test substance six hours a day, five days a week for 13 weeks. The target levels of test substance were 0, 100, 300, and 1000 mg/m^3 and the achieved concentrations were very near target levels. Clear treatment related effects were observed in rats from the high-dose group manifest as reduced body weight gains, increased lung weights and microscopic pulmonary morphology. Mid-dose group animals exhibited an increase in lung weigh only for males and microscopic effects that were considered by the examining pathologist to be indicative of a "physiological response to aerosol exposure" and of questionable toxicological significance. In light of the dose-response continuum and minimal microscopic effects at the low dose, the mid dose is considered a LOAEL and the low dose is considered a NOAEL. The only target organ identified was the respiratory tract where necrosis of olfactory-respiratory epithelium was observed in numerous treated animals but not in controls. Additionally, mid and high-dose animals showed interstitial inflammation of the lungs in rats. No changes attributed to treatment in any organ system related to reproductive function were

mentioned in the laboratory report although most reproductive organs from high dose and control animals underwent macroscopic and microscopic evaluation. The study is considered an adequate test of the repeated-dose toxicity of EP-290

Recommendation: No additional repeated-dose studies are recommended. The available inhalation study adequately fills the HPV required data element for repeated-dose toxicity.

3.6.0 Genetic Toxicity

The SIDS/HPV requirement for genetic toxicity screening is for two end-points, one sensitive to point mutation and one sensitive to chromosomal aberrations. In the case of this material, adequate tests have been conducted on several components of the mixture (indicating low genotoxic hazard) but not on the mixture as a whole to cover either of these endpoints.

Component	Point Mutation Tests		Chromosomal Structure Tests	
Alcohols				
Behenyl alcohol C-22	Negative [rs] Ames Test (25)	Negative [rs] HGPRT test V79 Cells	Negative [rs] CA test in V79 cells	Negative [rs] In vivo mouse micronucleus test
2-Ethylhexanol C-8	Negative Ames Test (26,27,28)	Negative Mouse lymphoma L5178Y cells (26)	Negative CA test in CHO cells (29)	Negative Cell transform test JB6 cells (30)
Acids				
Stearic acid	Negative Ames test (31)		Negative Mitotic Recombination (31)	Negative Aneuploidy induction test (31)
Esters				
Octyldodecyl stearoyl stearate	Negative Ames test (32)		Negative In vivo mouse micronucleus test (32)	
Olefins				
C20-C24 alkenes, branched and linear	Negative [rs] Ames test (33)		Negative [rs] Human lymphocyte CA test (34)	Negative [rs] In vivo mouse micronucleus test (35)
1-Octadecene	Negative Ames test (36)		Negative Mitotic Recombination (36)	Negative Rat liver cell CA (36)
Tetradecene	Negative [rs] UDS test (37)	Negative [rs] HGPRT test (38)	Negative [rs] Cell transform test BALB/3T3 (39)	
[rs] indicates that a robust summary is available in the appendix				

Table 10. Genetic Toxicity of EP-290 Components

Examination of the components of EP-290 (Table 1) and the materials tested for genotoxicity in Table 10 suggests that the components fall into two groups relative to potential for genotoxicity. The largest group is the aliphatic alcohols, esters, ethers and acetals. This type of structure is not associated with any structural alerts for genotoxicity. As was discussed in the metabolism section, all members of this group are oxidized to saturated fatty acids that proceed down a common metabolic pathway (beta and alpha oxidation) in the form of "nutrients". Olefins are the second group. Metabolically, after oxidation to carboxylic acids, they join the aliphatic compounds in the alpha-beta-oxidation pathways, where they are metabolized as nutrients. As shown in Table 11, a substantial amount of genotoxicity testing is available and none of these studies indicate genotoxic activity.

Another concern with any material characterized as a "distillation residue" is the potential for formation of aromatic and tar-like species in distillation kettle at high temperature. As EP-290 is produced in a continuous process, extreme temperatures that may cause aromatization are never reached. Thus the opportunity for an untoward genotoxic molecule to be produced is limited.

Two basic approaches are possible for genotoxicity hazard assessment for this particular mixture. The first is to gather what is known about the components and similar compounds and base the assessment on the genotoxicity of the individual components, grouping the components where it makes sense. The second approach is to actually conduct genotoxicity testing on the product.

The scientific rationale for conducting genotoxicity testing of EP-290 is weak because: 1. This is a variable mixture and what is tested may or may not be representative of future production. 2. If the material is tested and found to be either positive or negative the result does not advance our knowledge of mutagenic substances as no particular structure is identified with the activity.

Based on the concept that components of EP-290 fall into two groups regarding genotoxicity, enough definitive information is available on EP-290 components, or surrogates of components, to construct a scientifically defensible argument supporting a lack of genotoxic potential for EP-290. Specifically, genotoxicity data for the materials in Table 10 are available and these data are thought to comprise a sufficient data-set to allow a "read across" approach for the two HPV genotoxicity endpoints. The materials listed in the table cover the alcohols (both long chain and shorter chained), acids and esters subcategories of the aliphatic grouping and three representative olefins have been selected to provide additional assurance that structures typical of the olefinic components of EP-290 are not genotoxic. Robust summaries have been provided for representative materials and tests in the appendix of this testing plan.

Recommendation: No additional testing for genotoxicity is recommended. The required HPV endpoints are filled by numerous studies indication lack of genotoxicity for the components of EP-290.

3.7.0 Reproductive Toxicity

Data on reproductive toxicity of EP-290 are available from the 13-week repeated dose study and from various studies on chemicals representative of EP-290's major components. A robust summary for an OECD-422 study of tetradecene is provided as a representative higher alkene (higher alkenes could be up to 30% of EP-290 content). As is the case for genotoxicity, the alkenes are considered more suspicious as potential reproductive/developmental toxins than the long chain acid and alcohols as they have a double bond that could be activated to an epoxide. Results of this gavage OECD-422 screening test indicate a reproductive or developmental NOAEL of 1000 mg/kg-day (the maximum dose) while the NOAELs for systemic toxicity of the parental animals were 100 mg/kg for females and less than 100 mg/kg for males (40).

The long chain alcohols, acid, and esters would appear to be of lesser concern as this group of materials shares identical or similar structures with the nutritional fatty acids found in most foods. Confirming this is a recent reproductive toxicity study of behenyl alcohol (a 22 carbon saturated straight-chain normal alcohol) (41). In this study, administration of behenyl alcohol to rats (up to 1000 mg/kg) or rabbits (up to 2000 mg/kg) had no effect on fertility or reproduction. The study in rats included 71 days of pre-mating administration to males and 15 days Premating exposure to females followed by continued exposure during mating and up to gestation-day 17.

Reproductive effects have been adequately assessed through the combination of the negative reproductive and developmental toxicity studies on components of this complex mixture and the subchronic study of EP-290 itself in which reproductive organs were evaluated and found to be unaffected by treatment with EP-290 (24). Conduct of additional studies would not add significantly to our understanding of this material's reproductive toxicity.

Recommendation: No additional reproductive testing is recommended, as the available data are sufficient to assess the reproductive toxicity of this material according to the HPV guidelines.

3.8.0 Developmental Toxicity

While no developmental toxicity studies for EP-290 were located, major components have been tested for developmental toxicity. A mixture of alcohols known as C7-9-11 Alcohol (CAS RN 85566-14-9), derived from a hydroformylation reaction and consisting mainly of linear alcohols with significant amounts of alpha-methyl branched alcohols ranging in carbon chain length from C7 to C11 was tested for developmental toxicity (42). The study was conducted according to OECD 414 guidelines except that 10 animals instead of the recommended 20 per group were used. Test material was administered at doses of 144, 720, or 1440 mg/kg/day. Females were

sacrificed on gestation day 20. Fetuses were removed and evaluated for sex, weight, and any external, soft tissue, or skeletal findings. No adverse effects were observed at any dose of C7-9-11 Alcohol. This included changes in body weight and food consumption by the dams, reproductive parameters, and signs of fetal toxicity. The maternal and fetal NOAEL were determined to be 1,440 mg/kg-day.

Longer chain alcohols have also been show not to adversely affect the developing conceptus. The 22-carbon straight-chained alcohol, behenyl alcohol (docosanol CAS RN 30303-65-2) has been examined in a modern guideline developmental toxicity study in rabbits (41). Doses were 1, 125, 500 or 2000 mg/kg day from day 6 to 19 of gestation using 22 rabbits per group. No compound related effects were observed on maternal or developmental endpoints

A representative higher olefin tetradecene has also been studied in a modified OECD-422 combined repeated dose study with reproductive and developmental screen (40). Results of this gavage test indicate a developmental NOAEL of 1000 mg/kg-day (the maximum dose) while the NOAELs for systemic toxicity of the dams was 100 mg/kg. This indicates that the higher olefins present little developmental toxicity hazard.
Taken together, the developmental toxicity studies of major components and the lack of structural alerts indicate a low developmental toxicity hazard for EP-290.

Recommendation: No additional developmental toxicity testing is required as the available data are sufficient to assess the developmental toxicity of this material.

4.0 Conclusions

With regard to the parameters specified in the EPA HPV Challenge program, it is concluded that the available information on EP-290 fills all of the requirements for physicochemical parameters, fate information, aquatic toxicity and mammalian toxicity. Although the available studies do not meet all the requirements of the current OECD guidelines in all cases, taken together the information provided a reliable hazard assessment.

4.1 HPV Data Matrix

EP-290, CAS RN 68526-82-9			
ENDPOINT	**Value**	**Comment**	**Kl.**
Physico-chemical			
Melting point	-44°C	Technical Specification, variable	2
Boiling point	130 – 270°C @ 13 hPa	Technical Specification, variable	2
Vapor pressure	< 0.01 hPa @ 25°C	Extrapolated from technical specifications, variable	2
Partition coefficient (log Kow)	Range 3.1-11.7	EpiWin	2
Water Solubility	< 100 mg/L	EpiWin	2
Environmental fate			
Photodegradation	$t_{1/2}$ < 1 day	EpiWin	2
Hydrolysis	$t_{1/2}$ > 1 year	EpiWin	2
Transport between compartments	Variable	EQC Level 3	2
Ready Biodegradability	Variable	EpiWin	2
Ecotoxicity			
Acute Fish	> 1000 mg/L	Study	2
Acute daphnia	17 mg/L	Study	1
Algal Inhibition	< 1 mg/L	ECOSAR	2
Health Effects			
Acute Oral	> 15,800 mg/kg	Heavy oxo ends	2
Acute Dermal	> 7,940 mg/kg	Heavy oxo ends	1
Acute inhalation	> 4.9 mg/L	Heavy oxo ends	1
Gene Tox			
Ames test	negative	Components and/or surrogates	2
In-vitro Cytogenetic	negative	Components and/or surrogates	2
HGPRT	negative	Components and/or surrogates	2
Micronucleus	negative	Components and/or surrogates	2
DNA-damage	negative	Components and/or surrogates	2
Subchronic/Repro			
90-day (LOAEL)	300 mg/m^3	Inhalation	2
90-day (NOAEL)	100 mg/m^3	Inhalation	2
Reproduction	negative	Components and/or surrogates	2
Developmental	negative	Components and/or surrogates	2

5.0 References

1 Klimisch H-J ; Andreae M ; Tillmann U. A systematic approach for evaluating the quality of experimental toxicological and ecotoxicological data. Regulatory Toxicology and Pharmacology; 25: 1-5 (1997).

2 MSDS for EP-290 Heavy Oxo Ends, revised 2/2/2000. BASF Corporation.

3 Technical Bulletin for EP-290 Heavy Oxo Ends BASF Product number 526251, BASF Corporation, Freeport TX., printed 2/1991.

4 Exxon Biomedical Sciences Inc., Ready Biodegradability: OECD 301F Manometric Respirometry Test. 114794A. 1997. As cited in Revised Robust Summaries for the Olefin Hydroformylation Products Category 15 October 2002.

5 Exxon Biomedical Sciences Inc., Ready Biodegradability: OECD 301F Manometric Respirometry Test. 114994A. 1997. As cited in Revised Robust Summaries for the Olefin Hydroformylation Products Category 15 October 2002.

6 IUDLID-2000 document for 2-Ethylhexanol CAS RN 104-76-7, European Chemicals Bureau, 2000

7 Exxon Biomedical Sciences Inc., Ready Biodegradability: OECD 301F Manometric Respirometry Test. 180294A. 1997. As cited in Revised Robust Summaries for the Olefin Hydroformylation Products Category 15 October 2002.

8 IUDLID-2000 document for Fatty acids C10-14 CAS RN 90990-09-3, European Chemicals Bureau, 2000

9 IUDLID-2000 document for Dodecanedioic acid CAS RN 693-23-2, European Chemicals Bureau, 2000

10 IUDLID-2000 document for 2-Ethylhexyl Laurate CAS RN 20292-08-4, European Chemicals Bureau, 2000

11 Exxon Biomedical Sciences Inc., Ready Biodegradability: OECD 301F Manometric Respirometry Test. 1191294A. 1997. As cited in Revised Robust Summaries for the Olefin Hydroformylation Products Category 15 October 2002.

12 Exxon Biomedical Sciences Inc., Ready Biodegradability: OECD 301F Manometric Respirometry Test. 119294A. 1997. As cited in Revised Robust Summaries for the Olefin Hydroformylation Products Category 15 October 2002.

13 Hyman, Michael R. Final Report of EPA Grant Number: R823426, Title: Aerobic Cometabolism of Ether-bonded Compounds. EPA National Center for Environmental Research. http://es.epa.gov/ncer/index.html

14 Harris, J.C., Rate of Hydrolysis in *Handbook of Chemical Property Estimation Methods*, WJ Lyman ed. ACS publication 1990.

15 Vollhardt, K. Peter, *Organic Chemistry*, WH Freeman and Company, New York 1987, p 640.

16 Acute Toxicity of Heavy Oxo Ends to Rainbow Trout. Static Assay Report #29999 Analytical Bio-Chemistry Laboratories Inc, Submitted to Monsanto Chemical Co. January 28, 1983

17 Acute Toxicity of Heavy Oxo Ends to Bluegill Sunfish. Static Assay Report #29998 Analytical Bio-Chemistry Laboratories Inc, Submitted to Monsanto Chemical Co. January 28, 1983

18 Acute Toxicity of Heavy Oxo-Ends (HOE) to *Daphnia Magna*. Report Number ES-82-SS-63 of MIC Environmental Sciences, Monsanto Chemical Co, 9/10/1982

19 ECOSAR modeling program, version 0.99f, as found in EPIWIN v 3.05, Syracuse Research Corporation, Syracuse NY (April 2000).

20 Anthony S. Wierzbicki, Matthew D. Lloyd, Christopher J. Schofield, Michael D. Feher and F. Brian Gibberd. Refsum's disease: a peroxisomal disorder affecting phytanic acid alpha-oxidation. Journal of Neurochemistry, 2002, 80, 727-735

21 Toxicological Investigations of: Monsanto Heavy Oxo Ends. Younger Laboratories Inc. Monsanto Project number Y-71-174. Submitted to Monsanto Co. 12/1/1971

22 An Acute Inhalation Study of Heavy Oxo Ends in the Rat. Final Report. Bio/dynamics Inc. Project No 84-7726 Submitted to Monsanto. August 1, 1985.

23 Toxicological Investigations of: Monsanto Heavy Oxo Ends. Younger Laboratories Inc. Monsanto Project number Y-71-174. Submitted to Monsanto Co. 12/1/1971

24 A Thirteen-Week Inhalation Toxicity Study with Heavy Oxo Ends in Rats, Project No. 84-7737 (BD-84-359). BioDynamics Inc, sponsored by Monsanto Company, report dated 16 January 1987.

25 Iglesias G, Hlywka JJ, Berg JE, Khalil MH, Pope LE, Tamarkin D. The toxicity of behenyl alcohol. I. Genotoxicity and subchronic toxicity in rats and dogs. Regul Toxicol Pharmacol. 2002 Aug;36(1):69-79.

26 P E Kirby, R F Pizzarello, T E Lawlor, S R Haworth and J R Hodgson, Evaluation of Di-(2-Ethylhexyl)phthalate and its Major Metabolites in the Ames Test and L5178Y Mouse Lymphoma Mutagenicity Assay, Environ. Mutagenesis, 1983, 5, 657-663.

27 . H Shimizu, Y Suzuki, N Takemura, S Goto and H Matsushita, The Results of Microbial Mutation Test For Forty-Three Industrial Chemicals. Jap. J. Ind. Health, 1985, 27, 400-419.

28 J R Warren, N D Lalwani and J K Reddy, Phthalate Esters as Peroxisome Proliferator Carcinogens, Environ. Health Perspectives, 1982, 45, 35-40.

29 B J Phillips, T E B James and S D Gangolli, Genotoxicity Studies of Di(2-ethylhexyl)phthalate and Its Metabolites in CHO Cells, Mutat. Res., 1982, 102, 297-304.

30 J M Ward, B A Diwan, M Ohshima, H Hu, H M Schuller and J M Rice, Tumor-Initiating and Promoting Activities of Di(2-ethylhexyl) Phthalate in vivo and in vitro, Environ. Health Perspect., 1986, 65, 279-291.

31 Elder, R.L. Final Report ont eh Safety Assessment of oleic acid, lauric acid, palmitic acid, myristic acid and stearic acid. J. AM Coll. Toxicol, 1987, 4:107-146 .

32 Final Report on the Safety Assessment of Octyldodecyl Stearoyl Stearate. International Journal of Toxicology 2001 20 (suppl. 3):51-59.

33 Bacterial Reverse Mutation Test using C20-C24 alkenes, branched and linear (Safepharm Laboratories Limited 1998) as cited in The National (Australia) Industrial Chemicals Notification and Assessment Scheme Full Public Report for Gulfteen C14 Isomerized Olefins, 3 October 2000.

34 In Vitro Chromosomal Aberration Test: Human Lymphocytes using C20-C24 alkenes, branched and linear (Safepharm Laboratories Limited 1998). As cited in The National (Australia) Industrial Chemicals Notification and Assessment Scheme Full Public Report for Gulfteen C14 Isomerized Olefins, 3 October 2000.

35 Mammalian Erythrocyte Micronucleus Test Using C20-C24 alkenes, branched and linear (Safepharm Laboratories Limited 1998). As cited in The National (Australia) Industrial Chemicals Notification and Assessment Scheme Full Public Report for Gulfteen C14 Isomerized Olefins, 3 October 2000.

36 In Vitro Genotoxicity of 1-octadecene (EU 1995) as cited in HEDSET and as cited in The National (Australia) Industrial Chemicals Notification and Assessment Scheme Full Public Report for Gulfteen C14 Isomerized Olefins, 3 October 2000.

37 Genetic Toxicology: DNA Damage and Repair/Unscheduled DNA Synthesis (UDS) using Gulftene 12-16 In Vitro (Gulf Life Sciences Center 1984). As cited in The National (Australia) Industrial Chemicals Notification and Assessment Scheme Full Public Report for Gulfteen C14 Isomerized Olefins, 3 October 2000.

38 In Vitro Mammalian Cell Gene Mutation Test: Chinese Hamster Ovary Cell/Hypoxanthine Guanine Phosphoribosyl Transferase Assay (HPRT) using Gulftene 12-16, (Gulf Life Sciences Center 1982). As cited in The National (Australia) Industrial Chemicals Notification and Assessment Scheme Full Public Report for Gulfteen C14 Isomerized Olefins, 3 October 2000.

39 BALB/3T3 Transformation Test Using Gulftene 12-16 (Gulf Life Sciences Center 1983). As cited in The National (Australia) Industrial Chemicals Notification and Assessment Scheme Full Public Report for Gulfteen C14 Isomerized Olefins, 3 October 2000.

40 Combined Repeated Dose Toxicity Study with Reproduction/Developmental Screening Test and Neurotoxicity Study in Rats using 1-tetradecene (Springborn Laboratories Inc 1995) As reported in: National Industrial Chemicals Notification And Assessment Scheme, Full Public Report, Gulftene C14 Isomerised Olefins NA/844 26 February 2001

41 Iglesias G, Hlywka JJ, Berg JE, Khalil MH, Pope LE, Tamarkin D. The toxicity of behenyl alcohol. II. Reproduction Studies in Rats and Rabbits. Regul Toxicol Pharmacol. 2002 Aug;36(1):80-85.

42 Report: Study of the Prenatal Toxicity of Isodecanol, 2-Ethylhexanol, and 711 Alcohol (T.C.) in Rats After Oral Administration (Gavage); EPA OTS Doc #: 89-910000245.