201-15013

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To: NCIC OPPT@EPA, Rtk Chem@EPA
cc: Christopher Bradlee <bradlec@basf-corp.com>, Ralph Parod <parodr@basf.com>
Subject: HPV Submission CAS 68526-82-9

Michael O. Leavitt, Administrator

U. S. Environmental Protection Agency

P.O.Box 147

Merrifield, VA 22116

Dear Administrator Leavitt

On behalf of BASF Corporation (HPV registration number), I am submitting the attached test plan and robust summaries for "Alkenes, C6-10, hydroformylation products, high-boiling" CAS Number 68526-82-9, submitted under the United States Environmental Protection Agency's High Production Volume Chemical Challenge Program.

This document is being submitted in electronic format (Adobe Acrobat pdf file). If you require additional information or have problems with the electronic document please contact me by phone (618-539-5280) or email (erauckman@charter.net).

Sincerely,

Elmer Rauckman PhD, DABT

Consulting Toxicologist for BASF Corporation


EP-290 Test Plan MV.pdf


EP-290 RS Fin MV.pdf

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

U.S. EPA HPV Challenge Program Submission

December 29, 2003

Submitted by:

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Table of Contents

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.

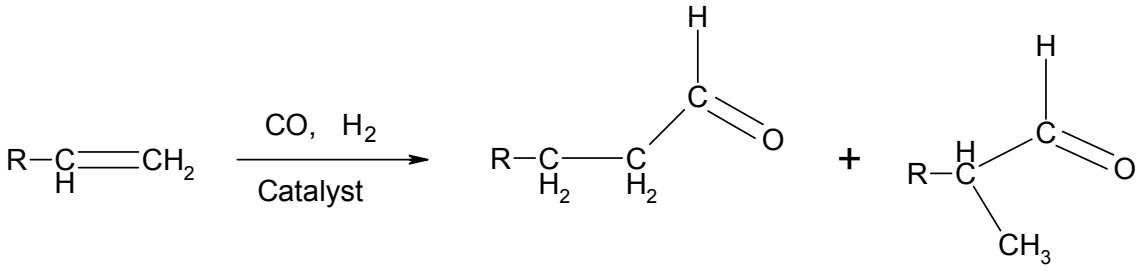
2.0 Chemistry

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.

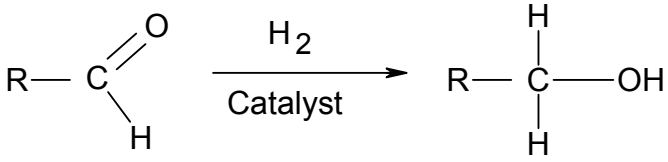
2.1 Production of EP-290

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:

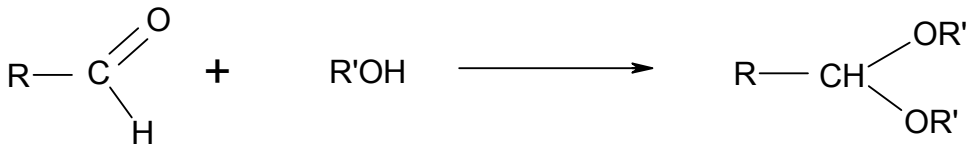


This aldehyde mixture is subsequently reduced under the reaction conditions to produce the desired alcohols.

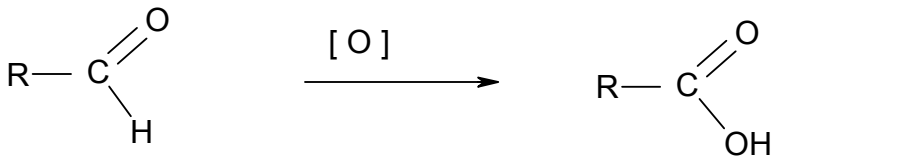


Mixture of alcohols

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.

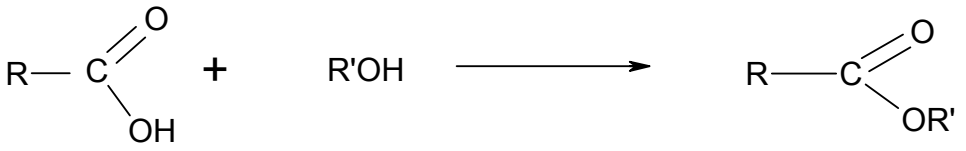


Aldehydes are readily converted to the corresponding carboxylic acid by any oxidizing equivalents.



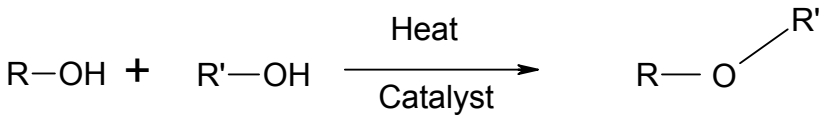
Alkyl Carboxylic Acids

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



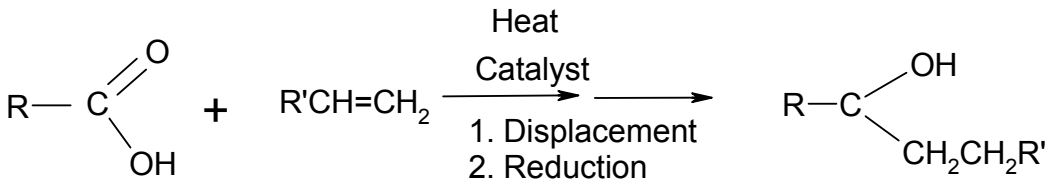
Alkyl Esters

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	CCCCCCCCCCCCCCCCCCCCO	8.6986
	CCCCCCCCCCCCCCCCCCC(C)CO	8.6251
	CCCCC(CC)CCCCCCCCCCCCCO	8.6251
	CCCCC(CC)CCCCCCCCCCC(C)CO	8.5516
C25 Alcohols	CCCCCCCCCCCCCCCCCCCCCCCCCO	11.1541
C18 Ether	CCCCCCCCCOCCCCCCCCC	7.9246
C22 Ether	CCCCCCCCCCCOCCCCCCCCCCC	9.8890
Hexedecene	CCCCCCCCCCCCCCC=C	8.0626
Eicosene	CCCCCCCCCCCCCCCCC=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	CCCCCCCCCCCCCCCCCCCCO	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	CCCCCCCCCCCCCCCCCCCCO	0.001	10.2	0.002	89.8
Octadecene	C18	CCCCCCCCCCCCCCCCC=C	0.0002	10.1	0.000003	89.9
Ethers, C_{18}-C_{22}	C20	CCCCCCCCCCOCCCCCCCCCC	0.0004	10.1	0.00002	89.9
Esters, C_{23} and higher	C28	CCCCCCCCCCCCC(=O)OCCCCCCCCCCCCC	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.

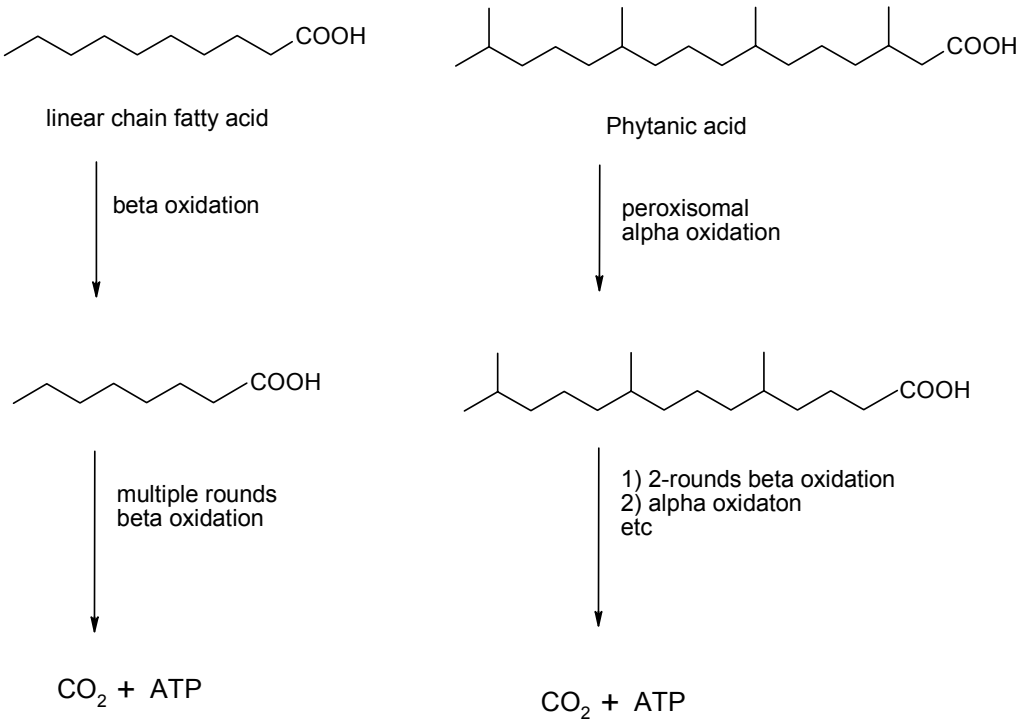


Figure 1. Oxidation of Linear and Branched Fatty Acids

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

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201-15013

HPV Data Set

EP-290

Robust Summaries

Existing Chemical	:	ID: 68526-82-9
Memo	:	Alkenes,C6-10, hydroformylation products, high boiling
CAS No.	:	68526-82-9

Producer related part

Company	:	BASF Corporation
Creation date	:	11.11.2002

Substance related part

Company	:	BASF Corporation
Creation date	:	11.11.2002
Status	:	
Memo	:	Prepared by Elmer Rauckman PhD DABT Toxicology and Regulatory Affairs Freeburg IL 62243 618-539-5280 rauckman@toxicsolutions.com
Printing date	:	30.12.2003
Revision date	:	
Date of last update	:	30.12.2003
Number of pages	:	52
Chapter (profile)	:	
Reliability (profile)	:	
Flags (profile)	:	

1.0.1 APPLICANT AND COMPANY INFORMATION

Type	:	manufacturer
Name	:	BASF Corporation
Contact person	:	
Date	:	
Street	:	3000 Continental Drive
Town	:	Mt. Olive, NJ 07828-1234
Country	:	
Phone	:	
Telefax	:	
Telex	:	
Cedex	:	
Email	:	
Homepage	:	

16.12.2003

1.2 SYNONYMS AND TRADENAMES

2.1 MELTING POINT

Value : ca. -44 °C

Method : Determined by an unknown method by BASF Corporation on product.
Test substance : EP-290 Heavy Oxo Ends BASF Product number 526251
Reliability : (2) valid with restrictions
26.10.2003 (29)

2.2 BOILING POINT

Value : ca. 130 - 273 °C at 13 hPa
Decomposition :
Method : other: distillation control
Year :
GLP :
Test substance :

Remark : This range represents the inital boiling point of the mixture to the boiling point after 80% of the product has been removed. A certain percent of residue would also remain.
Test substance : EP-290 Heavy Oxo Ends BASF Product number 526251
Reliability : (2) valid with restrictions
26.10.2003 (29)

2.3 DENSITY

Type : density
Value : = .845 g/cm³ at 20 °C

Remark : This is a measured value for typical product
Test substance : EP-290 Heavy Oxo Ends BASF Product number 526251
Reliability : (2) valid with restrictions
26.10.2003 (29)

2.4 VAPOUR PRESSURE

Value : < .01 hPa at 25 °C
Decomposition :
Method : other (calculated)
Year :
GLP :
Test substance :

Method : EPIWIN 3.05 was used to determine the vapor pressures of several typical components to gain an understanding of the components probable vapor pressure range.

Result :

Structures were input using standard SMILES notation.

Component	Vapor Pressure (mm Hg) Exp*	Calc	Higher VP(hPa)
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	0.0003

* Experimental vapor pressures as found in the SRC database contained in EPIWIN.

Test substance :

Representative model compounds

Conclusion

Most components are of very low volatility and have a vapor pressure below 0.01 hPa

Reliability : (2) valid with restrictions

EPIWIN estimates are assigned a reliability of 2

27.10.2003 (31)

Value : = .0035 hPa at 25 °C
Decomposition :
Method :
Year :
GLP :
Test substance : other TS

Remark : Most volatile alkene component
Test substance : 1-HEXADECENE (CASNO 629-73-2)
Reliability : (2) valid with restrictions
Handbook value

27.10.2003 (11)

2.5 PARTITION COEFFICIENT

Partition coefficient : octanol-water
Log pow : ca. 3 - 12 at 20 °C
pH value : -
Method : other (calculated)
Year :
GLP :
Test substance :

Method :

Calculation with EPIWIN

The Ko/w of each component (and isomer) was calculated with EPIWIN based on the SMILES notation. The relative quantity of each was used to construct a weighted average for the composite Ko/w. The utility of the composite Ko/w is questionable since the materials will distribute and interact with biological systems independently. The chart showing the entire range of Ko/w values provides an overview of the possible behavior of the components.

Result :

Component	SMILES	log Kow	fract	Rel %
C9	CCCCCCCCCO	3.2965	0.6	
	CCCCCCC(C)CO	3.223	0.2	
	CCC(CC)CCCCO	3.223	0.15	
	CCC(CC)CC(C)CO	3.1495	0.05	
				2
C11	CCCCCCCCCCCO	4.2787	0.6	
	CCCCCCCCC(C)CO	4.2052	0.2	
	CCC(CC)CCCCCCO	4.2052	0.15	
	CCC(CC)CCCC(C)CO	4.1317	0.05	
				12
C13	CCCCCCCCCCCCCO	5.2609	0.6	
	CCCCCCCCCCC(C)CO	5.1874	0.2	
	CCCCC(CC)CCCCCCO	5.1874	0.15	
	CCCCC(CC)CCCC(C)CO	5.1139	0.05	
				15
C20	CCCCCCCCCCCCCCCCCCCCO	8.6986	0.6	
	CCCCCCCCCCCCCCCCCC(C)CO	8.6251	0.2	
	CCCCC(CC)CCCCCCCCCCCCCO	8.6251	0.15	
	CCCCC(CC)CCCCCCCCCC(C)CO	8.5516	0.05	
				15
C25	CCCCCCCCCCCCCCCCCCCCCCCCCO	11.1541		2
Ethers				
C18	CCCCCCCCCOCCCCCCCCC	7.9246		3.5
C22	CCCCCCCCCCCCOCCCCCCCCCCC	9.889		3.5
Hexedecene	CCCCCCCCCCCCCCC=C	8.0626		7.5
Eicosene	CCCCCCCCCCCCCCCCC=C	9.0448		7
2-Bu-octol	CCCCCCC(CCCC)CO	4.6963		6.5
Ester C22	CCCCCCCCCCC(=O)OCCCCCCCCCCC	9.704		2.5
Ester C28	CCCCCCCCCCCCC(=O)OCCCCCCCCCCCC	11.6684		2.5

Using the weighted average the log $K_{o/w}$ = 7.07

Test substance :
Representative model compounds

Conclusion :
Major components have a Log Kow between about 3 and 12

Reliability : (2) valid with restrictions

EPIWIN estimates are assigned a reliability of 2

Flag : Critical study for SIDS endpoint

27.10.2003 (31)

Partition coefficient : octanol-water
Log pow : = 4.11 at 25 °C
pH value :
Method :
Year :
GLP :
Test substance : other TS

Remark : Most prevalent single alcohol
Test substance : 1-DECANOL (CASNO 112-30-1)
Reliability : (2) valid with restrictions
Calculated by acceptable method

12.11.2002 (25)

2.6.1 SOLUBILITY IN DIFFERENT MEDIA

Solubility in : Water

Value	:	< 100 mg/l at 20 °C
pH value	:	
concentration	:	at °C
Temperature effects	:	
Examine different pol.	:	
pKa	:	at 25 °C
Description	:	
Stable	:	
Deg. product	:	
Method	:	other: Calculated
Year	:	
GLP	:	
Test substance	:	

Method :

EPIWIN 3.05 was used to determine the water solubility of several typical components to gain an understanding of the components range of water solubilities.

Structures were input using standard SMILES notation.

Result :

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

* Experimental value found in SRC data base contained in EPIWIN 3.05

Test substance :

Representative model compounds

Conclusion :

The most water soluble components have a water solubility in the range of 100 mg/L. The mixture can be considered essentailly insoluble in water.

Reliability : (2) valid with restrictions

EPIWIN estimates are assigned a reliability of 2

Flag : Critical study for SIDS endpoint

27.10.2003 (31)

3.1.1 PHOTODEGRADATION

Type : air
Light source : Sun light
Light spectrum : nm
Relative intensity : based on intensity of sunlight

Method :

Calculated with AOP v1.90 Program based on SMILES structure

Result :

```
AOP Output

SMILES : CCCCCCCCCCCCCO
CHEM   :
MOL FOR: C13 H28 O1
MOL WT : 200.37

-------- SUMMARY (AOP v1.90): HYDROXYL RADICALS -------------------
Hydrogen Abstraction       =  19.4675 E-12 cm3/molecule-sec
Reaction with N, S and -OH =   0.1400 E-12 cm3/molecule-sec
Addition to Triple Bonds   =   0.0000 E-12 cm3/molecule-sec
Addition to Olefinic Bonds =   0.0000 E-12 cm3/molecule-sec
Addition to Aromatic Rings =   0.0000 E-12 cm3/molecule-sec
Addition to Fused Rings    =   0.0000 E-12 cm3/molecule-sec

   OVERALL OH Rate Constant =  19.6075 E-12 cm3/molecule-sec
   HALF-LIFE =     0.546 Days (12-hr day; 1.5E6 OH/cm3)
   HALF-LIFE =     6.546 Hrs

------ SUMMARY (AOP v1.90): OZONE REACTION ----------------------

               ******  NO OZONE REACTION ESTIMATION ******
               (ONLY Olefins and Acetylenes are Estimated)

Experimental Database:  NO Structure Matches




SMILES : CCCCCCCCCCCCCCCCCCCCO
CHEM   :
MOL FOR: C20 H42 O1
MOL WT : 298.56

--------- SUMMARY (AOP v1.90): HYDROXYL RADICALS -------------------
Hydrogen Abstraction       =  29.3588 E-12 cm3/molecule-sec
Reaction with N, S and -OH =   0.1400 E-12 cm3/molecule-sec
Addition to Triple Bonds   =   0.0000 E-12 cm3/molecule-sec
Addition to Olefinic Bonds =   0.0000 E-12 cm3/molecule-sec
Addition to Aromatic Rings =   0.0000 E-12 cm3/molecule-sec
Addition to Fused Rings    =   0.0000 E-12 cm3/molecule-sec

   OVERALL OH Rate Constant =  29.4988 E-12 cm3/molecule-sec
   HALF-LIFE =     0.363 Days (12-hr day; 1.5E6 OH/cm3)
   HALF-LIFE =     4.351 Hrs
-------- SUMMARY (AOP v1.90): OZONE REACTION ----------------------

               ******  NO OZONE REACTION ESTIMATION ******
               (ONLY Olefins and Acetylenes are Estimated)

Experimental Database:  NO Structure Matches
```

```
SMILES : CCCCCCCCCCCCCCCCC=C
CHEM   :
MOL FOR: C18 H36
MOL WT : 252.49
---------- SUMMARY (AOP v1.90): HYDROXYL RADICALS -------------------
Hydrogen Abstraction       =  20.8346 E-12 cm3/molecule-sec
Reaction with N, S and -OH =   0.0000 E-12 cm3/molecule-sec
Addition to Triple Bonds   =   0.0000 E-12 cm3/molecule-sec
Addition to Olefinic Bonds =  26.3000 E-12 cm3/molecule-sec
Addition to Aromatic Rings =   0.0000 E-12 cm3/molecule-sec
Addition to Fused Rings    =   0.0000 E-12 cm3/molecule-sec

   OVERALL OH Rate Constant =  47.1346 E-12 cm3/molecule-sec
   HALF-LIFE =     0.227 Days (12-hr day; 1.5E6 OH/cm3)
   HALF-LIFE =     2.723 Hrs

--------- SUMMARY (AOP v1.90): OZONE REACTION ----------------------
   OVERALL OZONE Rate Constant =     1.200000 E-17 cm3/molecule-sec
   HALF-LIFE =      0.955 Days (at 7E11 mol/cm3)
   HALF-LIFE =     22.920 Hrs

Experimental Database:  NO Structure Matches



SMILES : CCCCCCCCCCOCCCCCCCCCC
CHEM   :
MOL FOR: C20 H42 O1
MOL WT : 298.56
--------- SUMMARY (AOP v1.90): HYDROXYL RADICALS -------------------
Hydrogen Abstraction       =  41.6461 E-12 cm3/molecule-sec
Reaction with N, S and -OH =   0.0000 E-12 cm3/molecule-sec
Addition to Triple Bonds   =   0.0000 E-12 cm3/molecule-sec
Addition to Olefinic Bonds =   0.0000 E-12 cm3/molecule-sec
Addition to Aromatic Rings =   0.0000 E-12 cm3/molecule-sec
Addition to Fused Rings    =   0.0000 E-12 cm3/molecule-sec

   OVERALL OH Rate Constant =  41.6461 E-12 cm3/molecule-sec
   HALF-LIFE =     0.257 Days (12-hr day; 1.5E6 OH/cm3)
   HALF-LIFE =     3.082 Hrs

--------- SUMMARY (AOP v1.90): OZONE REACTION ----------------------

               ******  NO OZONE REACTION ESTIMATION ******
               (ONLY Olefins and Acetylenes are Estimated)

Experimental Database:  NO Structure Matches



SMILES : CCCCCCCCCCCCC(=O)OCCCCCCCCCCCCC
CHEM   :
MOL FOR: C26 H52 O2
MOL WT : 396.70
---------- SUMMARY (AOP v1.90): HYDROXYL RADICALS -------------------
Hydrogen Abstraction       =  31.6744 E-12 cm3/molecule-sec
Reaction with N, S and -OH =   0.0000 E-12 cm3/molecule-sec
Addition to Triple Bonds   =   0.0000 E-12 cm3/molecule-sec
Addition to Olefinic Bonds =   0.0000 E-12 cm3/molecule-sec
Addition to Aromatic Rings =   0.0000 E-12 cm3/molecule-sec
Addition to Fused Rings    =   0.0000 E-12 cm3/molecule-sec

   OVERALL OH Rate Constant =  31.6744 E-12 cm3/molecule-sec
   HALF-LIFE =     0.338 Days (12-hr day; 1.5E6 OH/cm3)
   HALF-LIFE =     4.052 Hrs
--------- SUMMARY (AOP v1.90): OZONE REACTION ----------------------

               ******  NO OZONE REACTION ESTIMATION ******
               (ONLY Olefins and Acetylenes are Estimated)

Experimental Database:  NO Structure Matches
```

Source :

Toxicology and Regulatory Affairs Calculation -2003

Test substance :

Representative model compounds

Reliability : (2) valid with restrictions

Calculated by an acceptable method

Flag : Critical study for SIDS endpoint
30.12.2003 (12)

3.1.2 STABILITY IN WATER

Type : abiotic
t1/2 pH4 : at °C
t1/2 pH7 : > 1 year at 25 °C
t1/2 pH9 : at °C

Method :

Water stability is estimated using chemical principles and EPIWIN modeling.

Most of the components do not contain a water-reactive or hydrolysable group. The following are considered water stable* for this reason:

-Olefins
-Aliphatic alcohols
-Aliphatic ethers
-Aliphatic carboxylic acids

The materials that are potentially hydrolysable are;
-Aliphatic esters
-Aliphatic acetals

These were entered into EPIWIN (HYDROWIN v1.67) in an attempt to estimate hydrolysis rates using the following SMILES notations

C-11,11 Ester CCCCCCCCCCC(=O)OCCCCCCCCCCC
C-9,9,9 Acetal CCCCCCCCC(OCCCCCCCCC)OCCCCCCCCC

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

Result :

The ester has an estimated Kb of 0.01077 L/mol-sec.
Estimated half-life for ester:
pH 8 = 2.0 years
pH 7 = 20.4 years

The program cannot estimate the hydrolysis rate for acetals. Although acetals are chemically considered more labile than esters, they are not hydrolyzed rapidly at neutral pH*. In addition, since the acetal is almost completely water insoluble (EPIWIN estimated water solubility 0.00000037 mg/L) it will remain with the organic phase and will not have the opportunity to hydrolyze under conditions where a significant amount of EP-290 is in contact with water. Furthermore, the acetal is a low-level component of EP-290 (2-4%) and its hydrolysis would not be a major factor in the overall water stability of the material.

Relative to hydrolysis of the model ester, limited water solubility (EPIWIN estimate 0.000036 mg/L) would severely limit the access of water to the ester in bulk material.

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

Test substance :

Representative model compounds

Conclusion :

The product is considered stable in water with a half-life >> 1 year

Reliability : (2) valid with restrictions

EPIWIN estimates are assigned a reliability of 2

Flag : Critical study for SIDS endpoint

27.10.2003 (31)

3.3.1 TRANSPORT BETWEEN ENVIRONMENTAL COMPARTMENTS

Type : fugacity model level III
Media : other: water
Air : % (Fugacity Model Level I)
Water : % (Fugacity Model Level I)
Soil : % (Fugacity Model Level I)
Biota : % (Fugacity Model Level II/III)
Soil : % (Fugacity Model Level II/III)
Method :
Year :

Method :

Because this is a complex mixture, when well mixed into the environment, individual components will distribute according to their individual physiochemical properties. To understand the relative distribution of components it is necessary to look at individual representative components. This was accomplished by selecting a range of materials thought to be most representative of various potentials for distribution. Two alcohols (C13 and C20) were selected as these are components and have differing water-solubility and volatility. One representative olefin (C18), one ether (C20) and one ester (C28) were selected. In the calculation procedure, various isomeric forms were examined and were not found to be greatly different. This selection of materials is considered representative of EP-290.

It was assumed that materials originated in water as this is considered the most likely manner in which EP-290 will enter the environment.

Result :

Alcohol C13 CCCCCCCCCCCCCO

Level III Fugacity Model (Full-Output):
==========

	Chem Name	:
	Molecular Wt	: 200.37
	Henry's LC	: 0.000128 atm-m3/mole (Henrywin program)
	Vapor Press	: 0.000237 mm Hg (Mpbpwin program)
	Liquid VP	: 0.000276 mm Hg (super-cooled)
	Melting Pt	: 31.7 deg C (Mpbpwin program)
	Log Kow	: 5.26 (Kowwin program)
	Soil Koc	: 7.46e+004 (calc by model)

	Concentration (percent)	Half-Life (hr)	Emissions (kg/hr)
Air	0.612	13.1	0
Water	50.6	360	1000
Soil	0.0395	360	0
Sediment	48.8	1.44e+003	0

	Fugacity (atm)	Reaction (kg/hr)	Advection (kg/hr)	Reaction (percent)	Advection (percent)
Air	3.52e-012	153	29	15.3	2.9
Water	6.83e-010	462	240	46.2	24
Soil	3.71e-015	0.361	0	0.0361	0
Sediment	2.06e-010	111	4.62	11.1	0.462

Persistence Time: 474 hr
Reaction Time: 652 hr
Advection Time: 1.73e+003 hr
Percent Reacted: 72.7
Percent Advected: 27.3

Half-Lives (hr), (based upon Biowin (Ultimate) and Aopwin):
Air: 13.09
Water: 360
Soil: 360
Sediment: 1440
Biowin estimate: 3.215 (weeks)

Advection Times (hr):
Air: 100
Water: 1000
Sediment: 5e+004

****

Alcohol C-20: CCCCCCCCCCCCCCCCCCCO

Level III Fugacity Model (Full-Output):
==========

	Chem Name	:
	Molecular Wt	: 298.56
	Henry's LC	: 0.000929 atm-m3/mole (Henrywin program)
	Vapor Press	: 5e-007 mm Hg (Mpbpwin program)
	Liquid VP	: 3.08e-006 mm Hg (super-cooled)
	Melting Pt	: 105 deg C (Mpbpwin program)
	Log Kow	: 8.7 (Kowwin program)
	Soil Koc	: 2.05e+008 (calc by model)

	Concentration (percent)	Half-Life (hr)	Emissions (kg/hr)
Air	0.000623	8.7	0
Water	10.2	360	1000
Soil	0.00198	360	0
Sediment	89.8	1.44e+003	0

	Fugacity (atm)	Reaction (kg/hr)	Advection (kg/hr)	Reaction (percent)	Advection (percent)
Air	5.28e-015	0.663	0.0833	0.0663	0.00833
Water	6.32e-012	261	136	26.1	13.6
Soil	9.28e-019	0.0509	0	0.00509	0
Sediment	1.89e-012	578	24	57.8	2.4

Persistence Time: 1.34e+003 hr
Reaction Time: 1.59e+003 hr
Advection Time: 8.36e+003 hr
Percent Reacted: 84
Percent Advected: 16

Half-Lives (hr), (based upon Biowin (Ultimate) and Aopwin):
Air: 8.702
Water: 360
Soil: 360
Sediment: 1440
Biowin estimate: 2.998 (weeks)

Advection Times (hr):
Air: 100
Water: 1000
Sediment: 5e+004

****

C-18 Olefin Octadecene : CCCCCCCCCCCCCCCCC=C

Level III Fugacity Model (Full-Output):
==========

Chem Name	:			
Molecular Wt	: 252.49			
Henry's LC	: 10.7 atm-m3/mole (Henrywin program)			
Vapor Press	: 0.00261 mm Hg (Mpbpwin program)			
Liquid VP	: 0.0029 mm Hg (super-cooled)			
Melting Pt	: 29.6 deg C (Mpbpwin program)			
Log Kow	: 9.04 (Kowwin program)			
Soil Koc	: 4.5e+008 (calc by model)			

	Concentration (percent)	Half-Life (hr)	Emissions (kg/hr)
Air	0.000207	4.4	0
Water	10.1	360	1000
Soil	2.83e-006	360	0
Sediment	89.9	1.44e+003	0

	Fugacity (atm)	Reaction (kg/hr)	Advection (kg/hr)	Reaction (percent)	Advection (percent)
Air	2.68e-015	0.437	0.0277	0.0437	0.00277
Water	3.94e-008	261	136	26.1	13.6
Soil	8.25e-018	7.28e-005	0	7.28e-006	0
Sediment	1.18e-008	579	24	57.9	2.4

Persistence Time: 1.34e+003 hr
Reaction Time: 1.59e+003 hr
Advection Time: 8.37e+003 hr
Percent Reacted: 84
Percent Advected: 16

Half-Lives (hr), (based upon Biowin (Ultimate) and Aopwin):
Air: 4.4
Water: 360
Soil: 360
Sediment: 1440
Biowin estimate: 2.940 (weeks)

Advection Times (hr):
Air: 100
Water: 1000
Sediment: 5e+004

****

C-20 Ether CCCCCCCCCCOCCCCCCCCCC

Level III Fugacity Model (Full-Output):
==========

Chem Name	:			
Molecular Wt	: 298.56			
Henry's LC	: 0.228 atm-m3/mole (Henrywin program)			
Vapor Press	: 0.000107 mm Hg (Mpbpwin program)			
Liquid VP	: 0.000345 mm Hg (super-cooled)			
Melting Pt	: 76.4 deg C (Mpbpwin program)			
Log Kow	: 8.91 (Kowwin program)			
Soil Koc	: 3.33e+008 (calc by model)			

	Concentration (percent)	Half-Life (hr)	Emissions (kg/hr)
Air	0.000382	6.16	0
Water	10.1	360	1000
Soil	1.75e-005	360	0
Sediment	89.9	1.44e+003	0

	Fugacity (atm)	Reaction (kg/hr)	Advection (kg/hr)	Reaction (percent)	Advection (percent)
Air	4.17e-015	0.574	0.0511	0.0574	0.00511
Water	9.57e-010	261	136	26.1	13.6
Soil	1.24e-018	0.00045	0	4.5e-005	0
Sediment	2.87e-010	578	24	57.8	2.4

Persistence Time: 1.34e+003 hr
Reaction Time: 1.59e+003 hr
Advection Time: 8.37e+003 hr
Percent Reacted: 84
Percent Advected: 16

Half-Lives (hr), (based upon Biowin (Ultimate) and Aopwin):
Air: 6.163
Water: 360
Soil: 360
Sediment: 1440
Biowin estimate: 3.127 (weeks)

Advection Times (hr):
Air: 100
Water: 1000
Sediment: 5e+004

```
**************************************************************************

C-26 Ester: CCCCCCCCCCCCC(=O)OCCCCCCCCCCCCC
Level III Fugacity Model (Full-Output):
=======================================
  Chem Name   :
  Molecular Wt: 396.7
  Henry's LC  : 0.315 atm-m3/mole (Henrywin program)
  Vapor Press : 9.28e-008 mm Hg  (Mpbpwin program)
  Liquid VP   : 1.42e-006 mm Hg  (super-cooled)
  Melting Pt  : 145 deg C (Mpbpwin program)
  Log Kow     : 11.7  (Kowwin program)
  Soil Koc    : 1.92e+011  (calc by model)

          Concentration   Half-Life    Emissions
            (percent)        (hr)       (kg/hr)
   Air       7.59e-007       8.1          0
   Water     10.1            360          1000
   Soil      4.14e-006       360          0
   Sediment  89.9            1.44e+003    0

             Fugacity    Reaction    Advection   Reaction    Advection
              (atm)      (kg/hr)      (kg/hr)    (percent)   (percent)
   Air       3.83e-018    0.000869    0.000102    8.69e-005   1.02e-005
   Water     1.73e-012    261         136         26.1        13.6
   Soil      5.31e-022    0.000107    0           1.07e-005   0
   Sediment  5.19e-013    579         24.1        57.9        2.41

   Persistence Time: 1.34e+003 hr
   Reaction Time:    1.59e+003 hr
   Advection Time:   8.38e+003 hr
   Percent Reacted:  84
   Percent Advected: 16

   Half-Lives (hr), (based upon Biowin (Ultimate) and Aopwin):
      Air:      8.105
      Water:    360
      Soil:     360
      Sediment: 1440
        Biowin estimate: 3.059  (weeks)

   Advection Times (hr):
      Air:      100
      Water:    1000
      Sediment: 5e+004
```

Test substance :

Representative model compounds

Conclusion :

The representative compounds if released into water, will distribute primarily to sediment and water depending on their individual Ko/w values. Except for the shorter chain alcoholic components of EP-290, which may distribute equally between water and sediment, the majority of material is expected to distribute to sediment. This is shown in the following summary table from the Level III calculations.

Component	C#	Distribution (Percent)			
		Air	Water	Soil	Sediment
Alcohol	C13	0.61	50.6	0.04	48.8
Alcohol	C20	0.001	10.2	0.002	89.8
Octadecene	C18	0.0002	10.1	0.000003	89.9
Ether	C20	0.0004	10.1	0.00002	89.9
Ester	C28	0.000001	10.1	0.000004	89.9

Reliability : (2) valid with restrictions
Calculated values are assigned a reliability of 2.

Flag : Critical study for SIDS endpoint

26.10.2003 (9)

3.5 BIODEGRADATION

Type : aerobic
Inoculum : activated sludge, domestic
Concentration : 42 mg/l related to Test substance

Degradation : = 21 (±) % after 28 day(s)

Result : other: limited biodegradation

Method : A Manometric Respirometry Test was preformed according to the OECD-301F test guideline (1992).
GLP: Yes

Result :

Approximately 21% biodegradation of the test material was measured on day 28. Approximately 10% biodegradation was achieved on Day 17.

By day 14, >60% biodegradation of the sodium benzoate positive control was observed, which meets the guideline requirement. No excursions from the protocol were noted. Biodegradation was based on oxygen consumption and the theoretical oxygen demand of the test material as calculated using results of an elemental analysis of the test material.

Percent degradation of test substance in triplicate flasks was: 20.9%, 19.9%, 22.6% (mean = 21.1%)

Test condition :

Non acclimated activated sludge and test medium were combined before adding test material. Test medium consisted of glass distilled water and mineral salts (Phosphate buffer, Ferric chloride, Magnesium sulfate, Calcium chloride).
Test vessels were 1L glass flasks placed in a waterbath and electronically monitored for oxygen consumption. Test material was tested in triplicate, controls and blanks were tested in duplicate. Test material concentration was approximately 42 mg/L. Sodium benzoate (positive control) concentration was 44mg/L. Test temperature was 22 +/-1 Deg C.

All test vessels were stirred constantly for 28 days using magnetic stir bars and plates.

Test substance :

Alkenes, C9-11, C10 Rich, CASNO 68526-56-7, component of EP-290

Reliability : (2) valid with restrictions

Assigned 2 because original report not available for review.

20.12.2003 (14)

Type : aerobic
Inoculum : activated sludge, domestic
Concentration : 57 mg/l related to Test substance
related to
Contact time :
Degradation : = 58 (±) % after 28 day(s)
Result :

Method :

A Manometric Respirometry Test was preformed according to the OECD-301F test guideline (1992).

GLP: Yes

Result :

Approximately 58% biodegradation of the test material was measured on day 28. Approximately 10% biodegradation was achieved on Day 7.

By day 14, >60% biodegradation of the sodium benzoate positive control was observed, which meets the guideline requirement. No excursions from the protocol were noted. Biodegradation was based on oxygen

consumption and the theoretical oxygen demand of the test material as calculated using results of an elemental analysis of the test material.

Percent degradation of test substance in triplicate flasks was: 60.1%, 60.7%, 53.7% (mean = 58.1%)

Test condition :

Non acclimated activated sludge and test medium were combined before adding test material. Test medium consisted of glass distilled water and mineral salts (Phosphate buffer, Ferric chloride, Magnesium sulfate, Calcium chloride).
Test vessels were 1L glass flasks placed in a waterbath and electronically monitored for oxygen consumption. Test material was tested in triplicate, controls and blanks were tested in duplicate. Test material concentration was approximately 57 mg/L. Sodium benzoate (positive control) concentration was 44mg/L. Test temperature was 22 +/-1 Deg C.

All test vessels were stirred constantly for 28 days using magnetic stir bars and plates.

Test substance :

Olefin hydroformylation products C11-14 iso, C13 rich (68526-86-3)

Reliability : (2) valid with restrictions

Assigned 2 because original report not available for review.

20.12.2003 (15)

Type : aerobic
Inoculum : activated sludge, domestic
Concentration : 2 mg/l related to Test substance
related to
Contact time :
Degradation : = 71 (±) % after 28 day(s)
Result : readily biodegradable

Method :

OECD Guide-line 301 D "Ready Biodegradability: Closed Bottle Test"

Year: (1981)

GLP: no

Test substance :

Dodecanedioic acid CASNO 693-23-2

Reliability : (2) valid with restrictions

Secondary source, IUCLID value from guideline study, assigned 2

20.12.2003 (23)

Type : aerobic
Inoculum : activated sludge, domestic
Concentration : 43 mg/l related to Test substance
related to
Contact time :
Degradation : = 71 (±) % after 28 day(s)
Result : readily biodegradable

Method :

A Manometric Respirometry Test was preformed according to the OECD-301F test guideline (1992).

Remark :

This mixture of alcohols is derived from an essentially identical hydroformylation reaction as that used to produce EP-290. This mixture of alcohols is a component of EP-290

Result :

The test material was determinded to be readily biodegradable. The half-life was reached by day 11. By day 28, 71.1% degradation of the test material was observed. 10% biodegradation was achieved on day 4. By day 14, >60% biodegradation of positive control was observed, which met the guideline requirement. No excursions from the protocol were noted. Biodegradation was based on oxygen consumption and the theoretical oxygen demand of the test material as calculated using results of an elemental analysis of the test material.

Replicate flasks containg test material showed the following percent degradation on day 28: 74.0%, 72.6%, 66.5% (mean = 71.1). The control substance, sodium benzoate, showed a 86% biodegradation on day 28.

Test condition :

Non acclimated activated sludge and test medium were combined prior to addition of test material. Test medium consisted of glass distilled water and mineral salts (Phosphate buffer, Ferric chloride, Magnesium sulfate, Calcium chloride). Test vessels were 1L glass flasks placed in a waterbath and electronically monitored for oxygen consumption. Test material was tested in triplicate, controls and blanks were tested in duplicate. Test material concentration was approximately 43 mg/L. Sodium benzoate (positive control) concentration was 44mg/L. Test temperature was 22 +/-1 Deg C.
All test vessels were stirred constantly for 28 days using magnetic stir bars and plates.

Test substance :

Olefin hydroformylation products C9-11 iso, C10 rich (68526-85-2)

Reliability : (2) valid with restrictions

Assigned 2 because original report not available for review.

20.12.2003 (13)

Type : aerobic
Inoculum : activated sludge, domestic
Concentration : 2 mg/l related to Test substance
related to
Contact time : 30 day(s)
Degradation : = 95 (±) % after 30 day(s)
Result : readily biodegradable

Method :

Directive 84/449/EEC, C.6 "Biotic degradation closed bottle test"

GLP:no

Test substance :

2-Ethylhexyl Laurate CASNO 20292-08-4

Reliability : (2) valid with restrictions

Secondary source, IUCLID value from guideline study, assigned 2

20.12.2003 (22)

Type : aerobic

Inoculum	:	activated sludge, non-adapted
Concentration	:	2 mg/l related to Test substance related to
Contact time	:	
Degradation	:	= 85 (±) % after 30 day(s)
Result	:	
Method	:	Directive 84/449/EEC, C.6 "Biotic degradation closed bottle test"
Test substance	:	Dodecanoic acid CASNO 143-07-7
Reliability	:	(2) valid with restrictions

Secondary source, IUCLID value from guideline study, assigned 2

20.12.2003 (24)

4.1 ACUTE/PROLONGED TOXICITY TO FISH

Type	:	static
Species	:	Lepomis macrochirus (Fish, fresh water)
Exposure period	:	96 hour(s)
Unit	:	mg/l
NOEC	:	= 1000 measured/nominal
LC0	:	> 1000 measured/nominal
LC50	:	> 1000 measured/nominal
Limit test	:	no
Analytical monitoring	:	no
Method	:	
Year	:	
GLP	:	no
Test substance	:	

Method :

After preliminary tests, 10 fish (bluegill sunfish, mean wt 0.30 g) were exposed to the test material at several closely spaced concentrations. Test containers were 5-gallon glass containers containing 15 liters of laboratory well water. Test material was added directly to the vessels without a carrier solvent. Ten fish were added to each container after the test material had been mixed with the test water for less than 30 minutes

Conditions were:

Temperature	21-23°C
Alkalinity	368 ppm as CaCO3
Hardness	255 ppm as CaCO3
Dissolved Oxygen	9.5 ppm
pH	8.0 (dilution water)
DOC	not reported

Remark :

Examination of the raw data indicates that the test material was not completely dissolved in the water. "Oil type" droplets were reported on the surface at all test concentrations. This may not be a significant issue with a mixture such as this which has components that vary in solubilities.

Result :

Not all of the test material dissolved in the water. It was reported that large-oily droplets remained on the surface of the water for the duration of the test at all concentrations.

In the definitive test, the following results were recorded

Conc (mg/L)	# fish	24hr	#dead at 48hr	72hr	96hr
0	10	0	0	0	0
100	10	0	0	0	0
180	10	0	0	0	0
320	10	0	0	0	0
560	10	0	0	0	0
1000	10	0	0	0	0

No adverse effects on fish were reported at any concentration.

Oxygen levels were determined in controls, the lowest and the highest

concentrations at 0, 48 and 96 hours and did not differ markedly control staying between 5.7 and 9.5 ppm (the lower DO reading were taken at study termination. Measurement of pH levels were done at the same concentrations and times and was from 8.0 to 8.2 for all measurements

Test substance : Heavy Oxo Ends, Monsanto Chemical, CASNO 68526-82-9, Average MW 283.4, clear, yellow to green liquid

Conclusion :

The LC50 for bluegill sunfish under these conditions is greater than 1000 mg/L.

Reliability : (1) valid without restriction

Well-documented study conducted under glp-like conditions with quality assurance audits of the data and report.

Flag : Critical study for SIDS endpoint

26.10.2003 (3)

Type : Static
Species : Salmo gairdneri (Fish, estuary, fresh water)
Exposure period : 96 hour(s)
Unit : mg/l
NOEC : = 560 measured/nominal
LC0 : > 1000 measured/nominal
LC50 : > 1000 measured/nominal
Limit test : No
Analytical monitoring : No
Method :
Year :
GLP : No
Test substance :

Method :

After preliminary tests, 10 fish (rainbow trout, mean wt 0.87 g) were exposed to the test material at several closely spaced concentrations. Test containers were 5-gallon glass containers containing 15 liters of laboratory well water. Test material was added directly to the vessels without a carrier solvent. Ten fish were added to each container after the test material had been mixed with the test water for less than 30 minutes

Conditions were:

Temperature	12-13°C
Alkalinity	368 ppm as CaCO3
Hardness	255 ppm as CaCO3
Dissolved Oxygen	9.2 ppm
pH	7.8 (dilution water)
DOC	not reported

Remark :

Examination of the raw data indicates that the test material was not completely dissolved in the water. "Oil type" droplets were reported on the surface at all test concentrations. This may not be a significant issue with a mixture such as this which has components that vary in solubilities.

Result : Not all of the test material dissolved in the water. It was reported that large-oily droplets remained on the surface of the water for the duration of the test at all concentrations.

In the definitive test, the following results were recorded

Conc (mg/L)	# fish	#dead at 24hr	48hr	72hr	96hr
0	10	0	0	0	0
32	10	0	0	0	0
56	10	0	0	0	0
100	10	0	0	0	0
180	10	0	0	0	0
320	10	0	0	0	0
560	10	0	0	0	0
1000	10	0	0	0	0

Effects on fish were limited to the 1000 mg/L group where a few fish were reported to be resting on the bottom at the 72 and 96 hour observation.

Oxygen levels were determined in controls and the lowest and the two highest concentrations at 0, 48 and 96 hours and was only different from control (8.2 ppm) at the 1000 mg/L level (6.0pm) at study termination. Measurement of pH levels were done at the same concentrations and times and either 8.0 or 8.1 for all measurements.

Test substance : Heavy Oxo Ends, Monsanto Chemical, CASNO 68526-82-9, Average MW 283.4, clear, yellow to green liquid

Conclusion :

The LC50 for rainbow trout sunfish under these conditions is greater than 1000 mg/L.

Reliability : (1) valid without restriction

Well-documented study conducted under glp-like conditions with quality assurance audits of the data and report.

Flag : Critical study for SIDS endpoint

20.10.2003 (4)

4.2 ACUTE TOXICITY TO AQUATIC INVERTEBRATES

Type : static
Species : Daphnia magna (Crustacea)
Exposure period : 48 hour(s)
Unit : mg/l
NOEC : = .1 measured/nominal
EC50 : = .17 measured/nominal
24 hour EC50 : > 1.6 measured/nominal
Limit Test : no
Analytical monitoring : no

Method :

A static toxicity test was conducted in 250 mL beakers which contained 200 mL test solution. The dilution water used in this study was well water from St. Peters, Missouri. For each test concentration, the appropriate amount of the test compound, dissolved in dimethylformamide was pipetted into 1000 mL of dilution water and shaken vigorously for 1 minute. This solution was then divided into three 200 mL aliquots in triplicate beakers to provide appropriate replication. The remaining 400 mL were used for 0-hour DO,

pH, alkalinity and hardness determinations. A control, consisting of the same dilution water and conditions but with no test compound was established. Also, a solvent control was employed which consisted of dilution water and the maximum amount of solvent used in the test concentrations. The amount of solvent used in this test was 0.5 mL dimethylformamide/L (DMF).

Nominal test concentrations were selected based on a rangefinding test. All test vessels were maintained at room temperature. Test solutions were not aerated during the test. Ten daphnids were randomly assigned to each test vessel within 30 minutes after the compound was added for a total of 30 daphnids per concentration.

During this test, the dissolved oxygen concentration, pH, alkalinity, hardness, and temperature of test solutions were monitored at the initiation and termination of the toxicity test in the high, middle, low and control test concentrations.

Statistical methods: In tests where the highest percentage of immobilized daphnids was >65 percent, the computer program of Stephan (1978) which calculates an EC50 by three methods, binomial, moving average, and probit analysis, was used.

Result :

During the 48-hour toxicity test, the pH and dissolved oxygen ranged from 7.6 to 8.5 and 5.3 to 8.6 mg/L, respectively. The average temperature was 21C and the alkalinity and hardness ranged from 198 to 290 mg/L and 232 to 322 mg/L.

Visual inspection of the beakers indicated that the water solubility was not exceeded at any concentrations. Both a control and a solvent control were used in this study. No mortality was observed in either set of control organisms.

	% Immobilized	
Conc (mg/L)	24 h	48 hr
Control	0	0
Solvent Cont	0	0
0.1	0	0
0.2	0	83.3
0.4	0	96.7
0.8	30	100
1.6	40	100

Test substance : Heavy Oxo Ends, Monsanto Chemical, CASNO 68526-82-9, Average MW 283.4, clear, yellow to green liquid. Lot number 1618258.

Conclusion :

The 48 hours EC50 was 0.17 mg/L with a 95% confidence interval of 0.15 to 0.19 mg/L.

The NOEC was 0.1 mg/L

Reliability : (1) valid without restriction
Well-documented, guideline-like study

Flag : Critical study for SIDS endpoint

23.10.2003 (5)

4.3 TOXICITY TO AQUATIC PLANTS E.G. ALGAE

4.4 TOXICITY TO MICROORGANISMS E.G. BACTERIA

5.1.1 ACUTE ORAL TOXICITY

Type	:	LD50
Value	:	> 15800 mg/kg bw
Species	:	rat
Strain	:	Sprague-Dawley
Sex	:	male/female
Number of animals	:	
Vehicle	:	other: Dosed neat
Doses	:	5010, 7940, 12600 and 15800 mg/kg bw
Method	:	
Year	:	
GLP	:	no
Test substance	:	

Method :

The undiluted test substance was administered undiluted to Sprague-Dawley rats in increasing dose at fractional log intervals. Treated animals were observed for seven days, survivors were sacrificed and subjected to an examination of the viscera. Body weights were only reported at the time of dosing (presumably used to determine the volume of test material to administer). Rats of each sex were used and all were in an initial weigh range of 225 to 270 grams. Dose levels and animals per group are given in the results.

Remark :

Study conducted in 1971

Result :

Dose levels and grouping were as follows:

Dose (mg/kg)	Animals (M = male, F = female)
5,010	1F
7,940	1M
12,600	1F
15,800	3M and 2F

All animals survived the 7-day observation period. Clinical signs reported were loss of appetite and activity for two to four days following administration. No abnormalities were noted at necropsy.

Test substance :

Monsanto Heavy Oxo Ends, lot 11.16.71, Monsantosample #174

Conclusion :

The Oral LD50 is greater than 15,800 mg/kg in Sprague-Dawley rats of each sex.

Reliability : (2) valid with restrictions

Good documentation for an older study. Although animals were sacrificed after seven days rather the currently recommended 14, animals had recovered from the initial signs of toxic effects. In addition, as the dose levels were almost 8 times the currently recommended maximum dose, this study is considered an adequate test of oral toxicity. Procedure is similar to current OECD-423 Acute Toxic Class Method. Downgraded to 2 due to only 7-day observation period.

21.10.2003 (30)

5.1.2 ACUTE INHALATION TOXICITY

Type	:	LC50
Value	:	> 4.9 mg/l
Species	:	rat
Strain	:	Crj: CD(SD)
Sex	:	male/female
Number of animals	:	20
Vehicle	:	
Doses	:	1.1 and 4.9 mg/L
Exposure time	:	4 hour(s)
Method	:	
Year	:	
GLP	:	yes
Test substance	:	

Method :

Groups of 5 Sprague-Dawley CD (Charles River) rats of each sex were exposed to test material for four hours as an aerosol at concentrations of 1.1 or 4.9 mg/L. Aerosol was produced using an air atomizing nozzle running at 19.7 or 20.2 L per minute and 26 psi pressure. Exposures were conducted in 100 l Plexiglas chambers which were monitored gravimetrically using filters at approximately hourly intervals. Particle size distributions were determined at 30 minute intervals using either a Battelle cascade impactor (4.9 mg/L group) or a TSI Model 3000 Aerodynamic particle sizer equipped with a TSI Model 3302 dilutor.

Rats were observed for physical signs before exposure, fifteen minutes after exposure began, and hourly thereafter. After the four-hour exposure, animals were allowed to remain in the chambers for 30 minutes to clear the chambers of test substance. Observations were continued on a once daily basis during the subsequent fourteen day post-exposure period. Body weights were recorded on day 1 before exposure and on days 2, 3, 5, 8, and 15. All rats that died on study or were sacrificed at termination of the study were necropsied.

Result :

It was determined that the mean gravimetric concentration of test substance aerosol at the high concentration was 4.9 mg/L with a range of 3.3 to 5.9 mg/L and that this aerosol was respirable with a MMAD of 2.6 microns and 91% of particles below 10 microns. The lower concentration group had a mean gravimetric concentration of 1.1 mg/L; however, the impactor data were found to be invalid for technical reasons and a particle size determination was not obtained. As the same nozzle and conditions were used to generate the lower concentration aerosol, it was assumed to be respirable as well.

One 4.9 mg/L group male died three days after the exposure and other rats in this group displayed irregular breathing, closed eyes, and matted coats during exposure. After the exposure period, rats were reported to have increased secretory responses, irregular breathing, matted coat, yellow anogenital area, and material on the coat. Rats exposed at 1.1 mg/L displayed similar signs with a lower incidence of irregular breathing. By the middle of the second post-exposure week, all rats were essentially free signs of toxicity. Body weights of 4.9 mg/L group rats were depressed (loss of bodyweight) on days 2 through 8. The bodyweights of the 1.1 mg/L animals were slightly depressed (loss of bodyweight) on days 2 though 5.

Body weight depression may have been related to treatment. The only necropsy finding considered to be treatment related was hair loss in the 4.9 mg/L group.

Test substance : Heavy Oxo Ends, Monsanto Chemical, CASNO 68526-82-9, Average MW 283.4, clear, yellow to green liquid

Conclusion :

The four hour LC50 for Heavy Oxo Ends is greater than 4.9 mg/L. 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, A NOAEL was not identified.

Reliability : (1) valid without restriction

Modern guideline-like study under glp with excellent documentation.

Flag : Critical study for SIDS endpoint

26.10.2003 (6)

5.1.3 ACUTE DERMAL TOXICITY

Type : LD50
Value : > 7940 mg/kg bw
Species : rabbit
Strain : New Zealand white
Sex : male/female
Number of animals : 4
Vehicle : other: neat application
Doses : 3160, 5010, 7940 mg/kg bw
Method :
Year :
GLP : no
Test substance :

Method :

The test substance was administered undiluted to the closely-clipped skin of New Zealand white male or female rabbits. The treated areas were covered with plastic that was held in place for 24 hours. Animals were observed for 14 days after treatment, sacrifices and necropsied. Increasing incremental doses were used to minimize animal usage. Animals weighed 2.4 to 2.7 kg at treatment. Body weights were determined 5 days after treatment but not at termination.

Result :

Dose levels and grouping were as follows:

Dose (mg/kg)	Animals	5-Day BW change
3,160	1M	-0.1 kg
5,010	1F	-0.2 kg
7,940	1M	-0.2 kg
7,940	1F	-0.3 kg

All animals survived the 14-day observation period. Clinical signs reported were loss of appetite and activity for three to seven days following administration. No abnormalities were noted at necropsy.

Test substance :

Monsanto Heavy Oxo Ends, lot 11.16.71, Monsanto sample #174

Conclusion :

The Dermal LD50 is greater than 7,940 mg/kg in New-Zealand rabbits of each sex

Reliability	:	(1) valid without restriction Good documentation for an older study. This study is considered an adequate test of dermal toxicity. Procedure is similar to current OECD-423 Acute Toxic Class Method.
Flag	:	Critical study for SIDS endpoint

23.10.2003 (30)

5.1.4 ACUTE TOXICITY, OTHER ROUTES

5.4 REPEATED DOSE TOXICITY

Type	:	Sub-chronic
Species	:	rat
Sex	:	male/female
Strain	:	Sprague-Dawley
Route of admin.	:	inhalation
Exposure period	:	13-weeks
Frequency of treatm.	:	5 days per week
Post exposure period	:	
Doses	:	target 100, 300 and 1000 mg per cubic meter
Control group	:	yes, concurrent vehicle
NOAEL	:	= 100 mg/m³
LOAEL	:	= 300 mg/m³
Method	:	
Year	:	
GLP	:	no data
Test substance	:	

Method :

Groups of 15 Sprague-Dawley rats of each sex were exposed to atmospheres containing the test substance (TS) six hours a day, five days a week for 13 weeks.

Chambers were one cubic meter steel and glass operated dynamically at calibrated initial airflows between 199 and 218 liters per min. Aerosol was generated from the neat test material using a Laskin nebulizer at backpressures of 5, 8, or 15 psi for low, mid and high dose groups respectively.

The target levels of TS were 0, 100, 300, and 1000 mg/m3. Rats were observed twice daily for signs of toxicity and were weighed at weekly intervals. Opthalmoscopic examinations were conducted prior to the start of treatment and at the end of the study. Blood was obtained from 10 rats/group for evaluation before the study, after about one month of treatment, and at the end of the study. The specific parameters evaluated are listed below. A complete necropsy was performed on all animals that died on test, or were sacrificed at study termination.

The following organs were weighed for all survivors: adrenals, brain, kidneys, liver, lungs, and reproductive organs (ovaries or testes with epididymides).

Hematology parameters examined were:
- hemoglobin
- hematocrit
- erythrocyte count
- platelet count
- total and differential leukocytes
- erythrocyte morphology

Clinical Chemistry parameters examined were
- total serum protein
- albumin
- albumin/globulin ratio
- serum glutamic pyruvic transaminase
- serum glutamic oxaloacetic transaminase
- alkaline phosphatase
- fasting glucose
- cholesterol
- triglycerides
- blood urea nitrogen
- lactic acid dehydrogenase
- creatinine
- uric acid
- total bilirubin
- direct bilirubin
- calcium
- phosphporus
- potassium
- sodium
- chloride

Tissues listed below were examined from rats in the control and high-dose group. The lungs, lymph nodes, and nasal turbinates were also examined in rats from the mid- and high-dose groups.
- abdominal aorta
- adrenals (2)
- bone and bone marrow (sternum)
- brain (three sections including frontal cortex and basal ganglia, parietal cortex and thalamus; cerebellum and pons)
- esophagus
- eyes (2)
- gonads
- ovaries (2) or testes with epididymides (2)
- heart
- intestine
- cecum
- colon
- duodenum
- ileum
- jejunum
- rectum
- kidneys (2)
- liver (2 sections, from separate lobes)
- lungs (each lobe and mainstem bronchi)
- lymph nodes (peribronchial and mesenteric)
- nasopharyngeal tissues (4 sections of head)
- pancreas

- pituitary
- salivary glands (submandibular)
- sciatic nerve
- spleen
- stomach
- thymic region
- thyroid/parathyroid
- trachea
- urinary bladder
- uterus (horns and cervix)

low and mid-dose groups also had the following examined

- lungs
- lymph nodes
- nasal turbinates

Result :

The gravimetrically measured levels of test substance (TS) for groups (male/female) were 105/105, 294/293 and 1014/1009 mg/m3. Analysis by a gas chromatographic method confirmed the accuracy of the gravimetric method. An analysis of the particle size distribution indicated that the test material was administered in a respirable aerosol. Impactor analysis showed a MMAD of 1.6, 1.4 or 1.6 microns for low, mid and high dose groups, respectively with 100% of the particles less than 10 micron.

One mid-dose female was accidentally killed during the interim blood sample collection and one high-dose male and two high-dose females died during the study. The high-dose group deaths were considered treatment related. An increased incidence of nasal discharge and rough coats were observed in rats from the mid- and high-dose groups. No treatment related opthalmoscopic findings were present. Body weights gains were slightly reduced in high-dose rats by about 8% throughout the study. This reduction was statistically significant only for females.

Few statistically significant hematological and clinical chemistry changes were observed and there was no pattern consistent with a treatment related effect; therefore, the following changes were not considered as toxicologically significant. High-dose males at interim sacrifice showed increased erythrocyte counts and serum phosphorus. High-dose males at terminal sacrifice showed increased BUN and decreased triglycerides.

Organ weights: Relative and absolute lung weights were increased for mid-dose males and rats of each sex in the high-dose group. This was associated with an increased incidence of intra-alveolar accumulation of macrophages and considered treatment related. Other changes in organ weights were observed for the mean relative weights of kidneys, adrenals and liver in the high-dose females. None of these were associated with evidence of organ damage or clinical-chemistry associated findings and were, thus, not considered toxicologically significant.

Pathology: A cytoplasmic accumulation of eosinophilic material, ranging from minimal to moderate in severity, was observed in the respiratory epithelial cells of almost all treated rats and a small number of control rats. The severity of this finding indicated a dose response relationship. Treated rats, but not controls, showed minimal to moderately severe necrosis of the respiratory-epithelium that was accompanied by an accumulation of eosinophilic particulate material on the luminal surface of the mucosa.

High-dose group animals showed subacute to chronic interstitial inflammation of mild to moderate severity. An increased intra-alveolar accumulation of macrophages was observed in the lungs of rats from the mid- and high-dose groups. Focal accumulation of foamy macrophages, which ranged in severity from minimal to moderate, was observed in treated rats. Other gross and microscopic changes, which were observed, either occurred in the treated and control rats or they occurred spontaneously.

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.

Test substance :

Heavy Oxo Ends, Monsanto Chemical, CASNO 68526-82-9, liquid, Lot number 1618277, received by laboratory 9 July 1984.

Conclusion :

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.

Reliability : (2) valid with restrictions

This is a modern, guideline-like, complete, and well documented study. No glp statement was found in the report. For this reason, the study is assigned a reliability score of 2.

Flag : Critical study for SIDS endpoint

26.10.2003 (2)

5.5 GENETIC TOXICITY 'IN VITRO'

Type : Ames test
System of testing : Reverse mutation, plate incorporation
Test concentration :
Cycotoxic concentr. :
Metabolic activation : with and without
Result : negative
Method :
Year :
GLP : yes
Test substance : other TS

Method :

The mutagenic potential of behenyl alcohol was evaluated using the S. typhimurium strains TA1535, TA1537, TA1538, TA98, and TA100 with and without metabolic activation. The tester strains were exposed to behenyl alcohol according to the direct plate incorporation method. Liver microsomal fractions from 8- to 12-week-old male Wistar rats were prepared according to established methods. Positive controls consisted of sodium azide and 4-nitro-Ophenylenediamine, tested without metabolic

activation, and aminoanthracene, tested with metabolic activation. Negative controls were untreated or exposed to only solvent. Behenyl alcohol was dissolved in ethanol and tested at concentrations of 10.0, 100.0, 333.3, 666.6, and 1000.0 mg/plate. The selection of doses was based on the results of a previously conducted range-finding study. Assays were performed in two independent experiments, using identical procedures, both with and without metabolic activation. Each concentration, including the controls, was tested in triplicate. The colonies were counted using a BIOTRAN 111 counter connected to a PC.

For a test substance to be considered positive in tester strain TA100, at least a twofold increase was required in the number of reversions. In tester strains TA1535, TA1537, TA1538, and TA98, a test substance was considered positive when the number of reversions was at least three times higher than the spontaneous reversion rate. In addition, a dose-dependent increase in the number of revertants was regarded as an indication of possible mutagenic potential, regardless of whether the highest dose induced a two- to threefold increase in the number of revertants.

Result :

Both assays demonstrated a lack of mutagenic activity by behenyl alcohol. No significant and reproducible increases in the number of revertants were found in any strain and behenyl alcohol treatment group combination relative to the solvent control. In addition, no concentration-dependent enhancement of the revertant number occurred, and no differences were observed between behenyl alcohol treatments with or without metabolic activation.

Test substance :

Behenyl alcohol (C-22 straight-chain alcohol) 1-Docosanol CASRN: 661-19-8
Purity 98%
source: Condea, Germany.

Reliability : (2) valid with restrictions
Published reports assigned a 2

21.12.2003 (17)

Type : Chromosomal aberration test
System of testing : Chinese Hamster V79 cells
Test concentration : without act: 0, 0.6, 10 or 20 mg/L; with act 0, 1.4, 10 or 20 mg/L
Cycotoxic concentr. : > 20 mg/L
Metabolic activation : with and without
Result : negative
Method :
Year :
GLP :
Test substance : other TS

Method :

The ability of behenyl alcohol to induce structural chromosome aberrations in Chinese hamster V79 cells was evaluated in vitro, with and without metabolic activation.

Behenyl alcohol was dissolved in ethanol. V79 cells were exposed to behenyl alcohol, both with and without metabolic activation. The liver microsomal fractions were obtained from 8- to 12-week-old male Wistar rats. Duplicate cultures were used. Preparations of chromosomes were completed 7, 18, and 24 hours after behenyl alcohol treatment started.

Cultures prepared at 7 and 24 hours were treated with 20 ug/ml behenyl alcohol, while cultures prepared at 18 hours were treated with 0.6, 10.0, and 20.0 ug/ml behenyl alcohol. Assays were initiated by seeding approximately 50000 to 100000 cells per dish in minimal essential medium (MEM). After 48 h (for cells harvested at 7 and 24 hours) and 55 hours (for cells harvested at 18 hours), the medium was replaced with serum-free medium containing behenyl alcohol at the appropriate dose, with and without metabolic activation.

All cultures were exposed to behenyl alcohol for four hours. Following the treatment interval, the medium was replaced with normal medium after rinsing twice with saline. Colcemia (0.2 ug/ml), a metaphase-arresting substance, was added to the cultures for the last two hours of incubation for cells harvested at 7 hours or for the last 2.5 hours of incubation for cells harvested at 18 and 28 hours. The cells were then treated on the slides in the chambers with a hypotonic solution for 20 min at 37 deg C. After incubation, the cells were fixed, stained with Giemsa, and examined microscopically. One hundred metaphases were scored for cytogenic damage per slide.

The concentrations used in this study were based on the results from a earlier range-finding study, which used the plating efficiency assay as an indicator for toxicity response. Positive controls consisted of EMS (without metabolic activation) and cyclophosphamide (with metabolic activation).

For the test substance to be scored positive, either a significant dose-related increase in the number of structural chromosomal aberrations or a significant positive response at one of the test points was required.

Statistical analysis included use of the chi-squared test, which was only performed for cells carrying aberrationsexclusive gaps. Both biological and statistical significance was considered in the assessment. Test substance significance was established where $P < 0.05$.

Result :

Treatment with the highest concentration of 20 ug/ml behenyl alcohol did not reduce the plating efficiency of the V79 cells nor the mitotic index; however, data from the range finding study indicate that higher doses would have been toxic to cells. No relevant increases in the number of cells with structural aberrations were observed after treatment with behenyl alcohol at any concentration or time interval were observed. Positive and negative controls gave the expected results, demonstrating sensitivity of the test system.

Test substance :

Behenyl alcohol (C-22 straight-chain alcohol) 1-Docosanol CASRN: 661-19-8
Purity 98%
source: Condea, Germany.

Conclusion :

Behenyl alcohol did not produce chromosome aberrations in V79 cells under these conditions using the highest practical non-cytotoxic concentration.

Reliability : (2) valid with restrictions
Published reports assigned a 2

21.12.2003 (17)

Type	:	HGPRT assay
System of testing	:	Chinese Hamster V79 cells
Test concentration	:	2.0, 7.5, 15.0, and 20.0 mg/ml
Cycotoxic concentr.	:	
Metabolic activation	:	with and without
Result	:	negative
Method	:	
Year	:	
GLP	:	no data
Test substance	:	other TS

Method :

The potential for behenyl alcohol to induce gene mutations, in vitro, at the HGPRT locus was evaluated in Chinese hamster V79 cells, with and without metabolic activation.

Behenyl alcohol was dissolved in ethanol and V79 cells were exposed to behenyl alcohol concentrations of 2.0, 7.5, 15.0, and 20.0 mg/ml for 4 h and monitored for the loss of functional HGPRT enzyme. The final concentration of ethanol in the culture medium did not exceed 1% v/v. The selection of doses was based on the results of a previously conducted rangefinding experiment. Each concentration was tested with and without metabolic activation and the cells were subcultured twice per week. The assay was performed in two independent experiments, using identical procedures, both with and without metabolic activation. Concurrent negative and solvent controls were included, and positive controls consisted of ethylmethanesulfonate (EMS) (Merk-Schuchardt) and 7,12-dimethylbenz(a)anthracene (DMBA) (Sigma). All incubations were conducted at 37°C in a humidified atmosphere with 4.5% C02. Methylene blue (10%) was used for staining in 0.01% KOH solution. Stained colonies with more than 50 cells were counted with a preparation microscope.

Mutant frequency was determined by seeding known numbers of cells in medium containing thioguanine to detect mutant cells, and in medium without thioguanine to determine the total number of surviving cells. For the test substance to be considered positive, a significant dose-related increase in the mutant frequency or a reproducible and significant positive response for at least one of the test points was required. The test substance also was considered to be mutagenic if there was a reproducible concentration-related increase in the mutation frequency. Such evaluation may be considered independently of an enhancement factor for induced mutants; however, this is dependent on the level of the corresponding negative control data.

Result :

Gene mutation assay in Chinese hamster V79 cells. No relevant increases in mutant colony numbers were found in both independent experiments at any concentration of behenyl alcohol tested, with or without metabolic activation

Test substance :

Behenyl alcohol (C-22 straight-chain alcohol) 1-Docosanol CASRN: 661-19-8
Purity 98%
source: Condea, Germany.

Reliability : (2) valid with restrictions
Published reports assigned a 2

21.12.2003 (17)

Type	:	other: Salmonella typhimurium and E coli reverse mutation test
System of testing	:	
Test concentration	:	
Cycotoxic concentr.	:	
Metabolic activation	:	
Result	:	negative
Method	:	other: OECD 471 and 472
Year	:	
GLP	:	yes
Test substance	:	other TS

Method :

Salmonella typhimurium strains: TA 1535, TA 1537, TA 98, TA 100; Escherichia coli strain: WP2uvrA-

Plate incorporation test

Metabolic activation system: Liver fraction (S9) from rats pretreated with Aroclor 1254

0, 15, 50, 150, 500, 1 500 and 5 000 µg/plate.

Each concentration was tested in triplicate with or without metabolic activation, in two independent experiments; appropriate strain specific positive control reference substances were used

Result :

Precipitate noted at and above 1500 µg/plate; No cytotoxicity was observed.
There were no significant increases in revertant colony numbers at any concentration, in the presence or absence of metabolic activation. Concurrent positive controls used in the test induced marked increases in the frequency of revertant colonies and the activity of the S9 fraction was found to be satisfactory

Test substance :

C20-C24 alkenes, branched and linear

Conclusion :

C20-C24 alkenes, branched and linear were not considered mutagenic in the bacterial strains tested

Reliability : (2) valid with restrictions

Modern guideline study under glp. Downgraded to a 2 as laboratory report was not available for review.

Flag : Critical study for SIDS endpoint

21.12.2003 (7)

Type	:	Chromosomal aberration test
System of testing	:	Human Peripheral Lymphocytes
Test concentration	:	
Cycotoxic concentr.	:	
Metabolic activation	:	with and without
Result	:	
Method	:	OECD Guide-line 473
Year	:	
GLP	:	no data
Test substance	:	other TS

Method :

Each concentration was tested in duplicate with or without metabolic activation (S9), in two independent experiments

Experiment 1 (repeat . see comment below):
without S9,
0*, 78.13, 156.25, 312.5*, 625*, 1 250* ,2 500*
5 000* µg/mL;
treatment/harvest time = 4/20 hours;
positive control: ethyl methanesulphonate 750µg/mL;

with S9,
0*, 39.06, 78.13, 156.25, 312.5*, 625*, 1 250*, 2 500*
5 000* µg/mL,
treatment/harvest time = 4/20 hours,
positive control: cyclophosphamide 25µg/mL;

Experiment 2:
without S9,
0*, 39.06, 78.13, 156.25, 312.5*, 625* 1 250*, 2 500*
5 000* µg/mL;
treatment/harvest time = 20/20 hours;
positive control: ethyl methanesulphonate 500µg/mL;

with S9 (increased to a final concentration of 2%),
0*, 39.06 , 78.13, 156.25, 312.5*, 625* 1 250*, 2 500*
5 000* µg/mL;
treatment/harvest time: 4/20 hours,
positive control: cyclophosphamide 25 µg/mL;

asterisk* indicates cultures selected for metaphase analysis

Result :

An initial experiment revealed:
doses of 2500 or 5000 g/mL were probably beyond the maximum practical dose; an aberrant cell at the highest dose
contained multiple aberrations; and weak responses in the positive control.
The experiment was repeated.
In the repeated Experiment 1 and Experiment 2, an oily layer was observed at and above 156.25 µg/mL and 312.5µg/mL in the presence and absence of metabolic activation, respectively.

No toxicity was observed at any concentration.
The test substance did not cause any significant increases in the incidence of cells with chromosomal aberrations, polyploidy or endoreplication, at the concentrations analysed in the presence or absence of metabolic activation.
Positive controls used in the test caused significant increases in the incidence of aberrant cells and the activity of the S9 fraction was found to be satisfactory.

Test substance :

C20-C24 alkenes, branched and linear

Conclusion : C20-C24 alkenes, branched and linear was not considered to

Reliability : (2) valid with restrictions

Modern guideline study under glp. Downgraded to a 2 as laboratory report was not available for review.

Flag : Critical study for SIDS endpoint

21.12.2003 (19)

Type : other: multiple tests
System of testing : Other: multiple
Test concentration :
Cycotoxic concentr. :
Metabolic activation :
Result : negative
Method :
Year :
GLP :
Test substance : other TS

Method :

The following data are taken from the HEDSET data sheet for 1-octadecene. The full study reports were not provided in the submission.

The HEDSET documents indicate these tests were not conducted in accordance with GLP or OECD or EC testing guidelines.

Result :

1-Octadecene was considered not mutagenic or clastogenic in the following test systems:

TEST	COMMENT	RESULT
Bacterial Rev. Muta Assay	S. typhimurium TA98, TA100, TA 1535, TA1537, TA1538. E.coli WP2, WP2uvrA. 0.2 to 2 000 mg/plate; with/without metabolic activation.	Negative
Mitotic Recombin.n	S.cerevisiae JD1. 0.01 to 5.0 mg/mL With/without metabolic activation	Negative
Chromosome Aberration	Rat liver RL1 cells. 0 to 500 µg/mL as acetone solution With/without metabolic activation.	Negative

Test substance :

1-Octadecene RN: 112-88-9

Reliability : (2) valid with restrictions

Original reports not available. HEDSET documents considered reliable

21.12.2003 (20)

Type : other: Cell Transformation
System of testing : BALB/3T3 Cells
Test concentration : 0, 10, 20, 30 or 1500 µg/mL
Cycotoxic concentr. : Cytotoxicity was evident at 20 µg/mL and above
Metabolic activation :
Result : negative
Method :
Year :
GLP :
Test substance : other TS

Method :

Mouse embryo cells BALB/3T3-A31-1-1 were treated with 0, 10, 20, 30, 1500 µg/mL of test substance in duplicate.

Positive Control: 3-methylcholanthrene 1 µg/mL;.

Cultures were exposed to test substance for two days.

Result :

Cytotoxicity was evident at 20 µg/mL and above leaving only one viable dose level, 10 g/ml.

The number and type of transformed foci at any test substance concentration was not increased above the negative control.

The positive control gave the expected response for transformation.

Test substance :

Tetradecene (Gulfteen C12-C16)

Conclusion :

Tetradecene (Gulfteen C12-16) did not cause cell transformation under these conditions.

Reliability : (2) valid with restrictions

21.12.2003 (8) (8)

Type : Unscheduled DNA synthesis
System of testing : Primary hepatocytes from Fischer 344 rats
Test concentration : 0, 100, 1000, 2000 or 4000 µg/ml
Cycotoxic concentr. : 256 µg/ml in range finder
Metabolic activation :
Result : negative
Method : OECD Guide-line 482
Year :
GLP : no data
Test substance : other TS

Method :

concentrations of 0, 100, 1000, 2000 or 4000 µg/mL of test substance was tested in triplicate.

Positive Control: 2-acetylaminofluorene 0.2 µg/mL.

Cultures were exposed to test substance and 1 mCi/mL 3H-thymidine for 18 hours.

Result :

In the range finding study, cytotoxicity was reported at and above 256 µg/mL.
Toxicity data were not available for the main test.

The test substance at any concentration did not elicit an increased mean net nuclear grain count above the concurrent negative control.

The positive control gave the expected response for UDS.

Test substance :

Tetradecene (Gulfteen C12-C16)

Conclusion :

Tetradecene (Gulftene 12-16) did not produce an increase in unscheduled DNA synthesis under these conditions.

Reliability : (2) valid with restrictions

Modern guideline study. Downgraded to a 2 as laboratory report was not available for review.

21.12.2003 (16)

Type	:	HGPRT assay
System of testing	:	CHO Cells
Test concentration	:	0, 4, 16, 128, 512, 1024 or 2048 µg/mL
Cycotoxic concentr.	:	1024
Metabolic activation	:	with and without
Result	:	negative
Method	:	OECD Guide-line 476
Year	:	
GLP	:	no data
Test substance	:	other TS

Method :

Cells:
Chinese Hamster Ovary (CHO)

Metabolic activation system:
Liver fraction (S9) from rats pretreated with Aroclor 1254

Dosing schedule:
0, 4, 16, 128, 512, 1024 or 2048 µg/mL each concentration was tested in triplicate with or without metabolic activation (S9)

Positive controls:
Without S9: ethyl methanesulphonate 100µg/mL;
With S9: benzo[a]pyrene 4 µg/mL;

Exposure period was 5 hours

Result :

Toxicity was observed at 1024 and 2048 µg/mL in the presence and absence of metabolic activation.

The test substance did not cause any significant increases in the incidence of mutant colonies in the presence or absence of metabolic activation.

Positive controls used in the test caused marked increases in the incidence of mutant colonies and the activity of the S9 fraction was found to be satisfactory.

Test substance :

Tetradecene (Gulfteen C12-C16)

Conclusion :

Tetradecene (Gulftene 12-16) did not induce gene mutations in CHO cells.

Reliability : (2) valid with restrictions

Modern guideline study. Downgraded to a 2 as laboratory report was not available for review.

21.12.2003 (21)

5.6 GENETIC TOXICITY 'IN VIVO'

Type	:	Micronucleus assay
Species	:	mouse
Sex	:	male
Strain	:	other: Crl:CD-1 (ICR) BR
Route of admin.	:	i.p.
Exposure period	:	24 and 48 hours
Doses	:	500, 1000 or 2000 mg/kg bw
Result	:	negative
Method	:	OECD Guide-line 474 "Genetic Toxicology: Micronucleus Test"
Year	:	
GLP	:	
Test substance	:	other TS

Method :

7 males/24 hour, vehicle and positive control, and mid, low and high dose group; 7 males/48 hour, vehicle control and high dose group; 5 males/positive control group.

administration:
Test substance: 500 mg/kg (low)
1000 mg/kg (mid)
2 000 mg/kg (high)

Positive control: cyclophosphamide 50 mg/kg;
Vehicle control: arachis oil;
TS administered via intraperitoneal injection at a constant volume of 10 mL/kg bw. Positive control was administered orally.

Sacrifice:
Vehicle and positive control, low, mid and high dose animals were sacrificed 24 hours after dosing.
Remaining animals of the vehicle control group and high dose animals were sacrificed 48 hours after dosing.

Result :

Clinical observations:
No mortality.
No clinical signs of toxicity.

Micronuclei score:
No significant increase in micronucleated PCE due to treatment with test substance at either sampling time. No statistically significant decrease in the PCE/NCE ratio at 24 or 48 hours.
The positive control caused a significant increase in micronucleated PCE.

Test substance :

C20-C24 Alkenes, branched and linear

Conclusion :

C20-C24 alkenes, branched and linear did not induce a significant increase in micronucleated PCE in bone marrow cells of the mouse in vivo.

Reliability : (2) valid with restrictions

Modern guideline study under glp. Downgraded to a 2 as laboratory report was not available for review.

17.12.2003 (26)

Type	:	Micronucleus assay
Species	:	mouse
Sex	:	male/female
Strain	:	NMRI
Route of admin.	:	gavage
Exposure period	:	24, 48 or 72 hours
Doses	:	0, 50, 150, or 500 mg/kg-bw
Result	:	negative
Method	:	
Year	:	
GLP	:	yes
Test substance	:	other TS:

Method :

The potential for behenyl alcohol to induce micronuclei in polychromatic erythrocytes (PCE) in bone marrow of NMRI mice was evaluated in vivo. Animals at least 10 weeks old (BRL Tierfarm Füllinsdorf, Switzerland) were individually housed in Markrolon Type 1 cages with wire mesh tops and granulated soft wood bedding. Aminals were housed in a room designed to maintain adequate environmental conditions (21°C, 12-h photocycle; relative humidity was not regulated). Animals were fed both a standard pellet diet and tap water, ad libitum, during the study.

Prior to treatment with behenyl alcohol, mice were fasted for 18 h, but continued to receive water ad libitum. Twelve mice (6 males and 6 females) were administered a single oral dose of 0, 50, 150, or 500 mg behenyl alcohol/kg body weight suspended in polyethylene glycol. Doses were based on the results from a previously conducted experiment in which 500 mg/kg body weight was estimated to be the maximum attainable dose. The volume administered was 10 ml/kg body weight. Cyclophosphamide (CPA) was used as the positive control at 40 mg/kg body weight.

At 24, 48, or 72 h after dosing, animals were killed and bone marrow cells were collected for micronuclei analysis. Only 5 mice/sex/dose group were evaluated in the event that remaining animals of each treatment group died spontaneously, or due to gavage error. Animals were killed by cervical dislocation. The femora were removed, the epiphyses were cut off, and the marrow was flushed out with fetal calf serum. The cell suspension was centrifuged at 1500 rpm for 5 min and the supernantant was discarded. A small drop of resuspended cell pellet was spread on a slide. The smear was air-dried, stained and coverslips were mounted. At least 1 slide per sample was made and scored for micronuclei and polychromatic-normochromatic (NCE) cell ratio. For each animal, 1000 PCEs were scored for micronuclei.

For the test substance to be classified as mutagenic, either a statistically significant dose-related increase in the number of micronucleated polychromatic erythrocytes or a reproducible statistically significant positive response for at least one of the test points was required.

Statistical analysis was conducted using the Mann-Whitney test; however, both biological significance and statistical significance were considered in the study. Significance was established where $P < 0.05$.

Result :

As shown below in the Table, there was no increase in the percentage micronucleated PCE, or in the PCE:NCE ratio of mice at any preparation interval after treatment with any dose level.

Treatment	Dose (mg/kg)	Harvest time(h)	percent micro nucleated (mean)	Ratio PCE:NCE (mean)
Vehicle control	0	24	0.03	1.27
		48	0.09	1.05
		72	0.09	1.41
CP (positive)	40	24	0.71	0.93
Behenyl alcohol	50	24	0.07	0.98
		48	0.10	1.06
		72	0.09	1.33
	150	24	0.08	1.07
		48	0.04	1.01
		72	0.05	1.55
	500	24	0.07	1.11
		49	0.05	1.23
		72	0.07	1.46

Test substance :

Behenyl alcohol (C-22 straight-chain alcohol) 1-Docosanol CASRN: 661-19-8
Purity 98%
source: Condea, Germany.

Conclusion :

Test material did not induce micronuclei in the bone marrow of mice under these conditions.

Reliability : (2) valid with restrictions

Guideline-like GLP study. Dosing rationale not provided. Published study assigned 2.

21.12.2003 (17)

5.8.1 TOXICITY TO FERTILITY

Type : One generation study
Species : rat
Sex : male/female
Strain : other: Crl:CD BR VAF/Plus
Route of admin. : gavage
Exposure period :
Frequency of treatm. :
Premating exposure period
Male : 28 days
Female : 14 days
Duration of test :
No. of generation studies : 1
Doses : 100, 500, 1000 mg/kg
Control group : yes, concurrent vehicle
NOAEL parental : <= 100 mg/kg bw
NOAEL F1 offspring : = 1000 mg/kg bw

Method :

Number/sex of animals: 12 males/group 20 females/group (12 females assigned to breeding phase and 8 females assigned as satellite females)

Method of administration: Oral (gavage)

Doses: 0, 100, 500 or 1000 mg/kg/day (dose volume 5mL/kg) for a minimum of 42 days;
Vehicle: corn oil.

Dosing Schedule: Males:
Day 0 to 28 - Pretreatment;
Day 29 to 42 - Mating;
Day 43 to 47 - Dosing after mating.

Satellite females:
Day 0 to 49 . Dosing period.

Breeding females:
Day 0 to 14 . Pretreatment;
Day 15 to 42 . Dosing during mating and lactation;
Day 43 to 51 - Dosing during lactation and until termination

Terminal kill schedule Day 43. euthanasia of unselected males (4 rats/sex/group).
Days 45 to 47. neurotoxicity and clinical pathology evaluations (8 rats/sex/group), histopathology (5 rats/sex/group).
Days 42 to 51 . euthanasia and necropsy of breeding females (F0)and F1 pups.

Test methods: OECD TG 422 (modified)

Result :

MORTALITY:
F0 males and satellite females: Nil.

F0 females: In the 500 mg/kg/day group, one female with evidence of mating failed to deliver and was euthanised on post breeding day 25 and one female was euthanised with total litter loss on Day 43.

CLINICAL OBSERVATIONS:
F0 males, satellite females and F0 females:
Urine stain and salivation noted in the 500 and 1000 mg/kg/day groups. No other consistent observations.
Functional Observation Battery (FOB) and Motor Activity:
F0 males and satellite females:
No compound related differences in the FOB and motor activity tests between control and treated groups.

CLINICAL PATHOLOGY:
F0 males and satellite females:
Serum Chemistry:
Significantly increased alanine transferase (ALT) activity in males. In females, significantly decreased sodium values at all treatment doses and significantly increased
cholesterol in the 500 and 1000 mg/kg/day groups.

HEMATOLOGY:

Slight decreases in mean erythrocyte count and haematocrit at all treatment doses and in haemoglobin and mean cell volume at 1000 mg/kg/day in rats of each sex. These changes were only significant in females.
Significantly increased mean cell haemoglobin concentration in females of the 100 and 1000 mg/kg/day group and in males of the 1000 mg/kg/day group.

PATHOLOGY:
F0 males and satellite females:
Organ Weights:
Significantly increased absolute liver weight and liver weight relative to brain weight in animals of the 500 and 1 000 mg/kg/day group.
Significant findings in females only were decreased spleen weight (relative to brain weights) in the 1000 mg/kg/day group and increased kidney weight in the 500 mg/kg/day group.
Macroscopic:
In males, pitted kidneys were observed in the 500 and 1000 mg/kg/day groups.
Microscopic:
Treatment related effects were observed in kidneys of all test males (dose-related increased eosinophillic hyaline droplets in the proximal convoluted tubules, a finding commonly associated with hydrocarbon nephropathy).
Minimal to moderate hepatocellular vacuolation was observed in animals of the 500 and 1000 mg/kg/day groups.

F0 females:
Macroscopic:
No test related findings were observed. The animal euthanized on post breeding Day 25 was found to be non gravid. The animal euthanized on Day 43 was found to have implantation sites.

FERTILITY, GESTATION, PARTURITION AND LACTATION:
Mating and fertility indices, precoital intervals and gestation length were comparable among the groups.

F1 GENERATION FINDINGS:
No treatment related developmental effects through to lactation Day 4.

Test substance :

1-Tetradecene CASNO 1120-36-1 (the substance used was blended from three different suppliers of 1-tetradecene)

Conclusion :

Based upon liver weight increase and hepatocyte cytoplasmic vacuolation observed at 500 and 1000 mg/kg/day, the NOAEL for systemic toxicity in satellite females was 100 mg/kg/day. No NOAEL for systemic toxicity was established for males because of hydrocarbon nephropathy noted at all dose levels. The NOAEL for reproductive, developmental or neurotoxicity was 1000 mg/kg/day in rats of each sex.

Reliability : (1) valid without restriction
Modified guideline study downgraded to 2 because original laboratory report was not available for review.

Flag : Critical study for SIDS endpoint
21.12.2003 (10)

Type : One generation study
Species : rat
Sex : male/female

Strain	:	Sprague-Dawley
Route of admin.	:	gavage
Exposure period	:	
Frequency of treatm.	:	daily
Premating exposure period		
Male	:	71 days
Female	:	14 days
Duration of test	:	
No. of generation studies	:	
Doses	:	10, 100, 1000 mg/kg
Control group	:	yes, concurrent vehicle
NOAEL F1 offspring	:	= 1000 ml/kg bw
NOAEL F2 offspring	:	= 1000 ml/kg bw
Result	:	No reproductive or developmental effects
Method	:	other: ICH Harmonized Tripartite Repro Effectx Medicinal Prod
Year	:	
GLP	:	yes
Test substance	:	other TS: surrogate

Method :

Adult Sprague-Dawley (Charles River, Margate, Kent, England) rats of each sex were obtained at approximately 5 to 6 weeks of age. Rats were acclimated to the laboratory environment for 6 days prior to the initiation of dosing. During the acclimation period, rats were observed daily. Male rats weighed between 193 and 240 g and were 6 to 7 weeks of age at study start. Female rats were obtained eight weeks after the males. Female rats weighed between 208 and 262 g and were 10 to 11 weeks of age at study start. During the acclimation and premating periods, 10 rats (5 males and 5 females) were housed per stainless-steel cage. During the mating period, 1 male and 1 female were housed in a polypropylene cage with stainless-steel mesh lids and floors. Five females were housed together during the gestation period, while 5 males were housed together after the mating period was complete. Cages were equipped with polyethylene or polycarbonate bottles and sipper tubes and were placed in rooms designed to maintain adequate environmental conditions (18°C; 55% relative humidity, 12-h photocycle).

Feed was an expanded rodent diet containing no added antibiotic, or other chemotherapeutic or prophylactic agent. Water was local tapwater. Both food and water were available to the rats ad libitum.

DOSAGE LEVELS. Eighty-eight CD male rats and eight-eight CD female rats were administered the test substance formulated to supply targeted dosages of 0, 10, 100, or 1000 mg behenyl alcohol/kg body weight/day (Groups 1, 2, 3, and 4, respectively). Each treatment group consisted of 44 rats (22 males and 22 females). Animals were dosed by gavage at 5 ml/kg body weight. The volume given to each animal was calculated from body weights measured immediately before each administration. Males were treated with behenyl alcohol daily for 71 days prior to mating, during mating, and until termination. Females were treated with the test substance for 15 days prior to mating, during mating, and up to Day 17 of gestation.

Dosing Solutions were prepared by weighing the required amount of behenyl alcohol into a glass container and heating the container to

approximately 80°C until the behenyl alcohol was molten. Vehicle (1% Tween 80) was heated in a water bath to at least 75°C and combined with the molten behenyl alcohol under continuous magnetic stirring, to a concentration of 20% behenyl alcohol. The resulting suspension was slowly cooled, with homogenization to a temperature below 60°C, and then further cooled in a water bath to a temperature of 30°C. Once the resulting suspension reached this temperature, it was again slowly homogenized for at least 2 min and allowed to cool to room temperature. The concentrated suspension was further diluted to achieve the proper dosage levels.

IN-LIFE DATA: Rats were observed daily at cage side for evidence of reaction and general health. A thorough macroscopic examination of the visceral organs was completed on any animal that died during the study. Prior to mating, food and water consumption for males and females was recorded weekly and daily, respectively. During the gestation period, food and water consumption was measured only for females during the following time periods: Gestation Days 0 to 2, 3 to 6, 7 to 9, 10 to 13, 14 to 17, and 18 to 19, inclusive. Male and female body weight gains were measured twice weekly until mating. Following mating, male body weight gains were measured twice weekly for the remainder of the study, and body weight gains for females were recorded on GD 0, 3, 7, 10, 14, 18, and 20. In addition, starting 10 days before the mating period, vaginal smear samples were obtained daily from all females to assess the regularity and duration of estrous cycles.

REPRODUCTIVE PERFORMANCE: Trays beneath the cages were checked for ejected copulation plugs every morning during the mating procedure. Vaginal smears from each female were also examined for the presence of spermatozoa. The length of the mating period was recorded (time elapsing between initial paring and detection of mating) and Gestation Day 0 was designated as the day in which evidence of mating was found.

REPRODUCTIVE ENDPOINTS. Females were killed on Day 20 of gestation using carbon dioxide, and uterine contents were examined. Each female was macroscopically examined for evidence of disease or adverse reaction to test substance. Corpora lutea in each ovary were counted. The reproductive tract, including the ovaries, was then dissected out. For each female, the numbers of pre- and post-implantation sites, early and late resorption sites, and viable fetuses, as well as the distribution of fetuses in each uterine horn, were examined. The uterus of any female that was not gravid was stained with ammonium sulfide solution and examined for implantation sites.

Each fetus was weighed, given a detailed external examination, and uniquely identified within the litter with respect to the uterine position. Placenta were weighted and examined macroscopically for any abnormalities. The neck, thoracic, and abdominal cavities were removed from half of the fetuses, the contents of the thoracic and abdominal cavities were examined, and the sex was recorded. These fetuses were eviscerated, fixed in methylated spirit, processed and stained with Alizarin Red, and subjected to a skeletal examination. The remaining fetuses were placed in Bouin's fixative and internally examined using a modification of the Wilson free-hand serial sectioning technique.

Following necropsy of the females, males were killed with carbon dioxide, and examined externally and internally. Reproductive organ weights were

recorded. The left vas deferens was ligated to obtain a 5-microliter sample from the cauda epididymis. The sample was diluted in medium and mixed to assess for motility. The number of spermatozoa was assessed using a hemocytometer after further diluting the sample with 4% v/v neutral buffered formaldehyde.

STATISTICS: : To test the statistical significance of suggestive intergroup differences, one-way analysis of variance and t test were performed on body weights, body weight changes, and food and water consumption. Organ weights were evaluated by Dunnett's or Behren's-Fisher's tests. Nested analysis of variance and weighed t test were conducted on fetal and placental weights. Differences with an associated probability of $P < 0.05$ were considered statistically significant.

Remark :

Result is supported by a rabbit reproduction study reported in the same publication.

Result :

All female rats survived to scheduled sacrifice. One male treated with 1000 mg/kg demonstrating severe adverse clinical signs and a decrease in body weight was killed during week 6. This was the only death that occurred in the study and it was not considered treatment related. No other remarkable clinical observations were seen in any of the treated animals. Body weight gains, food and water consumption for rats of each sex of all dose groups, were comparable to controls throughout the study. No compound-related differences in female estrous cycles or mating performance and fertility were observed in any of the treatment groups when compared to the control group. Macroscopic findings at terminal necropsy revealed no findings attributable to test substance. No differences were observed in the number of corpora lutea, pre- and postimplantation sites, early and late resorptions, and viable fetuses. Fetal and placental weights were not affected by treatment with behenyl alcohol. Fetal sex ratios were comparable between all treatment groups and controls.

	DOSE (mg/kg-day)			
Parameter	0	10	100	1000
Number pregnant	22	22	22	21
Corpora lutea	17.8	18.4	18.7	18.9
Implantations	17.2	17	18.1	18
Viable young				
Male	8.4	8.4	8.5	8.6
Female	8	7.5	8.5	8.3
Total	16.4	15.9	17	16.9
Resorptions				
Early	0.82	1.09	1.14	1.05
Late	0	0	0	0
Total	0.82	1.09	1.14	1.05
Implantation loss (%)				
Pre	3.3	8.3	3.2	5.8
Post	4.7	6.4	6.3	5.8

Macroscopic, internal, and skeletal examinations of the fetuses, revealed no variations that were not comparable to historical control values. There were no observed effects related to behenyl alcohol treatment in this study. No significant macroscopic findings were reported in males treated with

		behenyl alcohol. Absolute and relative body weights of reproductive organs were similar between the treatment groups and the control group. Evaluation of sperm number and motility revealed no findings attributable to behenyl alcohol treatment.
Test substance	:	Behenyl alcohol (C-22 straight-chain alcohol) 1-Docosanol CASRN: 661-19-8 Purity 98% source: Condea, Germany.
Conclusion	:	There were no observed effects related to behenyl alcohol treatment in this reproduction study.
Reliability	:	(1) valid without restriction Modern guideline study under GLPs

21.12.2003 (18)

5.8.2 DEVELOPMENTAL TOXICITY/TERATOGENICITY

Species	:	rat
Sex	:	female
Strain	:	Wistar
Route of admin.	:	gavage
Exposure period	:	Days 6 to 15 of gestation
Frequency of treatm.	:	Daily
Duration of test	:	
Doses	:	0, 144, 720 or 1440 mg/kg-day
Control group	:	yes, concurrent vehicle
NOAEL maternal tox.	:	= 1440 mg/kg bw
NOAEL teratogen.	:	= 1440 mg/kg bw
Method	:	OECD Guide-line 414 "Teratogenicity"
Year	:	
GLP	:	yes
Test substance	:	
Method	:	The study was conducted according to OECD 414 guidelines except that 10 animals instead of the recommended 20 per group were employed. I\Test material was administered at doses of 144, 720, or 1440 mg/kg/day. A standard dose volume of 5 ml/kg was used. Control group 1 was dosed with doubly distilled water. Control group 2 was dosed with emulsifier (doubly distilled water with 0.005% Cremophor EL). The state of health of the animals was monitored daily and food consumption and body weights of the animals were recorded regularly. Females were sacrificed on gestation day 20. Fetuses were removed and evaluated for sex, weight, and any external, soft tissue, or skeletal findings.
Remark	:	Statistial methods: Dunnett's test, Fisher's exact test
Test substance	:	Alcohols, C7-11-branched and linear, CASNO 85566-14-9 The test material consisted of linear alcohols and alpha-methyl branched alcohols ranging in carbon chain length from C7 to C11
Conclusion	:	C7-11 Alcohol does not produce signs of toxicity in the dam or the fetus at these dose levels. C7-11 Alcohol is not embryo or fetotoxic under the conditions of this study.
Reliability	:	(2) valid with restrictions Reliable with restrictions - Only 10 animals per group, instead of the recommended 20 (OECD 414), were employed

13.11.2002 (27) (28)

Species	:	rat
Sex	:	male/female
Strain	:	other: Crl:CD BR VAF/Plus
Route of admin.	:	gavage
Exposure period	:	Premating through gestation
Frequency of treatm.	:	daily
Duration of test	:	
Doses	:	100, 500, 1000 mg/kg
Control group	:	yes, concurrent vehicle
NOAEL maternal tox.	:	= 100 mg/kg bw
NOAEL teratogen.	:	= 1000 mg/kg bw
Result	:	negative
Method	:	other: OECD 422 (modified)
Year	:	
GLP	:	yes
Test substance	:	other TS

Method :

Number/sex of animals: 12 males/group 20 females/group (12 females assigned to breeding phase and 8 females assigned as satellite females)

Method of administration: Oral (gavage)

Doses: 0, 100, 500 or 1000 mg/kg/day (dose volume 5mL/kg) for a minimum of 42 days;
Vehicle: corn oil.

Dosing Schedule: Males:
Day 0 to 28 - Pretreatment;
Day 29 to 42 - Mating;
Day 43 to 47 - Dosing after mating.

Satellite females:
Day 0 to 49. Dosing period.

Breeding females:
Day 0 to 14. Pretreatment;
Day 15 to 42. Dosing during mating and lactation;
Day 43 to 51. Dosing during lactation and until termination.

Terminal kill schedule Day 43. Sacrifice of unselected males (4 rats/sex/group).
Days 45 to 47. Neurotoxicity and clinical pathology evaluations (8 rats/sex/group), histopathology (5 rats/sex/group).
Days 42 to 51. Sacrifice and necropsy of breeding females (F0) and F1 pups.

Result :

Mortality:

F0 males and satellite females: None

F0 females: In the 500 mg/kg/day group, one female with evidence of mating failed to deliver and was sacrificed on post breeding day 25 and one female was sacrificed with total litter loss on Day 43.

Clinical observations:
F0 males, satellite females and F0 females:
Urine stain and salivation was noted in the 500 and 1000 mg/kg/day groups. Other observations were noted sporadically.

Functional Observation Battery (FOB) and Motor Activity:
F0 males and satellite females:
No test-substance related differences in the FOB and motor activity tests between the control and treated groups.

Clinical Pathology:
F0 males and satellite females:
Serum Chemistry:
Significantly increased alanine transferase (ALT) activity in males. In females, significantly decreased sodium values at all treatment doses and significantly increased cholesterol in the 500 and 1 000 mg/kg/day groups.

Haematology:
Slight decreases in mean erythrocyte count and haematocrit at all treatment doses and in haemoglobin and mean cell volume at 1000 mg/kg/day in both sexes. These changes were only significant in females. Significantly increased mean cell haemoglobin concentration in females of the 100 and 1000 mg/kg/day group and in males of the 1000 mg/kg/day group.

Pathology:
F0 males and satellite females:
Organ Weights:
Significantly increased absolute liver weight and liver weight relative to brain weight in animals of the 500 and 1 000 mg/kg/day group.
Significant findings in females only were decreased spleen weight (relative to brain weights) in the 1 000 mg/kg/day group and increased kidney weight in the 500 mg/kg/day group.

Macroscopic:
In males, pitted kidneys were observed in the 500 and 1 000 mg/kg/day groups.

Microscopic:
Treatment related effects were observed in kidneys of all test males (dose-related increased eosinophillic hyaline droplets in the proximal convoluted tubules, a finding commonly associated with hydrocarbon nephropathy). Minimal to moderate hepatocellular vacuolation was observed in animals of the 500 and 1 000 mg/kg/day groups.

F0 females:
Macroscopic:
No test related findings were observed. The animal euthanised on post breeding Day 25 was found to be non gravid. The animal euthanised on Day 43 was found to have implantation sites.

Fertility, Gestation, Parturition and Lactation:
Mating and fertility indices, precoital intervals and gestation length were comparable among the groups.

F1 generation findings:
No treatment related developmental effects through to lactation Day 4.

Test substance :

1-Tetradecene CASNO 1120-36-1 (the substance used was blended from three different suppliers of 1-tetradecene)

Conclusion :

Based upon liver weight increase and hepatocyte cytoplasmic vacuolation observed at 500 and 1000 mg/kg/day, the NOAEL for systemic toxicity in satellite females was 100 mg/kg/day. No NOAEL for systemic toxicity was established for males because of hydrocarbon nephropathy noted at all dose levels. The NOAEL for reproductive, developmental or neurotoxicity was 1000 mg/kg/day in rats of each sex.

Reliability : (2) valid with restrictions

Modified guideline study downgraded to 2 because original laboratory report was not available for review

21.12.2003 (1)

(1) 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

(2) 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.

(3) 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

(4) 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

(5) 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

(6) 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.

(7) 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.

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

(9) Calculated by TRA using EPIWIN 3.05

(10) 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

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(12) EPIWIN 3.05, Syracuse Research Corporation, AOP Program v1.90

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(16) 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.

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

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(19) 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

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(22) IUDLID-2000 document for 2-Ethylhexyl Laurate CASNO 20292-08-4, European Chemicals Bureau, 2000

(23) IUDLID-2000 document for dodecanedioic acid CASNO 693-23-2, European Chemicals Bureau, 2000

(24) IUDLID-2000 document for Fatty acids C10-14 CASNO 90990-09-3, European Chemicals Bureau, 2000

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(27) 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.

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