SCREENING-LEVEL HAZARD CHARACTERIZATION OF HIGH PRODUCTION VOLUME CHEMICALS

CHEMICAL CATEGORY NAME
Neoacids C_5 TO C_{28}

SPONSORED CHEMICALS

Propanoic acid, 2,2-dimethyl-	**CAS No. 75-98-9**
Propanoic acid, 2,2-dimethyl-, methyl ester	**CAS No. 598-98-1**
Carboxylic acid, C_{6-8} neo	**CAS No. 95823-36-2**
Neodecanoic acid	**CAS No. 26896-20-8**
Fatty acids, C_9-C_{13} neo	**CAS No. 68938-07-8**
Fatty acids, C_9-C_{28} neo	**CAS No. 72480-45-6**

August 2007

Prepared by

High Production Volume Chemicals Branch
Risk Assessment Division
Office of Pollution Prevention and Toxics
Environmental Protection Agency
1200 Pennsylvania Avenue, NW
Washington, DC 20460-0001

SCREENING-LEVEL HAZARD CHARACTERIZATION OF HIGH PRODUCTION VOLUME CHEMICALS

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

The Environmental Protection Agency's Office of Pollution Prevention and Toxics (OPPT) is evaluating the data submitted in the HPV Challenge Program on approximately 1,400 sponsored chemicals. OPPT is using a hazard-based screening process to prioritize review of the submissions. The hazard-based screening process consists of two tiers described below briefly and in more detail on the Hazard Characterization website[3].

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

In Tier 2, a screening-level hazard characterization is developed by EPA that consists of an objective evaluation of the quality and completeness of the data set provided in the Challenge Program submissions. The evaluation is performed according to established EPA guidance[2,4] and is based primarily on hazard data provided by sponsors. EPA may also include additional or updated hazard information of which EPA, sponsors or other parties have become aware. The hazard characterization may also identify data gaps that will become the basis for a subsequent data needs assessment where deemed necessary. Under the HPV Challenge Program, chemicals that have similar chemical structures, properties and biological activities may be grouped together and their data shared across the resulting category. This approach often significantly reduces the need for conducting tests for all endpoints for all category members. As part of Tier 2, evaluation of chemical category rationale and composition and data extrapolation(s) among category members is performed in accord with established EPA[2] and OECD[5] guidance.

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

The screening-level hazard characterizations, as the name indicates, do not evaluate the potential risks of a chemical or a chemical category, but will serve as a starting point for such reviews. In 2007, EPA received data on uses of and exposures to high-volume TSCA existing chemicals, submitted in accordance with the requirements of the Inventory Update Reporting (IUR) rule. For the chemicals in the HPV Challenge Program, EPA will review the IUR data to evaluate exposure potential. The resulting exposure information will then be combined with the screening-level hazard characterizations to develop screening-level risk characterizations[4,6]. The screening-level risk characterizations will inform EPA on the need for further work on individual chemicals or categories. Efforts are currently underway to consider how best to utilize these screening-level risk characterizations as part of a risk-based decision-making process on HPV chemicals which applies the results of the successful U.S. High Production Volume Challenge Program and the IUR to support judgments concerning the need, if any, for further action.

---

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

SCREENING-LEVEL HAZARD CHARACTERIZATION
Neoacids C_5-C_{28} Category

Introduction

The sponsor, ExxonMobil Chemical Company, submitted a Test Plan and Robust Summaries to EPA for the Neoacids C_5-C_{28} Category on December 6, 2001. EPA posted the submission on the ChemRTK Web site on January 11, 2002 (http://www.epa.gov/chemrtk/pubs/summaries/neoc528/c13335tc.htm). EPA comments on the original submissions were posted to the website on October 10, 2002. Public comments were also received and posted to the website. The sponsor submitted revised and final documents on September 18, 2003 and November 6, 2006, which were posted to the ChemRTK website on November 3, 2003 and December 14, 2006 respectively. The neoacids C_5-C_{28} category consists of the following chemicals:

Propanoic acid, 2,2-dimethyl-	CAS No. 75-98-9
Propanoic acid, 2,2-dimethyl-, methyl ester	CAS No. 598-98-1
Carboxylic acid, C_{6-8} neo	CAS No. 95823-36-2
Neodecanoic acid	CAS No. 26896-20-8
Fatty acids, C_9-C_{13} neo	CAS No. 68938-07-8
Fatty acids, C_9-C_{28} neo	CAS No. 72480-45-6

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

Category Justification

The six members of the neoacids C_5-C_{28} category are complex mixtures, designated as Class 2 substances for TSCA Inventory Reporting. Class 2 substances, in general, have a complex and variable composition depending on their source or methods of derivation. The category members are trialkyl acetic acids ($R_1R_2R_3CCOOH$) produced by reacting a branched olefin with carbon monoxide and water at elevated temperatures and pressures in the presence of an acid catalyst. During this process, each hydrogen atom on the non-carboxyl carbon of acetic acid is replaced by an alkyl group. The number of carbon atoms in the category members ranges from C_5 to C_{28}. The sponsor grouped the chemicals based on the similarities in structure, physical-chemical properties, environmental fate and the same mode of action. Representative chemical structures of the sponsored substances are depicted in the appendix.

The revised test plan identified the category member CAS No. 26896-20-8 as neodecanoic acid with isomer composition information for the neo acid mixtures. Fatty acids, C_9-C_{13} neo (CAS No. 68938-07-8) is estimated to contain ~87% C_9 isomers, ~9% C_{13} isomers and ~4% of the remaining isomers within the range indicated. Fatty acids, C_9-C_{28} neo (CAS No. 72480-45-6) consists primarily of fatty acids having carbon numbers predominantly in the range of C_9 through C_{28} and boiling in the range of approximately 225°C to 387°C. Composition for the other category members is not provided. Additionally, the rationale for inclusion of 2,2-dimethylpropanoic acid, methyl ester in the category is based on its presumed rapid hydrolysis to the parent neoacid. This rationale was inconsistent with modeled data and did not support the grouping of the ester with the other category members. Although, the methyl ester metabolizes into the parent acid, 2,2-dimethylpropanoic acid, and methanol by endogenous esterases, no data were submitted in support of this conclusion. The other hydrolysis product, methanol, has intrinsic toxicological properties not characteristic of the category members. However, EPA agrees that using a conservative approach, the methyl ester can be considered part of the category as long as the contribution of methanol toxicity is delineated when characterizing the toxicological endpoints.

Justification for Supporting Chemicals

Data were submitted for supporting chemicals to address data gaps for the reproductive and developmental toxicity endpoints. The supporting chemicals are isononanoic acid (CAS No. 3302-10-1) and isooctanoic acid (CAS No. 25103-52-0). In its original comments, EPA stated that isooctanoic acid and isononanoic acid were unacceptable for read-across purposes because the supporting substances were not similar in structure to the category members and it was not clear if there was any substitution at the alpha position. A key feature of the category chemicals is the lack of the alpha hydrogen in their structures, which is a critical determinant of metabolism. It is also likely that the isooctanoic acid is a mixture. EPA recommended a combined repeated-dose/reproductive/developmental toxicity screening study (OECD TG 422) be conducted on category members with the shortest and longest chain lengths to address these data gaps in the submission. In its response, the sponsor stated that based on structure-activity relationships, neither category of acids produce reproductive effects because of the size of the methyl groups and proposed no additional reproductive or developmental testing. No additional information or data were provided to support this proposal; therefore, EPA considers the data from the proposed supporting chemicals inadequate for the purposes of the HPV Challenge Program.

Summary-Conclusion

The short carbon-chain category members have low log K_{ow} values, indicating that their potential to bioaccumulate is expected to be low. Log K_{ow} ranges that include values greater than 4 for category members that may contain longer carbon chains (e.g., fatty acids, C_9-C_{13} neo and fatty acids, C_9-C_{28} neo) indicate that the potential for these category members to bioaccumulate may be high, depending on the composition of the mixture. Members of the category are not readily biodegradable, indicating that they have the potential to persist in the environment.

The evaluation of available aquatic toxicity data for fish, aquatic invertebrates and aquatic plants indicates that the potential acute hazard of the neoacids C_5-C_{28} category members to aquatic organisms is low.

The acute oral toxicity for the members of this category is low to moderate. The category members are considered irritating to the skin and eye but are not sensitizers. Repeated oral exposure to propanoic acid, 2,2-dimethyl- and fatty acids, C_9-C_{13} neo resulted in the following clinical observations: head shaking, sneezing, nasal discharge and increased salivation at high doses. These responses are considered to be related to the irritating nature of the chemicals. Repeated dermal exposure to propanoic acid, 2,2-dimethyl-, carboxylic acid, C_6-C_8 neo and neodecanoic acid resulted in erythema, atonia and desquamation. No treatment-related systemic effects were observed at the doses tested. Repeated exposure to fatty acids, C_9-C_{13} neo resulted in nephropathy associated with hyaline-droplet formation in male rats only. Although the kidney toxicity observed in male rats is suggestive of an $alpha_{2u}$-globulin-mediated effect, one of the key events in this mode of action, $alpha_{2u}$-globulin accumulation has not been demonstrated. Therefore, a NOAEL for nephropathy in male rats was not established. A three-generation reproductive toxicity study with neodecanoic acid indicated no treatment-related effects on reproductive parameters and showed no developmental effects. However, maternal toxicity was evident by decreased food intake and increased incidence of rales when exposed to carboxylic acid, C_6-C_8 neo. Developmental effects with this chemical were microphthalmia (small eyes), anophthalmia (eye(s) did not form during development), fused cervical vertebrae and misaligned thoracic vertebrae, hydrocephalus, varying unossified structures, reduced fetal body weight, and mortality. The category members, propanoic acid, 2,2-dimethyl-, neodecanoic acid and fatty acids, C_9-C_{13} neo did not show mutagenic potential when tested in *Salmonella typhimurium.* No chromosomal aberrations were observed in cells tested with propanoic acid, 2,2-dimethyl-, neodecanoic acid and fatty acids, C_9-C_{13} neo, with or without metabolic activation. However, fatty acids, C_9-C_{13} neo induced chromosomal aberrations *in vitro* when tested with metabolic activation. Fatty acids, C_9-C_{13} neo did not induce cytogenetic damage when tested *in vivo* in a mouse micronucleus assay.

The potential health hazard of the neoacids C_5 to C_{28} category is moderate based on the limited data available for repeated-dose and reproductive toxicity and the findings in the developmental studies.

Available data for neodecanoic acid cannot be used as read-across for the propanoic acid and fatty acid moieties of the category. Therefore, data gaps exist for the reproduction and developmental toxicity endpoints for the propanoic acid and fatty acid moieties of the category.

1. Physical-Chemical Properties and Environmental Fate

A summary of physical-chemical properties and environmental fate data submitted is provided in Table 1. For the purpose of the screening-level hazard characterization, the review and summary of these data was limited to the octanol-water partition coefficient and biodegradation endpoints as indictors of bioaccumulation and persistence, respectively.

Octanol-Water Partition Coefficient

Propanoic acid, 2,2-dimethyl- (CAS No. 75-98-9)
Log K_{ow}: 1.5 (estimated)

Propanoic acid, 2,2-dimethyl-methyl ester (CAS No. 598-98-1)
Log K_{ow}: 1.8 (estimated)

Carboxylic acid, C_{6-8} neo (CAS No. 95823-36-2)
Log K_{ow}: 2.4 (estimated)

Neodecanoic acid (CAS No. 26896-20-8)
Log K_{ow}: 3.9 (estimated)

Fatty acids, C_9-C_{13} neo (CAS No. 68938-07-8)
Log K_{ow}: 3.3 – 5.2 (estimated)

Fatty acids, C_9-C_{28} neo (CAS No. 72480-45-6)
Log K_{ow}: 3.3 – 6.0 (estimated)

Biodegradation

Propanoic acid, 2,2-dimethyl- (CAS No. 75-98-9)
In a ready biodegradation test, the inoculum was non-acclimated activated domestic sludge. After 28 days, 24% of the test substance had degraded.
Propanoic acid, 2,2-dimethyl- is not readily biodegradable.

Propanoic acid, 2,2-dimethyl-methyl ester (CAS No. 598-98-1)
Propanoic acid, 2,2-dimethyl-methyl ester is not readily biodegradable, based on the data for propanoic acid, 2,2-dimethyl- (CAS No. 75-98-9) and carboxylic acid, C_{6-8} neo (CAS No. 95823-36-2).
Propanoic acid, 2,2-dimethyl-methyl ester is not readily biodegradable.

Carboxylic acid, C_{6-8} neo (CAS No. 95823-36-2)
In a ready biodegradation test, the inoculum was non-acclimated activated domestic sludge. After 28 days, 44% of the test substance had degraded.
Carboxylic acid, C_{6-8} neo is not readily biodegradable.

Neodecanoic acid (CAS No. 26896-20-8)
In a ready biodegradation test, the inoculum was non-acclimated activated domestic sludge. After 28 days, 11% of the test substance had degraded.
Neodecanoic acid is not readily biodegradable.

Fatty acids, C_9-C_{13} neo (CAS No. 68938-07-8)
In a ready biodegradation test, the inoculum was non-acclimated activated domestic sludge. After 28 days, 2.3% of the test substance had degraded.
Fatty acids C_9-C_{13} neo is not readily biodegradable.

Fatty acids, C_9-C_{28} neo (CAS No. 72480-45-6)
Fatty acids, C_9-C_{28} neo is not considered readily biodegradable, based on the data for fatty acids, C_9-C_{13} neo (CAS No. 68938-07-8).
Fatty acids, C_9-C_{28} neo is not readily biodegradable.

Conclusion: The short carbon-chain category members have low log K_{ow} values, indicating that their potential to bioaccumulate is expected to be low. Log K_{ow} ranges that include values greater than 4 for category members that may contain longer carbon chains (e.g., fatty acids, C_9-C_{13} neo and fatty acids, C_9-C_{28} neo) indicate that the potential for these category members to bioaccumulate may be high, depending on the composition of the mixture. Members of the category are not readily biodegradable, indicating that they have the potential to persist in the environment.

Table 1. Summary of Physical-Chemical Properties and Environmental Fate Data

Endpoints	Propanoic acid, 2,2-dimethyl- (75-98-9)	Propanoic acid, 2,2-dimethyl-methyl ester (598-98-1)	Carboxylic acid, C_{6-8} neo (95823-36-2)	Neodecanoic acid (26896-20-8)	Fatty acids, C_9-C_{13} neo (68938-07-8)	Fatty acids, C_9-C_{28} neo (72480-45-6)
Melting Point (ºC)	35(e)	-62.5 (e)	**24.6 (m)**	**57.1 (m)**	**37 – 76 (m)**[1]	**37 – 76 (m)**[1]
Boiling Point (ºC)	**163 – 165 (m)**	**101 (m)**	**207 – 210 (m)**	**250 – 257 (m)**	**236 – 247 (m)**[1]	**236 – 247 (m)**[1]
Vapor Pressure (hPa at 25°C)	2.05 (e)	47.6 (e)	0.325 (e)	0.009 (e)	0.001 – 0.061 (e)[1]	$< 2.3 \times 10^{-12}$ – 0.061 (e)[1]
Log K_{ow}	1.5 (e)	1.8 (e)	2.4 (e)	3.9 (e)	3.3 – 5.2 (e)[1]	3.3 – 6.0 (e)[1]
Water Solubility (mg/L at 25°C)	15,590 (e)	2,835 (e)	1,912 (e)	69 (e)	3.1 – 243 (e)[1]	< 1 – 243 (e)[1]
Direct Photodegradation (cm^3/molecule-sec)	1.0218×10^{-12}	0.7194×10^{-12}	3.2965×10^{-12}	7.5357×10^{-12}	0.103617×10^{-12}	0.202531×10^{-12}
Indirect (OH^-) Photodegradation $t_{1/2}$ (h)	126 (e)	178 (e)	38.9 (e)	17.0 (e)	12.4 (e)	12.4 (e)
Stability in Water (Hydrolysis) (year)	N/A	No data[2]	N/A	N/A	N/A	N/A
Fugacity (Level III Model)						
Air (%)	0.78	13.7	0.71			
Water (%)	98.7	86.0	98.2	66.7	41.5	20.3
Soil (%)	0.27	0.03		5.7	6.6	10.2
Sediment (%)	0.26	0.28	0.74	27.3	51.7	69.5
Biodegradation at 28 days (%)	**24 (m)**	No Data 24 – 44 (RA)	**44 (m)**	**11 (m)**	**2.3 (m)**	No Data 2.3 (RA)
Bioconcentration Factor	3.16 (e)	5.12 (e)	3.16 (e)	3.16 (e)	3.16 (e)	3.16 (e)

(m) = measured data (i.e., derived from testing); (e) = estimated data (i.e., derived from modeling); (RA) = read-across; N/A, not applicable; [1]EPA recommended that the sponsor provide measured values for C9, C13 and C28 fatty acid or for the major component of these mixtures instead of ranges of values; [2]Sponsor proposed providing estimated data for this category member in the original test plan.

2. Environmental Effects – Aquatic Toxicity

A summary of aquatic toxicity data submitted for SIDS endpoints is provided in Table 2. The table also indicates where data for tested category members are read-across (RA) to untested members of the category.

Acute Toxicity to Fish

Propanoic acid, 2,2-dimethyl- (CAS No. 75-98-9)
Goldfish (*Carassius auratus)* were exposed to the test substance (treatment levels not specified) for 96 hours under static conditions.
96-h LC_{50} = 380 mg/L

Carboxylic acid, C_{6-8} neo (CAS No. 95823-36-2)
(Tested using heptanoic C7 acid-approximately 70% n-heptanoic acid, 30% isoheptanoic acid)
Fathead minnows (*Pimephales promelas*; 20/concentration) were exposed to the test substance at nominal concentrations of < 0.79, 51.4, 124, 200, 436 and 882 mg/L for 96 hours under flow-through conditions. Measured concentrations were < 0.8, 51.4, 125, 200, 436 and 882 mg/L.
96-h LC_{50} = 630 mg/L

Neodecanoic acid (CAS No. 26896-20-8)
Rainbow trout (*Oncorhynchus mykiss*) were exposed to the test substance as water accommodated fractions (WAF) at concentrations of 0, 10.3, 13.6, 26.3, 52.5 and 102 mg/L WAF for 96 hours under semi-static conditions. Individual WAFs were prepared and analyzed for test substance concentration for each test treatment.
96-h LC_{50} = 37.2 mg/L

Fatty acids, C_9-C_{13} neo (CAS No. 68938-07-8)
Rainbow trout (*O. mykiss*) were exposed to the test substance as water accommodated fractions (WAF) at concentrations of 0, 5.18, 10.5, 23, 61 and 102 mg/L WAF for 96 hours under semi-static conditions. WAF was analyzed for test material concentration. The mortality at 96 hours was 0% up to 23 mg/L and 100% at higher concentrations.
96-h LC_{50} = 37.5 mg/L

Acute Toxicity to Aquatic Invertebrates

Propanoic acid, 2,2-dimethyl- (CAS No. 75-98-9)
Daphnia magna were exposed to the test substance at nominal concentrations of 0, 36, 60, 100, 170, 280 and 460 mg/L for 48 hours under static conditions. At 48 hours, mortality was observed at 100 mg/L (7%), 170 mg/L (13%), 280 mg/L (93%) and 460 mg/L (100 %).
48-h EC_{50} = 203 mg/L

Carboxylic acid, C_{6-8} neo (CAS No. 95823-36-2)
(Tested using heptanoic C7 acid-approximately 70% n-heptanoic acid, 30% isoheptanoic acid)
Daphnia magna were exposed to the test substance at measured concentrations of <0.82, 54.7, 107.7, 222, 476 and 903 mg/L for 48 hours under flow-through conditions. At 48 hours, immobilization was observed at <0.82 mg/L (10%), 107 mg/L (35%), 222 mg/L (90%) and 100% immobilization at higher concentrations.
48-h EC_{50} = 138 mg/L

Neodecanoic acid (CAS No. 26896-20-8)
D. magna were exposed to neodecanoic acid at nominal concentrations of 0, 13, 22, 36, 60, 100, 170 and 280 mg/L for 48 hours under static conditions. At 48 hours, mortality was observed at 13 mg/L (13%), 22 mg/L (13%), 36 mg/L (20%), 60 mg/L (67%) and 100 % mortality at higher concentrations.
48-h EC_{50} = 47.1 mg/L

Fatty acids, C_9-C_{13} neo (CAS No. 68938-07-8)
D. magna were exposed to the test substance as water accommodated fractions (WAF) at measured concentrations of 0, 6.22, 11.5, 23.5, 45.6 and 84.9 mg/LWAF for 48 hours under static conditions. WAF was analyzed for test

material concentrations. At 48 hours, immobilization (100%) was only observed at the highest concentration tested (84.9 mg/L).
48-h EC_{50} = 62.2 mg/L

Toxicity to Aquatic Plants

Propanoic acid, 2,2-dimethyl- (CAS No. 75-98-9)
Green algae (*Pseudokirchneriella subcapitata*) were exposed to the test substance as water accommodated fractions (WAF) at measured concentrations of 0, 62, 125, 250, 500 and 1000 mg/L WAF for 72 hours under static conditions. WAF was analyzed for test material concentrations. Incubation for 72 hours inhibited growth by 1.5, -3.0, -1.0, 24 and 64%, at to 62, 125, 250, 500 and 1000 mg/L, respectively.
72-h EC_{50} (biomass) = 878 mg/L
72-h EC_{50} (growth) = 979 mg/L

Carboxylic acid, C_{6-8} neo (CAS No. 95823-36-2)
(Tested using heptanoic C7 acid-approximately 70% n-heptanoic acid, 30% isoheptanoic acid)
Green algae (*P. subcapitata*) were exposed to the test substance at measured concentrations of 0, 3.03, 6.20, 12.24, 23.55 and 52.15 mg/L for 96 hours under static conditions. Incubation for 96 hours inhibited growth by 47.8, 79.1, 81.7 and 84.3%, at to 6.2, 12.24, 23.55 and 52.15 mg/L, respectively.
96-h EC_{50} (growth) = 6.49 mg/L

Fatty acids, C_9-C_{13} neo (CAS No. 68938-07-8)
Green algae (*P. subcapitata*) were exposed to the test substance as water accommodated fractions (WAF) at measured concentrations of 0, 62.4, 120, 226, 350 and 432 mg/L WAF for 72 hours under static conditions. WAF was analyzed for test material concentrations. Incubation for 72 hours inhibited growth by 3.9, 4.9, 27, 51 and 59%, at to 62.4, 120, 226, 350 and 432 mg/L, respectively.
72-h EC_{50} (biomass) = 216 mg/L
72-h EC_{50} (growth) = 388 mg/L

Chronic Toxicity to Aquatic Invertebrates

Carboxylic acid, C_{6-8} neo (CAS No. 95823-36-2)
(Tested using heptanoic C7 acid-approximately 70% n-heptanoic acid, 30% isoheptanoic acid)
Daphnia magna (10 per 4 replicates) were exposed to the test substance at measured concentrations of < 0.9, 54.7, 2.32, 4.78, 10.1, 21.7 and 44.4 mg/L for 21 days under flow-through conditions. After 21 days, the observation of immobilization was used to characterize the chronic toxicity endpoint.
21-day EC_{50} = 7.1 mg/L

Conclusion: The evaluation of available aquatic toxicity data or fish, aquatic invertebrates and aquatic plants indicates that the potential acute hazard of the neoacids C_5-C_{28} category members to aquatic organisms is low.

Table 2. Summary of Environmental Effects – Aquatic Toxicity Data						
Endpoints	**Propanoic acid, 2,2-dimethyl-** **(75-98-9)**	**Propanoic acid, 2,2-dimethyl-methyl ester** **(598-98-1)**	**Carboxylic acid, C_{6-8} neo** **(95823-36-2)**	**Neodecanoic acid** **(26896-20-8)**	**Fatty acids, C_9-C_{13} neo** **(68938-07-8)**	**Fatty acids, C_9-C_{28} neo** **(72480-45-6)**
Fish **96-h LC_{50} (mg/L)**	**380 (m)**	No Data 380 (RA)	**630 (m)**[1]	**37.2 (m)**	**37.5 (m)**	No Data 37.5 (RA)
Aquatic Invertebrates **48-h EC_{50} (mg/L)**	**203 (m)**	No Data 203 (RA)	**138 (m)**[1]	**47.1 (m)**	**62.2 (m)**	No Data 62.2 (RA)
Aquatic Plants **72-h EC_{50} (mg/L)** **(growth)** **(biomass)**	 **979 (m)** **878 (m)**	 No Data 979 878 (RA)	 **6.49 (m; 96-h)**[1]	 No Data 388 (m) 216 (m) (RA)	 **388 (m)** **216 (m)**	 No Data 388 216 (RA)
Chronic Toxicity to Invertebrates **21-day EC_{50} (mg/L)**	**–**	**–**	**7.1 (m)**[1]	**–**	**–**	**–**

(m) = measured data (i.e., derived from testing); (e) = estimated data (i.e., derived from modeling); (RA) = Read Across;
– indicates endpoint was not addressed for this chemical, but is only required on a case-by-case basis.
[1]Data are for a C7 branched and linear aliphatic acid product that does not contain a quaternary carbon

3. Human Health Effects

A summary of health effects data submitted for SIDS endpoints is provided in Table 3. The table also indicates where data for tested category members are read-across (RA) to untested members of the category.

Acute Oral Toxicity

Propanoic acid, 2,2-dimethyl- (CAS No. 75-98-9)
Male Sprague-Dawley rats were administered the test substance via oral gavage at doses of 34.6, 120, 417, 1450, 5000 and 10,000 mg/kg-bw and observed for 14 days. All animals in the 5000 and 10,000 mg/kg dose groups died within 48 hours of treatment. Severe depression, dyspnea, and prostration preceded death in all of the animals that died. Necropsy findings in high dose animals indicated congestion of lungs, liver, kidneys and adrenals.
LD_{50} = 2,000 mg/kg-bw

Carboxylic acid, C_{6-8} neo (CAS No. 95823-36-2)
Male Sprague-Dawley rats were administered the test substance via oral gavage at doses of 34.6, 120, 417, 1450, 5000 and 10,000 mg/kg-bw and observed for 14 days. At the two highest dose levels, all animals were dead within 24 hours. Prior to death, animals exhibited marked depression, sprawling of the limbs and depressed reflexes. Congestion of the lungs, kidneys and adrenals were observed in these animals.
LD_{50} = 1,860 mg/kg-bw

Neodecanoic acid (CAS No. 26896-20-8)
Male Sprague-Dawley rats were administered the test substance via oral gavage at doses of 34.6, 120, 417, 1450, 5000 and 10,000 mg/kg-bw and observed for 14 days. In the highest dose group, 4/5 animals died by 4 hours and all animals were dead by 24 hours post-treatment. Animals in the 5,000 and 10,000 mg/kg groups appeared to have depression, dyspnea, ataxia and sprawling of the limbs. Also at these two dose levels, necropsy findings indicated congestion of the lungs, liver, spleen, kidneys and adrenals.
LD_{50} = 2,000 mg/kg-bw

Acute Dermal Toxicity

Propanoic acid, 2,2-dimethyl- (CAS No. 75-98-9)
Male and female albino rabbits were administered dermal doses of the test substance at 50, 200, 794 and 3160 mg/kg mg/kg-bw and observed for 14 days. In the 794 mg/kg group, three of the four animals exhibited slight depression, dyspnea, unsteady gait with slight sprawling of the limbs at 24 hours after exposure to the test substance. However, by the third day post-exposure, all of the animals appeared normal.
$LD_{50} \geq 3160$ mg/kg-bw

Carboxylic acid, C_{6-8} neo (CAS No. 95823-36-2)
Male and female albino rabbits were administered dermal doses of the test substance at 50, 200, 794 and 3160 mg/kg mg/kg-bw and observed for 14 days. In the highest dose group, marked depression, dyspnea, ataxia, and sprawling of the limbs were observed 1 to 4 hours after application. However, the animals had completely recovered by 24 hours following exposure and exhibited normal appearance and behavior for the remainder of the 14-day post-exposure period. Necropsy revealed no significant signs of gross pathology in these animals.
$LD_{50} \geq 3160$ mg/kg-bw

Neodecanoic acid (CAS No. 26896-20-8)
Male and female albino rabbits were administered dermal doses of the test substance at 50, 200, 794 and 3160 mg/kg mg/kg-bw and observed for 14 days. At the 794 and 3160 mg/kg levels, a dose-dependent increase in the degree of irritation, consisting of slight to moderate erythema was observed.
$LD_{50} \geq 3160$ mg/kg-bw

Acute Inhalation Toxicity

Propanoic acid, 2,2-dimethyl- (CAS No. 75-98-9)
(1) Male Wistar rats were exposed the test substance vapor via whole-body vapor at 4.0 mg/L for 6 hours and observed for 14 days. No deaths occurred among any of the animals during the inhalation exposure. Two rats died on the second and fifth days. Rats displayed piloerection, epitasis and dyspnea following exposure.
$LC_{50} < 4.0$ mg/L

(2) Male Swiss albino mice were exposed the test substance vapor via whole-body vapor at 4.0 mg/L for 6 hours. No deaths occurred among any of the animals during the inhalation exposure. Hyperactivity followed by prostration was observed. All 10 mice died within the 24 hours following exposure.
$LC_{50} > 4.0$ mg/L

Neodecanoic acid (CAS No. 26896-20-8)
(1) Male Wistar rats and Swiss albino mice (10/sex/species) were exposed the test substance vapor via whole-body vapor at 3.0 mg/L for 6 hours and observed for 14 days. No mortality or significant signs of toxicity were observed during the 6-hour exposure period. No deaths occurred in mice or rats throughout the study and no significant observations were made at necropsy.
$LC_{50} > 3.0$ mg/L

(2) Male Wistar rats and Swiss albino mice (10/sex/species) were exposed to aerosolized test substance 511 mg/m^3 (0.511 mg/L) for 6 hours and observed for 14 days. No mortality or significant signs of toxicity were observed during the 6-hour exposure period. No deaths occurred in mice or rats throughout the study and no significant observations were made at necropsy.
$LC_{50} > 0.511$ mg/L

Repeated-Dose Toxicity

Propanoic acid, 2,2-dimethyl- (CAS No. 75-98-9)
(1) Male and female Fischer 344 rats (7/sex/dose) were administered the test substance at 0, 10, 30, 100 and 300 mg/kg-bw/day by oral gavage for 28 days. No adverse treatment-related effects on body weights, food consumption, hematological parameters or histopathology were observed. Immediately after dosing at concentrations > 30 mg/kg-bw/day, the animals shook their heads and sneezed, producing a dark nasal discharge.

These effects were transient and considered a response to the irritant effects of the test substance. Increases in alkaline phosphatase activity, cholesterol and bilirubin levels at concentrations of 30 mg/kg-bw/day were considered adaptive responses and did not correlate with any histopathological changes. In addition, increases in kidney and liver weights at 300 mg/kg-bw/day were not considered clinically relevant, as they did not correlate with any histopathological changes.
LOAEL > 300 mg/kg-bw/day
NOAEL = 300 mg/kg-bw/day (highest dose tested)

(2)Groups of four male albino rabbits were administered the test substance at 0, 30 and 300 mg/kg-bw/day daily by dermal application with isopropyl alcohol as the vehicle for 2 weeks (a total of 10 exposures). There was a 2-day rest period (weekend) between the fifth and sixth applications. Control animals exhibited slight erythema throughout the study with slight atonia and desquamation following the fifth application. Animals in the low-dose group had slight to moderate erythema and animals in the high-dose group also moderate erythema with moderate to marked atonia and desquamation. Three animals in the high-dose group had areas of necrosis that persisted throughout the study. In the high-dose group, gross pathological findings revealed parasitic infection of the liver in one animal, pitted kidneys in another and congestion in the pancreas and kidney of a third.
LOAEL > 300 mg/kg-bw/day
NOAEL = 300 mg/kg-bw/day (highest dose tested)

Carboxylic acid, C_{6-8} neo (CAS No. 95823-36-2)
In a 2-week repeated-dose toxicity study, groups of four male albino rabbits were administered the test substance at 0, 55.4 and 553.7 mg/kg-bw/day daily by dermal application with isopropyl alcohol as the vehicle. There was a 2-day rest period (weekend) between the fifth and sixth applications. Animals in the low dose group showed normal appearance and behavior throughout the study with the exception of one animal that showed a slight weight loss. Slight erythema was observed during the first week followed by moderate atonia and desquamation for the remainder of the study period. In the high dose group, three of the four animals showed normal appearance and behavior. From the fifth through ninth application, the fourth animal showed labored breathing, weight loss, and was found dead after the final application. Upon necropsy, the lungs were found to be congested and emphysematous with hemorrhagic areas in the renal medulla. The death was not considered treatment related by the study authors. Slight to moderate erythema and slight to moderate edema were present from second through fifth applications. There was also moderate to marked atonia, desquamation and fissuring observed following the fourth application. All animals showed areas of necrosis at the application site and two animals exhibited hypersensitivity to touch.
LOAEL > 553.7 mg/kg-bw/day
NOAEL = 553.7 mg/kg-bw/day (highest dose tested)

Neodecanoic acid (CAS No. 26896-20-8)
Groups of 4 male albino rabbits were administered the test substance at 0, 400 and 2280 mg/kg-bw/day daily by dermal application for 2 weeks. There was a two-day rest period (weekend) between the fifth and sixth applications. Animals in the low dose group showed normal appearance and behavior throughout the study with the exception of one animal that was wheezing. Slight erythema and moderate atonia and desquamation were observed from the first or fourth application and persisted for the remainder of the study period. In the high dose group, animals exhibited a slight reduction in weight by the end of the study. Necropsy revealed parasitic areas on the liver and/or mesentery of three animals, emphysema in three animals, and fluid in the cranial cavity and sinuses of one animal. These findings were not considered treatment related. Moderate erythema and moderate to marked atonia, desquamation and edema were present after the fifth application. After seven applications, slight fissures were observed in some of the animals and the exposed skin became sensitive to touch. All animals in the low and high dose groups had a decrease in terminal total leukocyte count. However, the values were within normal limits for rabbits and were not considered treatment related by the study authors.
LOAEL > 2280 mg/kg-bw/day
NOAEL = 2280 mg/kg-bw/day (highest dose tested)

Fatty acids, C_9-C_{13} neo (CAS No. 68938-07-8)
Male and female Sprague-Dawley rats (5/sex/dose) were administered the test substance at 0, 10, 55 and 300 mg/kg-bw/day daily by oral gavage for 28 days. No adverse treatment related effects on body weights, food consumption, hematological parameters or histopathology were observed. At the highest dose tested, increased salivation was

observed. In high dose males, kidney weights increased with abnormal organ appearance. Histologically, a dose-related hyaline-droplet formation was observed in males at all treatment levels. Although the kidney toxicity observed in male rats is suggestive of an alpha$_{2u}$-globulin[1]-mediated effect, one of the key events in this mode of action, alpha$_{2u}$-globulin accumulation has not been demonstrated. Therefore, a NOAEL for nephropathy in male rats was not established.[1]
LOAEL = 10 mg/kg-bw/day (based on nephropathy)
NOAEL = Not established

Reproductive Toxicity

Neodecanoic acid (CAS No. 26896-20-8)
In a three-generation reproductive toxicity study, male and female Sprague-Dawley rats were administered the test substance at 0, 100, 500 and 1500 ppm (approximately 0, 5, 25 and 75 mg/kg-bw/day, respectively) in the diet. No adverse effects were observed on survival, appearance, behavior, body-weight gain and food consumption in the parental, F1 or F2 generations. The reproductive performance of the parents was not affected. No treatment-related gross or microscopic pathological findings were observed at any of the dietary levels.
LOAEL (systemic/reproductive toxicity) >1500 ppm (~75 mg/kg-bw/day)
NOAEL (systemic/reproductive toxicity) = 1500 ppm (~75 mg/kg-bw/day) (highest dose tested)

Developmental Toxicity

Neodecanoic acid (CAS No. 26896-20-8)
In a three-generation reproductive toxicity study, male and female Sprague-Dawley rats were administered the test substance at 0, 100, 500 and 1500 ppm (approximately 0, 5, 25 and 75 mg/kg-bw/day, respectively) in the diet. No adverse effects were observed on survival, appearance, behavior, body weight gain and food consumption in parental, F1 or F2 generations. The F1 and F2 generation litter sizes, pup body weights, appearance and behavior were comparable between the treated groups and control group. According to the study authors, incidental findings (not specified) in F1 and F2 generations were not correlated to any treatment-related toxicity. At necropsy, there were no gross alterations that could be attributed to exposure to the test substance. No treatment-related abnormalities were observed.
LOAEL (maternal/developmental toxicity) > 1500 ppm (~75 mg/kg-bw/day)
NOAEL (maternal/developmental toxicity) = 1500 ppm (~75 mg/kg-bw/day) (highest dose tested)

Carboxylic acid, C_{6-8} neo (CAS No. 95823-36-2)
Pregnant female Sprague-Dawley rats were administered the test substance at 0, 50, 250, 600 and 800 mg/kg-bw/day by oral gavage on gestation days 6 – 15. The highest dose produced morbidity and mortality in 4 of the 22 females and caused lethargy, abnormal breathing, rales and staining around the muzzle and anogenital areas. Maternal body weight and uterine weight at term were significantly reduced (statistics not stated) reduced. A statistically significant (statistics not provided) incidence of rales was observed in animals exposed to 600 mg/kg-bw/day. There was also a statistically significant (*p* not stated) reduction in body weight gain during gestation day 6 – 9 and gestation day 0 – 20 in the 600 mg/kg-bw/day exposure group. Maternal food consumption was significantly (statistics not provided) reduced during gestation days 6 – 9 and 9 – 12 at 600 and 800 mg/kg-bw/day, respectively and also during gestation days 12 – 16 in the 800 mg/kg-bw/day group. There was a significant (statistics not provided) increase in the early embryonic absorptions at 800 mg/kg-bw/day with a corresponding decrease in the mean number of live fetuses. The remaining fetuses in the highest dose group had statistically significant (statistics not provided) reductions in fetal body weight and crown-rump distance. Microphthalmia (small eyes) and anophthalmia (an absence of eye(s)) were observed in 14% of the fetuses from the high dose group as well as fused cervical vertebrae and misaligned thoracic vertebra. Statistically significant (statistics not provided) incidences of

[1]The presence of nephropathy in association with the hyaline droplet accumulation in male rats suggests that the nephropathy in the males is occurring by an alpha$_{2u}$-globulin-mediated mechanism which is male rate-specific and not considered relevant to humans. EPA's Risk Assessment Forum has outlined the key events and the data that are necessary to demonstrate this mode of action (Alpha$_{2u}$-Globulin: Association with Chemically Induced Renal Toxicity and Neoplasia in the Rat, EPA/625/3-91/019F). One of the key events, alpha$_{2u}$-globulin accumulation, has not been demonstrated. Therefore, the nephropathy is assumed to be relevant to human health and it is concluded that a NOAEL for nephropathy in male rats was not established.

hydrocephalus and structural malformation of the thoracic ribs occurred in both the 600 and 800 mg/kg-bw/day dosed groups. There was also a statistically significant (statistics not provided) increase in the ratio of malformed fetuses/live fetuses in these groups. The increase in the ratio of implants affected at 250 mg/kg-bw/day was comparable to the control group. Other effects observed in the high dose group were a statistically significantly (statistics not provided) increased incidence of renal/ureter variation, unossified structures of the cranium, sternum, vertebrae, pelvis, and hindpaw, and incompletely ossified supraoccipital and cervical vertebrae in the 600 and 800 mg/kg-bw/day groups.
LOAEL (maternal toxicity) = 600 mg/kg-bw/day (based on decreased maternal body weight and uterine weight at term, increased incidence of rales)
NOAEL (maternal toxicity) = 250 mg/kg-bw/day
LOAEL (developmental toxicity) = 600 mg/kg-bw/day (based on incidence of malformations)
NOAEL (developmental toxicity) = 250 mg/kg-bw/day

Genetic Toxicity – Gene Mutation

In vitro
Propanoic acid, 2,2-dimethyl- (CAS No. 75-98-9)
In Ames assay, *Salmonella typhimurium* and *Escherichia coli* (strains not provided) were exposed to propanoic acid, 2,2-dimethyl- in the presence and absence of metabolic activation, up to 2,000 µg/plate. No increases in mutation frequency were reported at any concentration tested with or without metabolic activation. No information on controls was provided.
Propanoic acid, 2,2-dimethyl- was not mutagenic in this assay.

Neodecanoic acid (CAS No. 26896-20-8)
S. typhimurium strains TA100, TA1535, TA98 and TA1537 were exposed to neodecanoic acid, in the presence and absence of metabolic activation, up to 1,500 µg/plate. No increases in mutation frequency were reported at any concentration tested with or without metabolic activation. Positive controls gave the expected increase in the number of revertants.
Neodecanoic acid was not mutagenic in this assay.

Fatty acids, C_9-C_{13} neo (CAS No. 68938-07-8)
In an Ames assay *S. typhimurium* and *Escherichia coli* (TA1535, TA1537, TA98, TA100 and WP2uvrApKM101) were exposed to fatty acids, C9-C13 neo in the presence and absence of metabolic activation, up to 5,000 µg/plate. The solubility of the test substance was limited in the 2,000 to 5,000 µg/plate range. No evidence of cytotoxicity was observed and the control substance elicited the required response. No increases in mutation frequency were reported at any concentration tested with or without metabolic activation.
Fatty acids, C9-C13 neo was not mutagenic in this assay.

Genetic Toxicity – Chromosomal Aberrations

In vitro
Propanoic acid, 2,2-dimethyl- (CAS No. 75-98-9)
Cultured rat hepatocytes were exposed to using propanoic acid, 2,2-dimethyl- with and without metabolic activation, at concentrations ranging from 125 to 500 µg/mL. No information on the positive control was provided. The test substance did not induced chromosomal aberrations in cells exposed with or without metabolic activation.
Propanoic acid, 2,2-dimethyl- did not induce chromosomal aberrations in this assay.

Neodecanoic acid (CAS No. 26896-20-8)
Human lymphocytes were exposed to neodecanoic acid *in vitro*, with and without metabolic activation, at concentrations ranging from 100 to 800 µg/mL. Appropriate responses were seen for negative and positive controls. The test substance did not induce chromosomal aberrations in cells exposed with or without metabolic activation.
Neodecanoic acid did not induce chromosomal aberrations in this assay.

Fatty acids, C_9-C_{13} neo (CAS No. 68938-07-8)
Chinese Hamster Ovary (CHO) cells were exposed to fatty acids, C_9-C_{13} neo in an *in vitro* assay, with and without metabolic activation, at concentrations ranging from 13.67 to 1000 µg/mL. Appropriate responses were seen for

negative and positive controls. The test substance did not induce chromosome aberrations in cells exposed without metabolic activation up to cytotoxic concentrations (concentration not stated). However, with metabolic activation, chromosomal aberrations were observed at concentrations > 400 µg/mL.
Fatty acids, C_9-C_{13} neo did not induce chromosomal aberrations without metabolic activation in the absence of cytotoxicity and did induce chromosomal aberrations with metabolic activation.

In vivo
Fatty acids, C_9-C_{13} neo (CAS No. 68938-07-8)
In an *in vivo* micronucleus assay Swiss mice (Charles River CD-1) (10/sex/dose) were exposed to fatty acids, C_9-C_{13} neo at a single dose of 2,000 mg/kg-bw (limit dose). No differences were observed in the ratio of micronucleated polychromatic erythrocytes (MPE) to 1000 polychromatic erythrocytes (PE) and the ratio of PE per 1000 to associated mature erythrocytes. The test substance did not induce cytogenetic damage to the bone marrow of Swiss mice under these conditions.
Fatty acids, C9-C13 neo was not mutagenic in this assay..

Other Information

Skin Irritation

Propanoic acid, 2,2-dimethyl- (CAS No. 75-98-9)
Skin irritation studies in rabbits indicate that this compound is a moderate skin irritant.

Carboxylic acid, C_{6-8} neo (CAS No. 95823-36-2)
Skin irritation studies in rabbits indicate that this compound is a moderate skin irritant.

Neodecanoic acid (CAS No. 26896-20-8)
Skin irritation studies in rabbits indicate that this compound is a moderate skin irritant.

Eye Irritation

Propanoic acid, 2,2-dimethyl- (CAS No. 75-98-9)
Eye irritation studies in rabbits indicate that this compound is a moderate eye irritant.

Carboxylic acid, C_{6-8} neo (CAS No. 95823-36-2)
Eye irritation studies in rabbits indicate that this compound is a moderate eye irritant.

Neodecanoic acid (CAS No. 26896-20-8)
Eye irritation studies in rabbits indicate that this compound is a moderate eye irritant.

Sensitization

Propanoic acid, 2,2-dimethyl- (CAS No. 75-98-9)
Sensitization studies with guinea pigs indicate that this compound is not a sensitizer.

Fatty acids, C_9-C_{28} neo (CAS No. 72480-45-6)
Sensitization studies with guinea pigs indicate that this compound is not a sensitizer.

Conclusion: The acute oral toxicity for the members of this category is low to moderate. The category members are considered irritating to the skin and eye but are not sensitizers. Repeated oral exposure to propanoic acid, 2,2-dimethyl- and fatty acids, C_9-C_{13} neo resulted in the following clinical observations: head shaking, sneezing, nasal discharge and increased salivation at high doses. These responses are considered to be related to the irritating nature of the chemicals. Repeated dermal exposure to propanoic acid, 2,2-dimethyl-, carboxylic acid, C_6-C_8 neo and neodecanoic acid resulted in erythema, atonia and desquamation. No treatment-related systemic effects were observed at the doses tested. Repeated exposure to fatty acids, C_9-C_{13} neo resulted in nephropathy associated with hyaline-droplet formation in male rats only. Although the kidney toxicity observed in male rats is suggestive of an

alpha$_{2u}$-globulin-mediated effect[1], one of the key events in this mode of action, alpha$_{2u}$-globulin accumulation has not been demonstrated. Therefore, a NOAEL for nephropathy in male rats was not established. A three-generation reproductive toxicity study with neodecanoic acid indicated no treatment-related effects on reproductive parameters and showed no developmental effects. However, maternal toxicity was evident by decreased food intake and increased incidence of rales when exposed to carboxylic acid, C_6-C_8 neo. Developmental effects with this chemical were microphthalmia (small eyes), anophthalmia (eye(s) did not form during development), fused cervical vertebrae and misaligned thoracic vertebrae, hydrocephalus, varying unossified structures, reduced fetal body weight, and mortality. The category members, propanoic acid, 2,2-dimethyl-, neodecanoic acid and fatty acids, C_9-C_{13} neo did not show mutagenic potential when tested in *Salmonella typhimurium.* No chromosomal aberrations were observed in cells tested with propanoic acid, 2,2-dimethyl-, neodecanoic acid and fatty acids, C_9-C_{13} neo, with or without metabolic activation. However, fatty acids, C_9-C_{13} neo induced chromosomal aberrations *in vitro* when tested with metabolic activation. Fatty acids, C_9-C_{13} neo did not induce cytogenetic damage when tested *in vivo* in a mouse micronucleus assay.

The potential health hazard of the neoacids C_5 to C_{28} category is moderate based on the limited data available for repeated-dose and reproductive toxicity and the findings in the developmental studies.

[1] The presence of nephropathy in association with the hyaline droplet accumulation in male rats suggests that the nephropathy in the males is occurring by an alpha$_{2u}$-globulin-mediated mechanism which is male rate-specific and not considered relevant to humans. EPA's Risk Assessment Forum has outlined the key events and the data that are necessary to demonstrate this mode of action (Alpha$_{2u}$-Globulin: Association with Chemically Induced Renal Toxicity and Neoplasia in the Rat, EPA/625/3-91/019F). One of the key events, alpha$_{2u}$-globulin accumulation, has not been demonstrated. Therefore, the nephropathy is assumed to be relevant to human health and it is concluded that a NOAEL for nephropathy in male rats was not established.

Table 3. Summary of Human Health Data

Endpoints	Propanoic acid, 2,2-dimethyl- (75-98-9)	Propanoic acid, 2,2-dimethyl-methyl ester (598-98-1)	Carboxylic acid, C_{6-8} neo (95823-36-2)	Neodecanoic acid (26896-20-8)	Fatty acids, C_9-C_{13} neo (68938-07-8)	Fatty acids, C_9-C_{28} neo (72480-45-6)
Acute Oral Toxicity LD_{50} (mg/kg-bw)	**2000**	No Data 2000 (RA)	**1860**	**2000**	No Data 2000 (RA)	No Data 2000 (RA)
Acute Dermal Toxicity LD_{50} (mg/kg-bw)	**> 3160**	No Data 3160 (RA)	**> 3160**	**> 3160**	No Data > 3160 (RA)	No Data > 3160 (RA)
Acute Inhalation Toxicity LC_{50} (mg/L/6h/day)	**> 4.0**	No Data > 4.0 (RA)	No Data > 0.511 – > 3.0 (RA)	**> 0.511 – > 3.0**	No Data > 0.511 – > 3.0 (RA)	No Data > 0.511 – > 3.0 (RA)
Repeated-Dose Toxicity NOAEL/LOAEL (mg/kg-bw/day)	**NOAEL = 300 LOAEL > 300 (28-d)**	No Data NOAEL = 300 LOAEL > 300 (RA)	No Data[1] NOAEL =~75 LOAEL > ~75 (Repro.) (RA)	**NOAEL =~75 LOAEL > ~75 (Repro.)**	**NOAEL = Not established LOAEL = 10 (28-d)**	No Data NOAEL = Not established LOAEL = 10 (28-d) (RA)
Reproductive Toxicity NOAEL/LOAEL (mg/kg-bw/day) NOAEL/LOAEL)	No Data	No Data	No Data NOAEL = ~75 LOAEL > ~75 (RA)	**NOAEL = ~75 LOAEL > ~75**	No Data	No Data
Developmental Toxicity NOAEL/LOAEL (mg/kg-bw/day) (maternal toxicity) (developmental toxicity)	No Data	No Data	**NOAEL = 250 LOAEL = 600 NOAEL = 250 LOAEL = 600**	**NOAEL = ~75 LOAEL > ~75 NOAEL = ~75 LOAEL > ~75**	No Data	No Data
Genetic Toxicity – Gene Mutation *In vitro*	**Negative**	No Data Negative (RA)	No Data Negative (RA)	**Negative**	**Negative**	No Data Negative (RA)
Genetic Toxicity – Chromosomal Aberrations *In vitro*	**Negative**	No Data Negative (RA)	No Data Negative (RA)	**Negative**	**Negative w/o metabolic activation; Positive w/ metabolic activation**	No Data Negative w/o metabolic activation; Positive w/ metabolic activation (RA)
Genetic Toxicity – Chromosomal Aberrations *In vivo*	–	–	–	–	**Negative**	–
Irritation (skin)	**Moderate**	No Data Moderate (RA)	**Moderate**	**Moderate**	No Data Moderate (RA)	No Data Moderate (RA)
Irritation (eye)		No Data			No Data	No Data

Table 3. Summary of Human Health Data						
Endpoints	**Propanoic acid, 2,2-dimethyl- (75-98-9)**	**Propanoic acid, 2,2-dimethyl-methyl ester (598-98-1)**	**Carboxylic acid, C_{6-8} neo (95823-36-2)**	**Neodecanoic acid (26896-20-8)**	**Fatty acids, C_9-C_{13} neo (68938-07-8)**	**Fatty acids, C_9-C_{28} neo (72480-45-6)**
	Moderate	Moderate (RA)	**Moderate**	**Moderate**	Moderate (RA)	Moderate (RA)
Sensitization	**Negative**	No Data Negative (RA)	No Data Negative (RA)	No Data Negative (RA)	**Negative**	No Data Negative (RA)

Measured data in bold text; (RA) = Read Across; [1]Data available only for 2-week study.

4. Hazard Characterization

The short carbon-chain category members have low log K_{ow} values, indicating that their potential to bioaccumulate is expected to be low. Log K_{ow} ranges that include values greater than 4 for category members that may contain longer carbon chains (e.g., fatty acids, C_9-C_{13} neo and fatty acids, C_9-C_{28} neo) indicate that the potential for these category members to bioaccumulate may be high, depending on the composition of the mixture. Members of this category are not readily biodegradable, indicating that they have the potential to persist in the environment.

The evaluation of available aquatic toxicity data generated for fish, aquatic invertebrates and aquatic plants indicates that the potential acute hazard of the neoacids C_5-C_{28} category members to aquatic organisms is low.

The acute oral toxicity for the members of this category is low to moderate. The category members are considered irritating to the skin and eye but are not sensitizers. Repeated oral exposure to propanoic acid, 2,2-dimethyl- and fatty acids, C_9-C_{13} neo resulted in the following clinical observations: head shaking, sneezing, nasal discharge and increased salivation at high doses. These responses are considered to be related to the irritating nature of the chemicals. Repeated dermal exposure to propanoic acid, 2,2-dimethyl-, carboxylic acid, C_6-C_8 neo and neodecanoic acid resulted in erythema, atonia and desquamation. No treatment-related systemic effects were observed at the doses tested. Repeated exposure to fatty acids, C_9-C_{13} neo resulted in nephropathy associated with hyaline-droplet formation in male rats only. Although the kidney toxicity observed in male rats is suggestive of an alpha$_{2u}$-globulin-mediated effect[1], one of the key events in this mode of action, alpha$_{2u}$-globulin accumulation has not been demonstrated. Therefore, a NOAEL for nephropathy in male rats was not established. A three-generation reproductive toxicity study with neodecanoic acid indicated no treatment-related effects on reproductive parameters and showed no developmental effects. However, maternal toxicity was evident by decreased food intake and increased incidence of rales when exposed to carboxylic acid, C_6-C_8 neo. Developmental effects with this chemical were microphthalmia (small eyes), anophthalmia (eye(s) did not form during development), fused cervical vertebrae and misaligned thoracic vertebrae, hydrocephalus, varying unossified structures, reduced fetal body weight, and mortality. The category members, propanoic acid, 2,2-dimethyl-, neodecanoic acid and fatty acids, C_9-C_{13} neo did not show mutagenic potential when tested in *Salmonella typhimurium.* No chromosomal aberrations were observed in cells tested with propanoic acid, 2,2-dimethyl-, neodecanoic acid and fatty acids, C_9-C_{13} neo, with or without metabolic activation. However, fatty acids, C_9-C_{13} neo induced chromosomal aberrations *in vitro* when tested with metabolic activation. Fatty acids, C_9-C_{13} neo did not induce cytogenetic damage when tested *in vivo* in a mouse micronucleus assay.

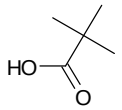
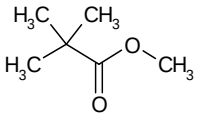
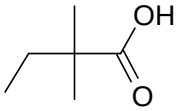
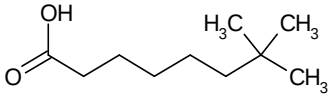
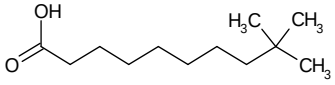
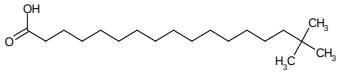
[1] The presence of nephropathy in association with the hyaline droplet accumulation in male rats suggests that the nephropathy in the males is occurring by an alpha$_{2u}$-globulin-mediated mechanism which is male rate-specific and not considered relevant to humans. EPA's Risk Assessment Forum has outlined the key events and the data that are necessary to demonstrate this mode of action (Alpha$_{2u}$-Globulin: Association with Chemically Induced Renal Toxicity and Neoplasia in the Rat, EPA/625/3-91/019F). One of the key events, alpha$_{2u}$-globulin accumulation, has not been demonstrated. Therefore, the nephropathy is assumed to be relevant to human health and it is concluded that a NOAEL for nephropathy in male rats was not established.

The potential health hazard of the neoacids C_5 to C_{28} category is moderate based on the limited data available for repeated-dose and reproductive toxicity and the findings in the developmental studies.

5. Data Gaps

Available data for neodecanoic acid cannot be used as read-across for the propanoic acid and fatty acid moieties of the category. Therefore, data gaps exist for the reproduction and developmental toxicity endpoints for the propanoic acid and fatty acid moieties of the category.

APPENDIX

Neoacids C_5 to C_{28}		
CAS No.	**Chemical Name**	**Structure**
SPONSORED CHEMICALS		
75-98-9	**Propanoic acid, 2,2-dimethyl-**	 CH_3-$C(CH_3)_2$-COOH (representative structure; may contain a variety of methyl branching patterns)
598-98-1	**Propanoic acid, 2,2-dimethyl-methyl ester**	 CH_3-$C(CH_3)_2$-COOH (representative structure; may contain a variety of methyl branching patterns)
95823-36-2	**Carboxylic acid, C_{6-8} neo**	 CH_3-CH2-$C(CH_3)_2$-COOH (representative structure is a C6 acid; may contain various branching patterns)
26896-20-8	**Neodecanoic acid**	 CH_3-$(CH_2)_4$-$C(CH_2$-$CH_3)$-CH_2-COOH (representative structure is a C10 acid; may contain various branching patterns)
68938-07-8	**Fatty acids, C_9-C_{13} neo**	 (representative structure is a C12 acid; may contain various branching patterns) C_9: CH_3-$C(CH_3)_2$-CH_2-$C(CH_3)_2$-COOH - C_{13}: CH_3-$C(CH_3)_2$-CH_2-$C((CH_2)_2$-$C(CH_3)_2)(CH_3)$-COOH
72480-45-6	**Fatty acids, C_9-C_{28} neo**	 (representative structure is a C19 acid; may contain various branching patterns) C_9: CH_3-$C(CH_3)_2$-CH_2-$C(CH_3)_2$-COOH - C_{28}:CH_3-$(CH_2$-$C(CH_3)$-$CH_2)_4$-CH_2-$C(CH_3)((CH_2)_6)$-$CH_3)$-COOH