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HIGH PRODUCTION VOLUME (HPV) CHEMICAL CHALLENGE PROGRAM

2-CYCLOHEXENE-1-OCTANOIC ACID, 5 (OR 6)-CARBOXY-4-HEXYL

CAS NO 53980-88-4

Submitted to the US EPA

by

MeadWestvaco Corporation

Table of Contents

2-cyclohexene-1-octanoic acid, 5 (or 6)-carboxy-4-hexyl

Information on 2-cyclohexene-1-octanoic acid, 5 (or 6)-carboxy-4-hexyl

Summary

MeadWestvaco Corporation is sponsoring 2-cyclohexene-1-octanoic acid, 5 (or 6)-carboxy-4-hexyl under the HPV Chemical Challenge Program.

This sponsored substance is a branched, C-21 dicarboxylic acid composed of saturated alkyl chains and a cyclohexene branch. The substance is supplied commercially as Westvaco DIACID® 1550. This is a class 2 product containing several components, being a mixture of about 60-70% of the C-21 diacid, 20-25% unreacted C-18 monoacid and 5-10% C-36 dimer acid.

In general, studies have been carried out using Westvaco DIACID® 1550. In some cases it is desirable to maximize the concentration of test substance dissolved in water and so the potassium salt has been used, as the commercial product Westvaco DIACID® H-240.

Westvaco DIACID® 1550 is manufactured by a patented process from tall oil fatty acids, which are obtained by the fractional distillation of crude tall oil, a by-product from the pulping of pine trees. Tall oil fatty acids and some other similar substances have been sponsored under the HPV chemical challenge program by the Pine Chemicals Association HPV task force (PCA), of which MeadWestvaco Corporation is a member.

Although there are some similarities between 2-cyclohexene-1-octanoic acid, 5 (or 6)-carboxy-4-hexyl and the chemicals sponsored by the PCA, there are also differences. Hence, data on tall oil fatty acids and other substances cannot be read across to meet SIDS endpoints for 2-cyclohexene-1-octanoic acid, 5 (or 6)-carboxy-4-hexyl. However, these data have been used as supporting information to gain a broader view of the properties of 2-cyclohexene-1-octanoic acid, 5 (or 6)-carboxy-4-hexyl in cases where specific data on 2-cyclohexene-1-octanoic acid, 5 (or 6)-carboxy-4-hexyl are not available.

Physicochemical properties

The **melting point** has not been determined because the substance is a liquid. Also, as a class 2 substance, it is unlikely to give a sharp freezing point.

The **boiling point** cannot be determined because the substance will decompose, possibly explosively, before it boils.

The **vapor pressure** is negligible under ambient conditions and has not been determined.

The log of the **octanol water partition coefficient** is estimated as 7.1.

The **water solubility** of Westvaco DIACID® 1550 has been assessed and both major components are only slightly soluble in water.

Environmental Fate

Adequate **biodegradation** data are available and these indicate that Westvaco DIACID® 1550 is substantially biodegradable in the environment.

Hydrolysis has not been determined because the substance has a very low solubility in water and lacks a functional group that would be susceptible to hydrolysis.

Determination of **photodegradation** is not relevant since the vapor pressure of the substance is essentially zero and it will not enter the atmosphere.

Transport and distribution between environmental compartments has not been determined due to the inability to provide usable inputs for the required modelling.

Ecotoxicity

The potassium salt has been used in tests to determine the **acute toxicity to fish, daphnia and algae.** The approximate 96 hour (48 hours for *Daphnia*) No Observed Effect Concentrations were 9.8 mg/l, 9.8 mg/l and 32 mg/l respectively.

Human health Effects (Mammalian) Toxicity

Adequate data are available for all SIDS endpoints for human health effects.

Westvaco DIACID® 1550 has a low **acute oral toxicity**, the LD_{50} to Sprague-Dawley rats, being >6000 mg/kg bw.

A combined test for **subchronic toxicity, toxicity to reproduction** and **developmental toxicity** has shown no reproductive, developmental or neurotoxic effects at a concentration of 15000 mg/kg bw/day. A NOEL for subchronic toxicity cannot be established as some effects on clinical chemistry, of unknown biological significance, were observed at the lowest dose level of 500 mg/kg bw/day.

Tests with Westvaco DIACID® 1550 have shown no evidence for **genotoxicity** in both **bacterial** and **non-bacterial** systems.

I Description of 2-cyclohexene-1-octanoic acid, 5 (or 6)-carboxy-4-hexyl

A 2-cyclohexene-1-octanoic acid, 5 (or 6)-carboxy-4-hexyl

The compound 2-cyclohexene-1-octanoic acid, 5 (or 6)-carboxy-4-hexyl (CAS Registry Number 53980-88-4) is being sponsored by MeadWestvaco Corporation under the US EPA HPV chemical challenge program. This substance is a branched, C-21 dicarboxylic acid composed of saturated alkyl chains and a cyclohexene branch. The substance is supplied commercially as Westvaco DIACID® 1550. This is a class 2 product containing several components, being a mixture of about 60-70% of the C-21 diacid, 20-25% unreacted C-18 monoacid and 5-10% C-36 dimer acid.

Westvaco DIACID® 1550 is manufactured by a patented process from tall oil fatty acids, which are obtained by the fractional distillation of crude tall oil, a by-product from the pulping of pine trees. Westvaco DIACID® 1550 is used as a surfactant in a wide range of applications. It also provides lubrication and corrosion protection in metalworking applications and acts as a hydrotrope for nonionic surfactants in alkaline cleaner formulations.

B Related Compounds

There are several related materials that should be considered, as data on the properties of these substances may potentially be read across to meet data requirements for 2-cyclohexene-1-octanoic acid, 5 (or 6)-carboxy-4-hexyl. These related substances have been sponsored under the HPV chemical challenge program by the Pine Chemicals Association HPV task force (PCA), of which MeadWestvaco Corporation is a member.

The first set of related compounds comprises six substances forming the "Tall Oil Fatty Acids and Related Substances" group. Tall oil fatty acids (CAS Registry Number 61790-12-3) are of obvious relevance since they are the precursor of 2-cyclohexene-1-octanoic acid, 5 (or 6)-carboxy-4-hexyl and are present in the Westvaco DIACID® 1550 product. Tall oil fatty acids are also the dominant member of the "Tall Oil Fatty Acids and Related Substances" group, being the substance with by far the greatest production volume of the substances in this group. Tall oil fatty acids typically contain a combined total of about 80% of oleic and linoleic acids. These are unsubstituted, linear, C-18, mono- or di- unsaturated monocarboxylic acids.

Also of some relevance in the "Tall Oil Fatty Acids and Related Substances" group are fatty acids, C-16 to C-18 and C-18 unsaturated, branched and linear (CAS Registry Number 68955-98-6), also known as monomer acid. This substance is a complex mixture. It typically contains about 36% oleic and elaidic acids, which are *cis* and *trans* forms of unsubstituted, linear C-18 monounsaturated monocarboxylic acids. Fatty acids, C-16 to C-18 and C-18 unsaturated, branched and linear also typically contain 28% of other branched C-18 acids and 24% of other C-18 acids, probably cyclic acids of unknown structure. Fatty acids, C-16 to C-18 and C-18 unsaturated, branched and linear have

similarities to tall oil fatty acids but contain a much lower level of unsaturation and also contain some branched and cyclic chains. Because of this, fatty acids, C-16 to C-18 and C-18 unsaturated, branched and linear share some characteristics with 2-cyclohexene-1-octanoic acid, 5 (or 6)-carboxy-4-hexyl. There are however differences in the numbers of carbon atoms and carboxylic acid groups in the molecules.

The original test plan for the "Tall Oil Fatty Acids and Related Substances" group was posted on the HPV web site on 14th June 2001 and the PCA responded to all comments with a revised test plan on 5th March 2002. The final submission containing the robust study summaries of all data was posted on the EPA web site on 20th September 2004.

This revised test plan for the "Tall Oil Fatty Acids and Related Substances" group provides data on the water solubility, partition coefficient and biodegradability of all six members. However, toxicological testing was only carried out on tall oil fatty acids. The toxicological properties of the other group members were read across from this substance.

The other group of chemicals sponsored by the PCA that is of interest is the "Fatty Acid Dimers and Trimer" group. The dimer is manufactured from C-18 unsaturated fatty acids and consists of many geometric isomers of C-36 dicarboxylic acids with a low level of unsaturation. The compounds may be acyclic, cyclic, aromatic or polycyclic. Apart from the presence of C-36 dimer in Westvaco DIACID® 1550, the relevance of dimer is that it is also composed of branched dicarboxylic acids, although they have a much higher molecular weight than 2-cyclohexene-1-octanoic acid, 5 (or 6)-carboxy-4-hexyl and a wide range of isomeric structures.

The proposed test plan for this category was posted on the HPV web site on 4th April 2002, and following the receipt of comments, a revised test plan was posted on the EPA HPV web site on 10th November 2002. Dimer is the primary substance in this group, which has three other members. It is proposed that water solubility, partition coefficient and biodegradation data will be developed for these other three members but that toxicological data will be read across from that for dimer.

C Use of Data on Related Compounds

Taken together, these related substances (tall oil fatty acids, dimer and fatty acids, C-16 to C-18 and C-18 unsaturated, branched and linear) share some characteristics with 2-cyclohexene-1-octanoic acid, 5 (or 6)-carboxy-4-hexyl. They are all long chain alkyl carboxylic acids with various degrees of branching and unsaturation. The major feature that distinguishes 2-cyclohexene-1-octanoic acid, 5 (or 6)-carboxy-4-hexyl from all the related compounds is that it is a C-21 compound. Also, it is a diacid, a feature shared only with the dimer molecule.

Hence any proposed read across of data from these other substances to 2-cyclohexene-1-octanoic acid, 5 (or 6)-carboxy-4-hexyl needs to be supported by evidence of comparability. This additional information must show that other, relevant, properties of 2-cyclohexene-1-octanoic acid, 5 (or 6)-carboxy-4-hexyl are similar to those of the compounds from which data are being read across. This is an important consideration since in comments on the original test plan the EPA expressed reservations about the

reading across of data from tall oil fatty acids to fatty acids, C-16 to C-18 and C-18 unsaturated, branched and linear, even although these substances are within a single chemical category.

In view of these concerns regarding the read across of data and the differences and similarities between the molecules, it is considered that it is not possible to read data directly across from these related substances to 2-cyclohexene-1-octanoic acid, 5 (or 6)-carboxy-4-hexyl. However, the test plan for to 2-cyclohexene-1-octanoic acid, 5 (or 6)-carboxy-4-hexyl bears many similarities to the test plans for the related substances, reflecting the common features of all four substances.

D Choice of Test Substance

The sponsored chemical, 2-cyclohexene-1-octanoic acid, 5 (or 6)-carboxy-4-hexyl is not supplied and used as an isolated molecule but as the major constituent of a commercial product, Westvaco DIACID® 1550. Therefore, testing, in general, will be carried out using Westvaco DIACID® 1550 as the test substance as this is the substance used commercially.

However, 2-cyclohexene-1-octanoic acid, 5 (or 6)-carboxy-4-hexyl and Westvaco DIACID® 1550 have only low solubilities in water. For the evaluation of some properties, the test substance used was Westvaco DIACID® H-240. This is a 40% solution of the potassium salt of Westvaco DIACID® 1550 and maximizes the solubility of the test substance. A similar approach to provide greater solubility of the test substance has been adopted by the PCA in the revised test plan for the "Tall Oil Fatty Acids and Related Substances" group, with fatty acids, C-16 to C-18 and C-18 unsaturated, branched and linear being tested as the sodium salt.

II Review of Existing data and Development of Test Plan

A Overview

The data available on the SIDS endpoints of concern for 2-cyclohexene-1-octanoic acid, 5 (or 6)-carboxy-4-hexyl have been subject to a comprehensive review. Both the then-current state of knowledge and the reliability of the data were assessed, together with corresponding data and test plans for the related compounds. A test plan was subsequently drawn up so that all relevant SIDS endpoints may be addressed satisfactorily to meet the commitment of MeadWestvaco Corporation in sponsoring 2-cyclohexene-1-octanoic acid, 5 (or 6)-carboxy-4-hexyl under the EPA HPV Chemical Challenge Program.

The current availability of data for 2-cyclohexene-1-octanoic acid, 5 (or 6)-carboxy-4-hexyl (as Westvaco DIACID® 1550) is shown in Table 1. This table also shows the

corresponding data availability and plans from the PCA for tall oil fatty acids, dimer and fatty acids, C-16 to C-18 and C-18 unsaturated, branched and linear.

Table 1
Matrix of Available Adequate Data and Testing on 2-cyclohexene-1-octanoic acid, 5 (or 6)-carboxy-4-hexyl and Related Substances.

SIDS endpoint	Westvaco DIACID® 1550	Tall Oil Fatty Acids	Monomer Acid (b)	Dimer (revised plan)
melting point	not tested	not tested	not tested	not tested
boiling point	not tested	not tested	not tested	not tested
vapor pressure	not tested	not tested	not tested	not tested
water solubility	tested	tested	tested	test
partition coefficient	available	tested	available	test
biodegradation	available (a)	available	tested	available
hydrolysis	not tested	not tested	not tested	not tested
photodegradation	not tested	not tested	not tested	not tested
transport / distribution	not tested	not tested	not tested	not tested
toxicity to fish	available (a)	tested	tested	test
toxicity to *Daphnia*	available (a)	tested	tested	test
toxicity to algae	available (a)	tested	tested	test
acute toxicity	available	available	not tested	available
subchronic toxicity	tested(c)	available	not tested	available
mutagenicity – bacterial	available	available	not tested	available
mutagenicity – mammalian	available	available	not tested	available
toxicity to reproduction	tested (c)	available	not tested	test
developmental toxicity	tested (c)	available	not tested	test

(a) – test carried out on potassium salt, Westvaco DIACID® H-240
(b) – "monomer acid" is alternative name for "fatty acids, C-16 to C-18 and C-18 unsaturated, branched and linear"
(c) – combined test following OECD guideline 422

As may be seen, the test plan has resulted in data availability for 2-cyclohexene-1-octanoic acid, 5 (or 6)-carboxy-4-hexyl that is identical (except for some reading across of toxicological data within the tall oil fatty acids and related substances group) to that of the related substances (tall oil fatty acids, dimer and fatty acids, C-16 to C-18 and C-18 unsaturated, branched and linear) in the two test groups sponsored by the PCA.

B Evaluation of Physicochemical Data

The basic physicochemical data required in the SIDS battery are melting point, boiling point, vapor pressure, partition coefficient and water solubility.

Class 2 substances are composed of a complex mixture of molecules that are often difficult to characterize. Westvaco DIACID® 1550 is derived from natural sources of variable composition that cannot be represented by a definite chemical structure. Due to this complex composition some measurements of physical properties are likely to produce results that are erroneous, difficult to interpret or meaningless.

In principle, testing of physicochemical properties could be carried out on 2-cyclohexene-1-octanoic acid, 5-carboxy-4-hexyl or 2-cyclohexene-1-octanoic acid, 6-carboxy-4-hexyl, if these compounds were isolated from the Westvaco DIACID® 1550 product. However, such information would be of little practical use in evaluating the properties of 2-cyclohexene-1-octanoic acid, 5 (or 6)-carboxy-4-hexyl under the HPV Chemical Challenge Program. Isolation and testing using 2-cyclohexene-1-octanoic acid, 5 (or 6)-carboxy-4-hexyl will therefore not be carried out within the test programme.

B1 Melting Point

Westvaco DIACID® 1550 is a liquid under normal conditions and determination of the melting point is not applicable. While consideration can be given to measurement of a freezing point, this is not likely to provide any useful information since Westvaco DIACID® 1550 is a complex mixture. It is therefore likely not to provide a defined freezing point but to display freezing behavior over a range of temperatures. Therefore, determination of the melting point has not been attempted.

B2 Boiling Point

Westvaco DIACID® 1550 is a non-volatile liquid at ambient temperatures and will decompose if heated to high temperatures. According to the material safety data sheet, the boiling point is in excess of 260°C, while the flash point is 235°C. Explosive mixtures may be formed at temperatures at, above, or, in some circumstances, below the flash point. Hence the boiling point has not been determined as such measurements serve no value within the HPV Chemical Challenge Program, while performing the required experiment could have been potentially dangerous.

B3 Vapor Pressure

The vapor pressure of Westvaco DIACID® 1550 at ambient temperatures is effectively zero, and experimental measurement is inappropriate.

B4 Water Solubility

The solubility in water of Westvaco DIACID® 1550 has been determined following OECD guideline 105. The C-21 diacid and the C-18 monoacid were tested individually. Both were found to be slightly soluble. Similar results are reported by the PCA for substances tested in the tall oil fatty acids and related substances category.

B5 Octanol – Water Partition Coefficient

Testing has been performed to generate adequate data showing that the log K_{ow} for Westvaco DIACID® 1550 at pH 2 is approximately 7.09, this being the mean of two peaks observed under the experimental conditions. No further testing to ascertain the partition coefficient has been undertaken, although the report notes that the values obtained are outside the specified range (0 to 6) for the method used. Multiple values for the partition coefficient would be expected since the substance is a mixture of several compounds. This value for Westvaco DIACID® 1550 is similar to that reported by the PCA for tall oil fatty acids.

C Evaluation of Environmental Data

The fate and behavior of a chemical in the environment is determined by the rates of the most important transformation (degradation) processes. The basic environmental fate data covered by the HPV Chemical Challenge Program include biodegradation, stability in water (hydrolysis as a function of pH), photodegradation and transport and distribution between environmental compartments.

C1 Biodegradation

Data and robust study summaries are available. Because of the low solubility in water of Westvaco DIACID® 1550, the tests were carried out using the potassium salt, Westvaco DIACID® H-240. When tested for ready aerobic biodegradability following OECD guideline 301E the material was found not to be readily biodegradable, showing 63% degradation after 35 days. However, when tested for biodegradation using anaerobic sludge as specified in EPA OTS method 40 CFR 796.3140 (now EPA OPPTS harmonized guideline 835.3400), biodegradation of up to 84% was observed within 56 days. This method is used for screening for the anaerobic biodegradability of organic compounds. A high biodegradability result in this test provides evidence that the test substance will be biodegradable in sewage treatment plant anaerobic digestors and in many natural anaerobic environments such as swamps, flooded soils, and surface water sediments.

Westvaco DIACID® H-240 contains not only the potassium salts of 2-cyclohexene-1-octanoic acid, 5 (or 6)-carboxy-4-hexyl but also the salts of the unreacted C-18 monoacid and C-36 dimer acid. Information on the biodegradability of the C-18 monoacid and its potassium salt and C-36 dimer acid has been previously submitted by the PCA under the HPV Chemical Challenge Program. The available information shows that the C-18 monoacid and its salt typically demonstrate 56 to 84% biodegradability over 28 days whereas the dimer acid demonstrated only around 6.5 % biodegradability over the same period. While the various results cannot be directly compared because of the differences in test methods and conditions, it nevertheless appears that the biodegradability of Westvaco DIACID® H-240 is similar to that of the C-18 monoacid and much greater than that of the C-36 dimer acid. This suggests that although 2-cyclohexene-1-octanoic acid, 5 (or 6)-carboxy-4-hexyl may not meet the criterion of being readily biodegradable, it nevertheless does exhibit a significant degree of biodegradability.

On this basis, the available data are considered adequate and no further testing is justified.

C2 Hydrolysis

Hydrolysis as a function of pH is a measure of the stability of a substance in water. Westvaco DIACID® 1550 does not contain any organic functional groups susceptible to hydrolysis. In addition, low solubility in water often limits the ability to determine hydrolysis and Westvaco DIACID® 1550 has a very low solubility in water. Therefore, this test material is expected to be stable in water and testing of hydrolytic stability as a function of pH has not been assessed experimentally.

C3 Photodegradation

No information is available on the photodegradation of Westvaco DIACID® 1550. However, since the substance is not volatile, it will not enter the atmosphere and be subject to photodegradation. Additionally, the chemical structures suggest that the molecules would not be susceptible to breakdown by a photodegradative mechanism. For these reasons, experimental testing for photodegradation is not considered applicable.

C4 Transport and Distribution

Transport and distribution between environmental compartments is intended to determine the ability of a chemical to move and partition in the environment. Such information is generated from models such as the level III model from the Canadian Environment Modelling Centre at Trent University. Use of these models requires the input of a range of parameters. For class 2 substances the required inputs are often not available or impossible to determine. Use of the model would not only require the input of multiple parameters but also potentially present multiple outputs for individual constituents of the product. These would not form a reasonable representation of the environmental distribution of the product. For these reasons, even although no information is available on the environmental transport and distribution of Westvaco DIACID® 1550, no work to assess the environmental transport and distribution of this substance has been performed.

D Evaluation of Ecotoxicity Data

The basic ecotoxicity data that are part of the HPV Chemical Challenge Program are acute toxicity to fish, daphnia and algae. Because of the low solubility in water of Westvaco DIACID® 1550, these tests were carried out using the potassium salt, Westvaco DIACID® H-240. This maximizes the concentration of test material to which the test organisms can be exposed while minimizing the potential for physical toxicity arising from the formation of features such as dispersions or critical micelles.

D1 Acute Toxicity to Fish

Testing has been performed and a robust test summary is available. The 96 hour LC_{50} to the fresh water minnow, *Pimephales promelas*, was found to be 15 mg/l. The No Observed Effect Concentration was 9.8 mg/l.

D2 Acute Toxicity to Daphnia

Testing has been performed and a robust test summary is available. The 48 hour LC_{50} to the water flea, *Daphnia pulex*, was found to be 22.5 mg/l. The No Observed Effect Concentration was 9.8 mg/l.

EPA guidance (*Federal Register,* Vol 65 No 248 page 81695) recommends that, for chemicals with a log K_{ow} value greater than 4.2, a test of chronic toxicity to *Daphnia* is carried out rather than tests of the acute toxicity of the material to *Daphnia* and fish. This is due to concerns about the potential for bioaccumulation of such test materials. However, the very high partition coefficient and the very low water solubility of Westvaco DIACID® 1550 together indicate that bioaccumulation is unlikely. Since data from acute tests are already available, it is considered that a 21-day test with *Daphnia* would produce no additional data of benefit, although considerable practical difficulties could arise in attempting to perform such a test.

D3 Acute Toxicity to algae

Testing has been performed and a robust test summary is available. The 96 hour EC_{50} to *Selenastrum capricornutum* was found to be 87.6 mg/l. The approximate No Observed Effect Concentration was 32 mg/l.

E Evaluation of Human Health Effects

The basic toxicity data required under the HPV Chemical Challenge Program are acute and repeated dose toxicity, bacterial and non-bacterial genotoxicity and developmental and reproductive toxicity.

E1 Acute Oral Toxicity

Testing has been performed with Westvaco DIACID® 1550 and a robust test summary is available. The LD_{50} to Sprague-Dawley rats, following a non-standard protocol, was found to be 6176 mg/kg bw. This study has a Klimish Reliability code of 2 – reliable with restrictions.

In other testing reported by the PCA, the acute oral toxicity of dimer, in three tests following the OECD 401 protocol, has been found be >5000 mg/kg bw for Wistar rats and >2000 mg/kg bw for Sprague-Dawley rats. The acute oral toxicity of tall oil fatty acids, also following the OECD 401 protocol, was >10000 mg/kg bw.

Although existing data on the acute oral toxicity of Westvaco DIACID® 1550 were generated using a non-standard protocol, all currently available test results indicate that

these long chain fatty acids have low acute oral toxicity. Therefore, no further testing of Westvaco DIACID® 1550 has been performed.

E2 Subchronic Toxicity

The PCA has reported that tall oil fatty acids have been tested for repeat dose toxicity in a 90 day study and found to have low toxicity, with a no observed effect level (NOEL) of approximately 2500 mg/kg bw/day. Dimer has been similarly tested and also found to be of low toxicity. Although a NOEL was not established, the tests revealed a no observed adverse effect level (NOAEL) of approximately 100 mg/kg bw/day.

The need to establish the subchronic toxicity of 2-cyclohexene-1-octanoic acid, 5 (or 6)-carboxy-4-hexyl was carefully considered. All available data for acute and subchronic toxicity of 2-cyclohexene-1-octanoic acid, 5 (or 6)-carboxy-4-hexyl, tall oil fatty acids and dimer indicated low toxicities. However, since subchronic toxicity is a basic data requirement within the HPV Chemical Challenge Program, the absence of data for this end-point, together with the limited reliability of the available acute toxicity data, represented a serious gap in knowledge and so the subchronic toxicity of Westvaco DIACID® 1550 has been determined experimentally. For the reasons described below in sections E5 and E6, a combined subchronic toxicity and reproductive / developmental toxicity screen test (OECD 422) of Westvaco DIACID® 1550 has been performed. The adoption of this combined test guideline to address the SIDS endpoints for subchronic toxicity, toxicity to reproduction and developmental toxicity is in accordance with EPA guidance (*Federal Register,* Vol 65 No 248 page 81695).

A robust study summary is available. The results of this test indicated changes in clinical chemistry parameters, of unknown biological significance, at the lowest dose level of 500 mg/kg bw/day and so a No Observed Effect Level cannot be established. No neurotoxicological effects were seen at the highest dose level of 15000 mg/kg bw/day.

E3 Bacterial Genotoxicity

Testing has been performed on Westvaco DIACID® 1550 and a robust test summary is available. The results show no evidence of mutagenicity against a range of bacteria in either the presence or absence of metabolic activation when tested at the limits of solubility and cytotoxicity.

E4 Non-bacterial Genotoxicity

Testing has been performed on Westvaco DIACID® 1550 and a robust test summary is available. The results show no significant increase in chromosomal aberrations in cultured Chinese hamster ovary cells in either the absence or presence of metabolic activation.

E5 Toxicity to Reproduction

The PCA has reported that tall oil fatty acids have been tested for reproductive toxicity in a procedure consistent with OECD method 415. Tall oil fatty acids have no effect upon reproductive capabilities at doses of approximately 5000 mg/kg bw/day. The PCA has also reported that the test for the subchronic toxicity of dimer included histopathology of

the reproductive organs and showed no evidence of toxicity to these organs at any dose level.

The toxicity to reproduction of 2-cyclohexene-1-octanoic acid, 5 (or 6)-carboxy-4-hexyl has been assessed, as described in sections E2 and E6, by a combined subchronic toxicity and reproductive / developmental toxicity screen test (OECD 422) of Westvaco DIACID® 1550. No effects on reproductive performance were observed at the highest dose level of 15000 mg/kg bw/day.

E6 Developmental Toxicity

The PCA has reported that tall oil fatty acids have been tested for developmental toxicity in a procedure consistent with OECD method 415. Tall oil fatty acids have no effect upon developmental capabilities at doses of approximately 5000 mg/kg bw/day.

The developmental toxicity of 2-cyclohexene-1-octanoic acid, 5 (or 6)-carboxy-4-hexyl has been assessed, as described in sections E2 and E5, by a combined subchronic toxicity and reproductive / developmental toxicity screen test (OECD 422) of Westvaco DIACID® 1550. No effects on development were observed at the highest dose level of 15000 mg/kg bw/day