AR201-13055

PINE CHEMICALS ASSOCIATION
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May 23, 2001

Administrator
US EPA
P.O. Box 1473
Merrifield, VA 22116

Re: HPV Test Plans and Robust Summaries for Tall Oil and Related Substances and Tall Oil Fatty Acids and Related Substances

Dear Ms Whitman;
On behalf of the member companies of the Pine Chemicals Association's High Production Volume Chemical Task Force, I am pleased to submit the Test Plans and Robust Summaries for the chemical categories designated as;

"Tall Oil and Related Substances"

"Tall Oil Fatty Acids and Related Substances"

The submission includes one electronic copy of each in pdf format, and a hard copy which will be mailed to EPA Headquarters. The registration number for our Consortium is

Should you have any questions concerning our submission please feel free to contact me at (770) 209-7534 or at wjones@tappi.org.

Sincerely,

Walter L. Jones
President & COO

MR 48236

HIGH PRODUCTION VOLUME (HPV) CHEMICAL CHALLENGE PROGRAM

TEST PLAN

for

TALL OIL FATTY ACIDS AND RELATED SUBSTANCES

CAS No. 61790-I 2-3
CAS No. 65997-03-7
CAS No. 68955-98-6
CAS No. 68201-37-6
CAS No. 61790-44-I
CAS No. 61790-45-2

Submitted to the US EPA

By

The Pine Chemicals Association, Inc.
HPV Task Force
Consortium Registration #

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Test Plan For Tall Oil Fatty Acids and Related Substances

Test Plan for Tall Oil Fatty Acids and Related Substances

Summary

The Pine Chemicals Association, Inc. (PCA) is sponsoring 36 HPV chemicals. This Test Plan addresses the following six chemicals, known collectively as Tall Oil Fatty Acids and Tall Oil Fatty Acid Salts:

61790-l 2-3, Fatty acids, tall-oil
65997-03-7, Fatty acids, tall-oil, low boiling
68955-98-6, Fatty acids, Cl 6-C18 and Cl 8 unsaturated, branched and linear
68201-37-6, Octadecanoic acid, branched and linear
61790-44-1, Fatty acids, tall oil, potassium salts
61790-45-2, Fatty acids, tall oil, sodium salts

These substances are all derived from or closely related to tall oil fatty acids, a substance obtained by the fractional distillation of crude tall oil, a by-product from the pulping of pine trees. Tall oil fatty acids and their derivatives are all complex mixtures (Class 2 substances) derived from a natural product. Each species of pine tree has a somewhat different mix of fatty acids, and even within a species, the mix of fatty acids could be influenced by the climate and local terrain.

While these are Class 2 substances, all the members of this group are similar in chemical composition, being predominantly Cl 8 unsaturated and saturated fatty acids, or their salts. Thus, PCA has elected to treat the group as a category for purposes of the HPV program. Where applicable, PCA will conduct physical/chemical property and environmental fate testing on all six substances. However, a representative of the category will be used for ecotoxicity and ***in vitro*** mammalian toxicity testing. Due to the existence of available data on a representative chemical that satisfy the SIDS human health endpoints, no animal testing will be conducted.

Tall oil fatty acids (CAS# 61790-12-3) ("TOFA") has been selected as the representative substance in this group for testing for the additional SIDS data. This selection is based upon several factors, including the fact that TOFA represents by far the greatest production volume, with almost four times more TOFA manufactured than all other substances in this group combined. In addition, TOFA is the raw material from which all the other group members, except fatty acids, tall oil, low boiling, are derived. Consequently, test results obtained on TOFA will be most representative of the category. TOFA and the other members of this group are used primarily as raw materials for the production of other chemicals. For example, the largest use of TOFA is in the production of dimer acids, which are converted into coatings, adhesives and printing inks. TOFA salts are widely used as surfactants in liquid soaps. Other members of the group are used as intermediates in the production of isostearic acid.

PCA has reviewed existing data on these compounds. Available data show that TOFA has low toxicity. It is non-toxic following acute oral exposure and a number of repeat dose studies also show low toxicity. TOFA is not mutagenic in the Ames test. A full two-generation reproductive/developmental toxicity study has been performed, and there were no treatment-related effects. Thus, because adequate data already exist for most of the SIDS endpoints, particularly those requiring the use of animals, no additional testing in animals will be necessary.

A brief summary of the available data for the substances in this category, and the anticipated additional testing, is described below and in Table 1.

Physical/Chemical Properties

Physical and chemical properties will be determined when appropriate; however, many of the physical and chemical properties are either inappropriate or cannot be measured for these compounds:

- The melting point will not be determined because these substances will either not give a sharp melting point when heated or will decompose before they melt.
- Boiling points cannot be determined because these substances will decompose before they boil.
- Under ambient conditions, the vapor pressure of these chemicals is essentially zero and experimental measurement is not possible.
- The partition coefficients will be tested for the four substances where this has not been determined. Partition coefficient testing can yield a range of values representing the various components, rather than a single value representing the mixture.
- The water solubility of all six of the compounds in this grouping category will be determined.

Environmental Fate

With respect to the SIDS environmental fate endpoints:

- Determination of photodegradation is not relevant, since the vapor pressure of these compounds is essentially zero and they could not enter the atmosphere.
- Hydrolysis in water will not be determined for any of the six compounds in this category because the members of this category have low water solubility and lack a functional group that would be susceptible to hydrolysis.
- Biodegradation data will be generated for two of the six compounds for which data are not already available.
- Transport and distribution between environmental compartments will not be determined due to the inability to provide usable inputs to the required model.

Ecotoxicity

- Existing ecotoxicitv data are not reliable due to inconsistencies in, or artificial methods of, sample preparation. Consequently, using TOFA, acute toxicity to fish, daphnia and algae will be retested under conditions that maximize solubility, but reduce exposure to insoluble fractions, which may cause nonspecific toxicological effects.

Mammalian Toxicity

- For the SIDS human health endpoints, there are sufficient data on acute and repeat dose toxicity, *in vitro* qenotoxicitv in *Salmonella* (i.e., Ames test), and reproductive and developmental effects for tall oil fatty acid. Consequently, no additional testing for these endpoints will be conducted so no animals will be used.
- Because the required SIDS battery calls for two tests for mutagenicity, tall oil fatty acid will be tested for genotoxicity in an *in vitro* mammalian chromosome aberration test (OECD 473) both with and without metabolic activation.

Table 1
Matrix of Available Adequate Data and Proposed Testing
On Tall Oil Fatty Acids and Tall Oil Fatty Acid Salts'

Chemical and CAS #	Reauired SIDS Endpoints										
	Partition Coef.	Water Sol.	Biodeg.	Acute Fish	Acute Daph.	Acute Algae	Acute oral	Repeat Dose	In vitro genetox (bact.)	In vitro genetox (non-bact)	Repro/ develop
61790-12-3, Fatty acids, tall-&l	Test	Test	Adeq.	Test	Test	Test	Adeq.	Adeq.	Adeq.	Test	Adeq./ Adeq.
65997-03-7, Fatty acids, tail-oil, low boiling	Adeq.	Test	Adeq.	C	C	C	C	C	C	C	C
68955-98-6, Fatty acids, Cl 6-C18 and Cl 8 unsat., branched & linear	Adeq.	Test	Adeq.	C	C	C	C	C	C	C	C
68201-37-6, Octadecanoic acid, branched and linear	Test	Test	Test	C	C	C	C	C	C	C	C
61790-44-I) Fatty acids, tall oil, potassium salts	Test	Test	Adeq.	C	C	C	C	C	C	C	C
61790-45-2, Fatty acids, tall oil, sodium salts	Test	Test	Test	C	C	C	C	C	C	C	C

Adeq. Indicates adequate existing **data**
Test Indicates proposed testing
C Indicates category read-down from existing or proposed test data on tall oil fatty acid.
*No testing will be conducted for melting point, boiling point, vapor pressure, hydrolysis, photodegradation, and transport and distribution between environmental compartments as explained in the test plan.

The Pine Chemicals Association, Inc. HPV Task Force includes the following companies:

Akzo Nobel Resins
Akzo Nobel - Eka Chemicals Incorporated
Arizona Chemical Company
Asphalt Emulsion Manufacturers Association
Boise Cascade Corporation
Cognis Corporation
Eastman Chemical Co. (including the former Hercules Inc. Resins Division)
Georgia-Pacific Resins Inc.
ICI Americas (including the former Uniqema)
Inland Paperboard & Packaging, Inc.
International Paper Co. (including the former Champion International Corporation)
Koch Materials Co.
McConnaughay Technologies, Inc.
Mead Corp.
Packaging Corporation of America
Plasmine Technology, Inc.
Raisio Chemicals
Rayonier
Riverwood International
Smut-fit – Stone Container Corporation
Westvaco
Weyerhaeuser Co.

The Task Force will be filing multiple test plans covering various chemicals. Not all members of the Task Force produce the substances covered by this test plan.

I. Description of Tall Oil Fatty Acids and Related Substances

The Pine Chemicals Association, Inc. (PCA) is sponsoring six HPV chemicals known collectively as Tall Oil Fatty Acids and Tall Oil Fatty Acid Salts. This group of chemicals consists of the following:

61790-I 2-3, Fatty acids, tall oil
65997-03-7, Fatty acids, tall oil, low boiling
68955-98-6, Fatty acids, Cl6 - Cl8 and Cl8 unsaturated, branched and linear
68201-37-6, Octadecanoic acid, branched and linear
61790-44-1, Fatty acids, tall oil, potassium salts
61790-45-2, Fatty acids, tall oil, sodium salts

This group of chemicals are all derived from or closely related to tall oil fatty acids (TOFA), a substance obtained by the fractional distillation of crude tall oil, a by-product from the pulping of pine trees. All the members of this group are similar in chemical composition, being predominantly Cl 8 unsaturated and saturated fatty acids, or their salts, As a complex mixture derived from a natural product, TOFA and its derivatives are all considered Class 2 substances.

Fatty acids are present in the pine tree as glycerol esters and are saponified to sodium salts during the pulping process. These sodium salts are the major component of tall oil soap that is skimmed from spent pulping liquor and acidulated to form **crude** tall oil. Crude tall oil is then fractionally distilled at high temperatures under vacuum to yield several fractions, two of which are included in this group. Fatty acids, tall oil, low boiling (CAS# 65997-03-7) is the most volatile fraction, and TOFA is the second most volatile. The remaining members of this group are all derived from TOFA (Zinkel and Russell 1989).

A. Composition

Each species of pine tree has a somewhat different mix of fatty acids. Even within a species, the mix of fatty acids may be influenced by the climate and local terrain. Consequently, product specifications for these substances are not given in terms of chemical components, but in general terms such as acid number and iodine value, which are measures of aggregate chemical reactivity (Zinkel and Russell 1989). Provided below is some general information on the typical compositions of each of the six substances in this category.

1. Fatty Acids, Tall Oil (CAS# 61790-12-3)

The actual composition of a given tall oil fatty acid depends on factors such as the origin of the tall oil and the fractionation conditions used for its production. The composition of a typical tall oil fatty acid (TOFA) is shown in Table 2.

Table 2

Composition of a Typical Tall Oil Fatty Acid

Common Name	*Chemical Structure*	*Percent Composition*
Palmitic acid	$CH_3(CH_2)_{14}COOH$	1%
Stearic acid	$CH_3(CH_2)_{16}COOH$	2%
Oleic acid	$CH_3(CH_2)_7CH=CH(CH_2)_7COOH$	48%
Linoleic acid	$CH_3(CH_2)_4CH=CH\text{-}CH_2CH=CH(CH_2)_7COOH$	35%
Conjugated linoleic acid"	$CH_3(CH_2)_XCH=CHCH=CH\text{-}(CH_2)_YCOOH$	7%
Other acids[b]		4%
Unsaponifiable matter		2%

a: x usually 4 or 5; y usually 7 or 8; but x + y = 12
b: 5,9,12-octadecatrienoic acid; linolenic acid; 5,11,14-eicosatrenoic acid; cis,cis-5,9-octadecadienoic acid; eicosadienoic acid; elaidic acid; cis-11 octadecanoic acid; C-20, C-22, C-24 saturated acids.

2. Fatty Acids, Tall Oil, Low Boiling (CAS# 65997-03-7)

The composition of tall oil, low boiling, better known as "tall oil heads," is even more complex. As with TOFA, the composition of heads depends on the origin of the tall oil and the fractionation conditions. The TSCA Inventory defines tall oil heads as, *"the low boiling fraction obtained by the distillation of tall oil. Contains fatty acids such as palmitic, stearic, oleic and linoleic as well as neutral materials."* The neutral component is also complex, and contains small amounts of various terpenic hydrocarbons, alcohols, aldehydes, phenolics, lignin-derived materials, and other neutral materials. The composition of a typical tall oil heads is shown in Table 3.

Table 3

Composition of a Typical Tall Oil Heads

Common Name	*Chemical Structure*	*Percent Composition*
Palmitic acid	$CH_3(CH_2)_{14}COOH$	36%
Stearic acid	$CH_3(CH_2)_{16}COOH$	1%
Oleic acid	$CH_3(CH_2)_7CH=CH(CH_2)_7COOH$	32%
Linoleic acid	$CH_3(CH_2)_4CH=CH\text{-}CH_2CH=CH(CH_2)_7COOH$	23%
Other acids[a]		8%
Unsaponifiable matter		10%

a: These are the same as indicated in Table 2 except the amounts of C20, C22, and C24 will be negligible.

3. Fatty Acids, C16-C18 and Cl8 Unsaturated, Branched and Linear (CAS# 68955-98-6)

Fatty acids, C16-C18 and Cl8 unsaturated, branched and linear (CAS# 68955-98-6) is better known as monomer acid. It is a co-product obtained in the production of dimer acid from TOFA. It has some of the characteristics of TOFA, except that it has a much **lower** level of unsaturation and also contains some branched chains. Monomer acid is a complex mixture of fatty acids; the major components are shown in Table 4.

Table 4

Composition of a Typical Monomer Acid

Common Name	*Chemical Structure*	*Percent Composition*
Palmitic acid	$CH_3(CH_2)_{14}COOH$	3%
Stearic acid	$CH_3(CH_2)_{16}COOH$	3%
Branched Cl8 acids		28%
Oleic acid (cis)	$CH_3(CH_2)_7CH=CH(CH_2)_7COOH$	12%
Elaidic acid (trans)	$CH_3(CH_2)_7CH=CH(CH_2)_7COOH$	24%
Other Cl8 acids[a]		24%
Unsaponifiable matter		1%

a: Probably cyclic acids of unknown structure.

4. Octadecanoic Acid, Branched and Linear (CAS# 68201-37-6)

Octadecanoic acid, branched and linear (CAS# 68201-37-6) is also known as hydrogenated monomer acid. It is an intermediate in the conversion of monomer acid into isostearic acid. Its composition is similar to the typical monomer acid shown in Table 4 except that all the acids are saturated.

5. Fatty acids, Tall Oil, Potassium Salt (CAS# 61790-44-l) and Sodium Salt (CAS# 61790-45-2)

Fatty acids, tall oil, potassium salt (CAS# 61790-44-I) and fatty acids, tall oil sodium salt (CAS# 61790-45-2) are simple salts of tall oil fatty acids. The salts are made by treating tall oil fatty acids with the appropriate base. As they are salts of a weak acid and a strong base, solutions of these salts are alkaline, with the pH depending on the concentration.

B. Commercial Uses of Tall Oil Fatty Acids and Tall Oil Fatty Acid Salts

Tall oil fatty acids (TOFA) is by far the most important member of this group from a commercial standpoint. The main use of TOFA is as a raw material for the production of a wide variety of other chemicals. TOFA has few, if any, uses in its unmodified form. The largest single use of TOFA is for the production of dimer acids that are then converted into coatings, adhesives, and printing inks. (Dimer acids will be addressed in another test plan.) Another important end use for tall oil fatty acids is in the production of alkyd resins that go into paints and printing inks. In all of these applications, TOFA improves the film forming properties and drying characteristics of the products into which it is formulated.

The salts of TOFA are widely used as surfactants. The sodium or potassium salts are used in liquid soaps for both industrial and household cleaning and disinfectant products, They also find uses in metal working fluids and in lubricants.

Tall oil heads are generally consumed for their fuel value. When the fatty acid content is sufficiently high, the heads can be used in some of the same markets as lower grades of TOFA.

Monomer acid is used in the production of isostearic acid, a liquid Cl8 acid. In addition, monomer acid can be used in some of the same applications as TOFA, such as soaps and lubricants.

Octadecanoic acid, branched and linear (hydrogenated monomer) is an intermediate in the production of isostearic acid from monomer acid and does not have any other specific commercial use.

C. Complexity of Analytical Methodology

All of the substances in this group are Class 2 substances. This, combined with the fact that fatty acids are essentially insoluble in water and decompose on heating at high temperature, create a variety of analytical issues. Gas chromatography of methylated derivatives is the accepted method for the analysis of the members of this group. However, the solubility of the free acids is very low (about 10 ppm). PCA has verified the reliability of the standard analytical methods at such low concentrations. Based on the method validation work to date, it appears that the analytical procedures will be adequate for the proposed testing.

II. Rationale for Selection of Representative Compound for Testing

TOFA (CAS# 61790-I 2-3) has been selected as the representative substance in this group for testing for the applicable SIDS ecotoxicity and *in vitro* mammalian genotoxicity tests, as shown in Table 5 (identical to Table 1). As also shown in Table 5, pertinent physical/chemical properties and environmental fate endpoints will

be determined for all six members of this group (for which data are not already available).

All the substances in this group are similar in chemical composition, being predominantly Cl 8 unsaturated and saturated fatty acids, or their salts. The selection of TOFA as the substance to be tested is based on several factors. It has by far the greatest production volume, with almost four times more TOFA manufactured than all other substances in this group combined (i.e., 4, 64, and 28 times greater volume than the low boiling fraction, octadecanoic acid, and fatty acids, Cl 6-18, respectively). EPA guidance suggests that testing the substance produced at the greatest volume as the representative chemical of a category would be appropriate. Clearly, TOFA fits this criterion. In addition, TOFA is the raw material from which all the other group members, except for tall oil heads, are derived.

Another criterion listed by EPA for grouping chemicals into a category is the use of the "family approach" of examining related chemicals when they are acids or acid salts. Although the salts of tall oil fatty acids have quite different physical characteristics, they are included in this group because they are quickly converted into the free acids when they are neutralized by acid or by dilution, as they would be under typical toxicity testing conditions, In summary, this group of chemicals fits the requirements of the EPA's HPV Challenge program for a chemical category, and TOFA is the most appropriate representative test material from this group.

III. Review of Existing Data and Development of Test Plan

PCA has undertaken a comprehensive evaluation of all relevant data on the SIDS endpoints of concern for the chemicals in this category. Considerable data are available that satisfy most of the SIDS endpoints for this category. The availability of the data on the specific SIDS endpoints is summarized in Table 5 (identical to Table 1). Table 5 also shows data gaps that will be filled by additional testing, and areas where data from TOFA will be generalized to other category members. Because adequate data already exist for most of the SIDS endpoints, no additional testing in animals will be necessary.

Table 5
Matrix of Available Adequate Data and Proposed Testing
On Tall Oil Fatty Acids and Tall Oil Fatty Acid Salts*

Chemical and CAS #	Required SIDS Endpoints										
	Partition Coef.	Water Sol.	Biodeg.	Acute Fish	Acute Daph.	Acute Algae	Acute oral	Repeat Dose	In vitro genetox (bact.)	In vitro genetox (non-bact)	Repro/ develop
61790-I 2-3, Fatty acids, tall-oil	**Test**	**Test**	**Adeq.**	**Test**	Test	Test	Adeq.	Adeq.	Adeq.	Test	Adeq./ **Adeq.**
65997-03-7, Fatty acids, tall-oil, low boiling	**Adeq.**	**Test**	**Adeq.**	C	C	C	C	C	C	C	C
68955-98-6, Fatty acids, Cl 6-C18 and Cl 8 unsat., **branched & linear**	Adeq.	Test	Adeq.	C	C	C	C	C	C	C	C
68201-37-6, Octadecanoic acid, branched and linear	**Test**	**Test**	**Test**	C	C	C	C	C	C	C	C
61790-44-1, Fatty acids, tall oil, potassium salts	**Test**	**Test**	**Adeq.**	C	C	C	C	C	C	C	C
61790-45-2, Fatty acids,' tall oil, sodium salts	Test	Test	Test	C	C	C	C	C	C	C	C

Adeq. Indicates adequate existing data
Test Indicates proposed testing
C Indicates category read-down from existing or proposed test data on tall oil fatty acid
* No testing will be conducted for melting point, boiling point, vapor pressure, hydrolysis, photodegradation, and transport and distribution between environmental compartments as explained in the test plan.

A. Evaluation of Existing Physicochemical Data and Proposed Testing

The basic physicochemical data required in the SIDS battery includes melting point, boiling point, vapor pressure, partition coefficient **(K_{ow}),** and water solubility.

Class 2 substances are composed of a complex mixture of substances and are often difficult to characterize. Tall oil fatty acids and their derivatives are Class 2 substances that are derived from natural sources. Their composition is variable and cannot be represented by a definite chemical structural diagram. Due to this "complex mixture" characteristic of tall oil fatty acids and their derivatives, some physical property measurements, such as the partition coefficient are not appropriate because the methodology used to determine these properties will actually separate the Class 2 substances into their various component fractions. Rather than

producing accurate measurements, the results of such testing are likely to be erroneous and difficult or impossible to interpret.

1. Melting Point

TOFA and the other non-salts in this grouping category are liquids at room temperature. In addition, a sharp melting point cannot be obtained due to the complex nature of these substances. Even though the two salts are solids under ambient conditions, heating them to determine the melting point would cause thermal decomposition. Consequently, the melting point will not be determined for any members of this grouping category.

2. Boiling Point

All of the non-salt members of this category are produced by high temperature, high vacuum distillation and are non-volatile at ambient temperatures, A boiling point has no significance because these materials will thermally decompose before they boil, when heated to high temperatures. The two salts in this group are solids, When heated to high temperatures, they will also thermally decompose before boiling. Accordingly, measurement of this property is inappropriate for all the substances in this category.

3. Vapor Pressure

Vapor pressures for the fatty acids at ambient temperatures are effectively zero, and their experimental measurement is inappropriate. The salt members of the group are solids and thus have no vapor pressure, so this end point cannot be measured. When dissolved in water their solutions will reflect the vapor pressure of the water rather than the salt, and therefore measurement of this property is inappropriate.

4. Water Solubility

The water solubility of all six compounds in this group will be determined using OECD (105).

5. Partition Coefficient

For the three members of this group for which partition coefficient data (i.e., K,,) do not already exist (octadecanoic acid, branched and linear CAS# 68201-37-6; fatty acids, tall oil, potassium salts CAS# 61790-44-I; and fatty acids, tall oil, sodium salts CAS# 61790-45-2) the K_{ow} will be determined. Adequate data exist for TOFA although this will be retested with the other compounds in this category. As noted above, because all of these substances are Class 2 mixtures, the procedure (OECD 107) to determine the K_{ow} yields a number of separate K_{ow} values rather than a single value representative of the mixture. Existing data for TOFA reveals numerous K_{ow} values: at pH 2, seven K_{ow} values ranging from 4.4 to 8.3 and at pH 7.5, six K_{ow} values ranging from 3.6 to 7.4 reflecting the partition coefficients of the individual

fatty acid constituents of this complex mixture. In this regard, it is reported that the partition coefficients for palmitic acid, stearic acid, oleic acid, and linoleic acid are 8.2, 8.2, 7.6, and 7.1, respectively. It should be noted that all of these fatty acids are well-recognized constituents of living organisms.

Summary of Physicochemical Properties Testing: The water solubility of all members of this group will be determined. The partition coefficients for the three members of this group for which there are no data will also be determined. While there are adequate data on the partition coefficient for TOFA, this will be retested along with the other compounds. Tests for the melting point, boiling point and vapor pressure are inappropriate.

B. Evaluation of Existing Environmental Fate Data and Proposed Testing

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

1. Biodegradation

Biodegradability can help to determine the fate of chemicals in the environment because it provides a measure for the potential of compounds to be degraded by microorganisms. Depending on the nature of the test material, several standard test methods are available to assess potential biodegradability.

Of the six chemicals in this group, four (TOFA; tall oil fatty acids, low boiling; fatty acids, C16-C18 and Cl8 unsaturated, branched and linear; and fatty acids, potassium salts) have existing data on the biodegradation endpoint. Biodegradation for octadecanoic acid, branched and linear and tall oil fatty acids, sodium salts will be determined.

2. Hydrolysis

Hydrolysis as a function of pH is used to assess the stability of a substance in water. Hydrolysis is a reaction in which a water molecule (or hydroxide ion) substitutes for another atom or group of atoms present in an organic molecule. If there is no group suitable to be displaced, then the organic compound is considered to be resistant to hydrolysis. None of the substances in the tall oil fatty acids category contains an organic functional group that might be susceptible to this physical degradative mechanism. Therefore, hydrolysis need not be measured.

In addition, low water solubility often limits the ability to determine hydrolysis as a function of pH. All of the tall oil fatty acids have very low solubility in water. Therefore, these materials are expected to be stable in water and it would be unnecessary to attempt to measure the products of hydrolysis. With respect to the

fatty acid salts, since they exist in an aqueous medium they hydrolyze (ionize) immediately, but form stable species. Consequently, it would also be unnecessary to measure this endpoint for the fatty acid salts.

3. Photodegradation

Due to their low water solubility and lack of any vapor pressure, there is no opportunity for any of these chemicals to enter the atmosphere. Thus, photodegradation is irrelevant. In addition, based on the constituents in these complex mixtures, there is no reason to suspect that they would be subject to breakdown by a photodegradative mechanism. Consequently, this endpoint will not be determined for any of the substances in this category.

4. Transport and Distribution Between Environmental Compartments

The transport and distribution between environmental compartments is intended to determine the ability of a chemical to move or partition in the environment. The determination of this property requires the use of various models (e.g., level III model from the Canadian Environment Modeling Centre at Trent University). For Class 2 substances such as TOFA and related compounds, the required inputs to the model are either not available or impossible to determine including molecular mass, reaction half-life estimates for air, water, soil, sediment, aerosols, suspended sediment, and aquatic biota. In addition, while the partition coefficient is also required and can be determined, the multiple K_{ow} values typically derived for these substances (e.g., seven K_{ow} values for TOFA) are a consequence of sample fractionation and reflect various components in the mixture and are not representative of the mixture itself. Consequently, due to the inability to provide usable inputs to the required model, no determination of transportation and distribution between environmental compartments will be undertaken for TOFA and related compounds.

Summary of Environmental Fate Testing: Biodegradation data will be generated for two of the six compounds in this group for which data are not already available. Photodegradation, hydrolysis, and transport and distribution between environmental compartments are inapplicable to these chemicals.

C. Evaluation of Existing Ecotoxicity Data and Proposed Testing

The basic ecotoxicity data that are part of the HPV Program includes acute toxicity to fish, daphnia and alga. While there are existing data on these endpoints for some of the substances in this grouping category, these data are conflicting and it is impossible to determine which, if any, of these findings is representative of true ecotoxicity. The inconsistencies in how water samples were prepared for testing these endpoints render these data inadequate. Consequently, acute toxicity to fish, daphnia and alga will be retested for TOFA under conditions that maximize the solubility under the specific test exposure conditions, but reduce exposure to insoluble fractions, which may cause nonspecific toxicological effects. In addition, the effect of both filtering, to further minimize nonspecific physical effects, and of

reducing the pH to the lower end of the acceptable range for test organism survival, will also be investigated for changes in toxicological effects. The results of preliminary tests will be used to select the most appropriate test conditions for the definitive test for each species.

It should be noted that in EPA's latest guidance concerning the HPV Challenge Program (EPA 2000), there is a recommendation that chemicals with a log K_{ow} greater than 4.2 should be tested in a chronic toxicity to daphnia study (in place of the acute toxicity tests in fish and daphnia) and toxicity to algae. This is due to concerns about the possibility of bioconcentration for chemicals with a K_{ow} greater than 4.2. These concerns would not hold for TOFA and related chemicals since the high K_{ow} values are due to the various fatty acid constituents of these complex mixtures, which would not bioaccumulate. Consequently, the proposed acute ecotoxicity tests in daphnia, fish and algae are adequate to satisfy the requirements of the HPV program.

Summary of Ecotoxicity Testing: The acute toxicity of TOFA to fish, daphnia and algae will be tested under conditions that maximize its solubility, but reduce exposure to insoluble fractions, which may cause nonspecific toxicological effects.

D. Evaluation of Existing Human Health Effects Data and Proposed Testing

1. Acute Oral Toxicity

Acute oral toxicity studies investigate the effect(s) of a single exposure to a relatively high dose of a substance. This test is conducted by administering the test material to animals (typically rats or mice) in a single gavage dose. Harmonized EPA testing guidelines (August 1998) set the limit dose for acute oral toxicity studies at 2000 mg/kg body weight. If less than 50 percent mortality is observed at the limit dose, no further testing is needed. A test substance that shows no effects at the limit dose is considered essentially nontoxic. If compound-related mortality is observed, then further testing may be necessary.

Summary of Available Acute Oral Toxicity Data

TOFA is non-toxic following acute oral exposure. TOFA was tested for acute oral toxicity in Sprague-Dawley rats. Animals received a single oral (gavage) dose of 10,000 mg/kg and were observed for 14 days. Parameters evaluated included clinical signs, mortality, body weight, and gross pathology. None of the animals died. One hour post-dosing, piloerection was observed in one male and abnormal stance was observed in one male and one female. By four hours, these effects had resolved. No body weight effects were observed. Gross necropsy revealed no treatment-related effects. The acute oral LD_{50} was greater than 10,000 mg/kg.

Summary of Acute Oral Toxicity Testing: TOFA has been tested for acute oral toxicity and found to be non-toxic (i.e., LD_{50} > 10,000 mg/kg) well above the

guideline of 2000 mg/kg. Consequently, additional testing for this endpoint is not necessary.

2. Repeat Dose Toxicity

Subchronic repeated dose toxicity studies are designed to evaluate the effect of repeated exposure to a chemical over a significant period of the life span of an animal. Typically, the exposure regimen in a subchronic study involves daily exposure (at least 5 consecutive days per week) for a period of not less than 28 days or up to 90 days (i.e., 4 to 13 weeks). The HPV program calls for a repeat dose test of at least 28 days. The dose levels evaluated are lower than the relatively high limit doses used in acute toxicity (i.e., LD_{50}) studies. In general, repeat dose studies are designed to assess systemic toxicity, but the study protocol can be modified to incorporate evaluation of potential adverse reproductive and/or developmental effects.

Summary of Available Repeat Dose Toxicity Data

There are existing data that demonstrate a lack of toxicity for TOFA. Tall oil fatty acid (CAS #61790-12-3) was tested in a 90-day subchronic toxicity study in rats. The test material was administered to Charles River rats in the diet at concentrations 0, 5, 10, or 25% for 90 days. The approximate doses were 0, 2500, 5000, or 12,500 mg/kg/day. Parameters evaluated included clinical signs, mortality, body weight, body weight gain, food consumption, hematology, clinical chemistry, urinalysis, gross pathology, organ weights, and microscopic pathology.

There were no deaths attributable to the test compound and no clinical signs were observed. Body weight and body weight gain were not affected by treatment, but food consumption was slightly decreased at dietary levels of IO and 25%. No changes in hematology, clinical chemistry or urinalysis parameters were measured at any dose level. At gross pathology, no treatment-related effects were noted. No consistent organ weight changes and no histopathological effects were reported. Based on these data, the No Observed Effect Level (NOEL) was 5% (approximately 2500 mg/kg/day).

Other subchronic studies for 28 and 40 days confirm the low toxicity of TOFA. In these studies, the only effect noted was depression of body weight gain at the highest doses tested.

Summary of Repeat Rose Toxicity Testing: TOFA has been tested for repeat dose toxicity in a 90-day study. in this study, the NOEL was approximately 2500 mg/kg/day, indicating that this compound has low toxicity. Other studies support this result. Consequently, no additional testing for this endpoint will be conducted.

3. Genotoxicity – In vitro

Genetic testing is conducted to determine the effects of substances on genetic material (i.e., DNA and chromosomes). The gene, which is composed of DNA, is the simplest functional genetic unit. Mutations can occur spontaneously or as a consequence of exposure to chemicals or radiation. Genetic mutations are commonly measured in bacterial and mammalian cells, and the HPV program calls for completing both types of tests.

Summary of Available Genotoxicity Data

TOFA was not mutagenic in the Ames assay. It was tested for mutagenicity in *S. typhimurium* strains TA98, TA100, TA1535, TA1537 and TA1538 at concentrations of 100, 333, 1000, 3333 and 10,000 µg/plate, with and without metabolic activation. No increases in mutation frequency were reported at any concentration, with or without metabolic activation. Tall oil fatty acid was not mutagenic in this assay. There are no *in vitro* genotoxicity data on mammalian cells.

Summary of Genotoxicity Testing: TOFA was not mutagenic in the Ames (bacteria) test. Consequently, no additional in vitro bacterial mutagenicity testing is necessary. The SIDS battery also includes an in vitro mammalian mutagenicity test. Therefore, TOFA will be tested for genotoxicity in an in vitro mammalian chromosome aberration test (OECD 473), both with and without metabolic activation.

4. Reproductive and Developmental Toxicity

Reproductive toxicity includes any adverse effect on fertility and reproduction, including effects on gonadal function, mating behavior, conception, and parturition. Developmental toxicity is any adverse effect induced during the period of fetal development, including structural abnormalities, altered growth and post-partum development of the offspring.

The "toxicity to reproduction" aspect of the HPV Challenge Program can be met by conducting a reproductive/developmental toxicity screening test or adding a reproductive/developmental toxicity screening test to the repeated dose study (OECD 421 or OECD 422, respectively). The one-generation reproduction toxicity study (OECD 415) is a more comprehensive protocol for the study of the effect of a test material on reproduction and development that also meets the SIDS and the HPV Program requirements.

Summary of Reproductive/Developmental Toxicity Data

TOFA had no effects when tested for reproductive and developmental toxicity in Sprague-Dawley rats in a full two-generation study. The test compound was administered in the diet at concentrations of 0, 5 or 10% to 30 females/group and 15 males/group. The approximate doses were 0, 2500, or 5000 mg/kg/day. Males and

females in the first generation (F_0) began treatment at 80 days of age and were mated at 100 days of age. Treatment of the F_0 animals continued through the weaning of the first generation (F_1). After weaning, the F_1 males and females were maintained on the treatment diet. At 100 days of age, they were mated and allowed to deliver pups (F_2).

There were no treatment-related effects on reproductive performance, or on any parameter measured in either the F_1 or F_2 pups. No treatment-related changes in fertility, viability, lactation, or gestation indices were observed. Hematology, clinical chemistry and urinalysis parameters were similarly unchanged, and there were no developmental effects in any F_1 or F_2 offspring. TOFA did not alter or otherwise affect the reproduction or development of rats in this study at doses as high as 10% (approximately 5000 mg/kg/day).

Summary of Reproductive/Developmental Testing: TOFA demonstrated no effects when tested for reproductive and developmental toxicity in a full two-generation study. Consequently, no additional reproductive/developmental toxicity testing is necessary.

References

EPA. 2000. Data Collection and Development on High Production Volume (HPV) Chemicals. Fed. Reg. Dec. 26, Vol. 65(248): pp. 81686-81698.

Zinkel, D.F. and Russell, J., Eds. 1989. Naval Stores. Production, Chemistry, Utilization. Pulp Chemicals Association, New York.

May 2001

IV. Robust Summaries of Existing Data

PHYSICO-CHEMICAL PROPERTY – OCTANOL/WATER PARTITION COEFFICIENT	
Test Substance	
Chemical Name	Tall oil fatty acid
CAS #	61790-I 2-3
Remarks	This substance is also referred to as TOFA in the test plan for Tall Oil Fatty Acids and Related Substances.
Method	
Method/Guideline followed	Testing was conducted according to OECD Test Method 117, *"Partition Coefficient (n-Octanol/Water) High Performance Liquid Chromatograph (HPLC) Method"*
Test Type	Partition coefficient
GLP (YIN)	Y
Year (Study Performed)	1993
Test conditions	Tall oil fatty acid was dissolved in methanol and the solution was analyzed by HPLC with UV detection using a mobile phase of methanol:buffer (3:1) at pH 2 and pH 7.5. A mixture of seven materials with known log P_{ow} values was used for reference.
Results	At pH 2, the log P_{ow} values of seven components in tall oil fatty acid were 4.4, 7.0, 7.3, 7.5, 7.7, 8.0, and 8.3. At pH 7.5, the log K_{ow} values of six components in tall oil fatty acid were 3.6, 3.8, 4.2, 4.5, 4.7, and 7.4.'
Data Quality	Reliable without restrictions – Klimisch Code 1 a
Reference	Dybdahl, H.P. 1993. Determination of log P_{ow} for single components in tall oil fatty acid. GLP Study No. 408335/472. Water Quality Institute, Horshplm, Denmark.

PHYSICO-CHEMICAL PROPERTY - OCTANOL/WATER PARTITION COEFFICIENT	
Test Substance	
Chemical Name	Tall oil fatty acids, low boiling
CAS #	65977-03-7
Remarks	This substance is also referred to as tall oil heads in the test plan for Tall Oil Fatty Acids and Related Substances.
Method	
Method/Guideline followed	Testing was conducted according to OECD Test Method 117, ***"Partition Coefficient (n-Octanol/Water) High Performance Liquid Chromatograph (HPLC) Method"***
Test Type	Partition coefficient
GLP (Y/N)	Y
Year (Study Performed)	1993
Test conditions	Tall oil heads was dissolved in methanol and the solution was analyzed by **HPLC** with UV detection using a mobile phase of methanol:buffer (3:1) at pH 2 and pH 7.5. A mixture of seven materials with known log P_{ow} values was used for reference.
Results	At pH 2, the log P_{ow} values of nine components in tall oil heads were 4.4, 6.7, 6.9, 7.0, 7.2, 7.2, 7.4, 7.7, and 7.8. At pH 7.5, the log P_{ow} values of seven components in tall oil heads were 4.6, 6.5, 6.9, 6.9, 7.3, 7.4, and 8.0.
Data Quality	Reliable without restrictions - Klimisch Code 1 a
Reference	Dybdahl, H.P. 1993. Determination of log Pow for single components in tall oil heads. GLP Study No. 408335/474. Water Quality Institute, Horshplm, Denmark.

PHYSICO-CHEMICAL PROPERTY - OCTANOL/WATER PARTITION COEFFICIENT	
Test Substance	
Chemical Name	Fatty acids, C16-C18 and Cl8 unsaturated, branched and linear
CAS #	68955-98-6
Remarks	This substance is also referred to as monomer acid in the test plan for Tall Oil Fatty Acids and Related Substances.
Method	
Method/Guideline followed	Testing was conducted according to Method A8 of Commission Directive 92/69/EEC
Test Type	Partition coefficient
GLP (Y/N)	N
Year (Study Performed)	1994
Test conditions	Not specified
Results	Fatty acids, Cl6 - Cl8 and Cl8 unsaturated, branched and linear had a partition coefficient of 7.93 x 10^4 at 25°C, or a $Log_{10} P_{ow}$ of 4.90.
Data Quality	Reliable with restrictions – Klimisch Code 2a
Reference	Mullee, D.M. 1994. Determination of partition coefficient. Project ID No. 5081027. SafePharm Laboratories Ltd., Derby, England.

ENVIRONMENTAL FATE - BIODEGRADATION	1
Test Substance	
Chemical Name	Tall oil fattv acid
CAS #	61790-l 2-i
Remarks	This substance is also referred to as TOFA in the test plan for Tall Oil Fatty Acids and Related Substances.
Method	
Method/Guideline followed	Testing was conducted according to OECD Test Method 301 D, ***"Ready Biodegradability: Closed Bottle Test"***
Test Type (aerobic/anaerobic)	Aerobic
GLP (Y/N)	Y
Year (Study Performed)	1993
Contact time	***28*** days
Inoculum	Secondary effluent from Rungsted Treatment plant
Test conditions	Inoculum: Secondary effluent was collected from Rungsted Treatment plant. Concentration of test chemical: A stock solution of the test material (2 g/L) was prepared in demineralized water by ultra sonication for 5 minutes. Test Setup: Test medium was prepared by adding 1 mL each of four solutions (potassium phosphate, magnesium sulfate, calcium chloride, ferric chloride) to 1 liter of demineralized water, which was aerated to an initial oxygen concentration of 9 mg O_2/L and inoculated with 1 drop of secondary effluent per liter. The test article was added at 2 mg/L to a part of the inoculated test medium, equivalent to a chemical oxygen demand of 5.03 mg O_2/L. Sodium benzoate, the reference compound, was added at 2 mg/L to another part of the inoculated medium (to assess the activity of the inoculum), equivalent to a theoretical oxygen demand of 3.34 mg O_2/L. Both the test and reference articles (2 mg/L) were added to a third part of the inoculated medium (to assess possible inhibitory effects of the test article), at a theoretical oxygen demand of 8.37 mg O_2/L. Blank controls were prepared using the inoculated medium without test or reference materials. After the samples were prepared, the medium was transferred to calibrated respirometric bottles (BOD bottles), and placed in the dark at 20°C. The study was performed in triplicate. Sampling frequency: Samples were collected for BOD analysis on days 0, 7, 14, 21, and 28. Controls: Yes. Method of calculating oxygen demand: Oxygen demand was calculated as the difference between the measured oxygen concentrations at time t and the start of the test. Biological oxygen demand was calculated by subtracting the oxygen demand for the blank controls from the oxygen demand in the bottles containing test and reference compounds.

Results Degradation % after time	50% after 7 days and 56% after 28 days (test article); 63% after 7 days and 77% after 28 days (sodium benzoate)
Conclusions	The biological oxygen demand for tall oil fatty acid was 50 and 56% of the theoretical oxygen demand after 7 and 28 days, respectively. The rapid oxygen consumption in the first week and the total oxygen demand at the termination of the experiment indicate that the test material was dominated by readily biodegradable compounds. Tall oil fatty acid did not inhibit the respiratory activity of the inoculum.
Data Quality	Reliable without restrictions- Klimisch Code 1 a
Reference	Madsen, T. 1993. Biodegradation of tall oil fatty acid. GLP Study No. 308067/472. Water Quality Institute, Horshplm, Denmark.

ENVIRONMENTAL FATE – BIODEGRADATION	
Test Substance	
Chemical Name	Tall oil fatty acid
CAS #	61790-I 2-3
Remarks	This substance is also referred to as TOFA in the test plan for Tall Oil Fatty Acids and Related Substances.
Method	
Method/Guideline followed	Testing was conducted according to OECD Test Method 301 F, ***"Manometric respiratory test for biological degradation"***
Test Type (aerobic/anaerobic)	Aerobic
GLP (Y/N)	Y
Year (Study Performed)	1999
Contact time	28 days
Inoculum	Activated sludge from a municipal sewage treatment plant
Test conditions	Inoculum: Activated sludge from the municipal sewage treatment plant in Reutlingen was washed twice with tap water and centrifuged. Concentration of test chemical: A stock solution of the test material (101.5 mg/L) was prepared. Test Setup: Mineral medium was prepared by adding 10 mL of a potassium phosphate solution and 1 mL each of three other solutions (magnesium sulfate, calcium chloride, ferric chloride) to make a total volume of 1 liter in demineralized water. Six flasks were prepared: two of the test article in mineral medium with inoculum (24 mg/L); two of the mineral medium plus the inoculum (24 mg/L); one of the reference substance [sodium benzoate (98.5 mg/L)] with inoculum (24 mg/L); and one of the test article in water with sterilized medium. Sampling frequency: Samples were collected for analysis on days 14 and 28. Controls: Yes. Method of calculating oxygen demand: Biological oxygen demand was calculated by subtracting the oxygen demand for the blank controls from the oxygen demand in the flasks containing test and reference compounds.
Results	
Degradation % after time	84% after 28 days (test article); 97% after 28 days (sodium benzoate)
Conclusions	Eighty-four percent of tall oil fatty acid was biodegraded after 28 days indicating that the organic portion of the test material was readily biodegradable.
Data Quality	Reliable without restrictions- Klimisch Code 1 a
Reference	Aniol, S. 1999. Biological degradation (Manometric respirometry test). STZ Project No. 03/99. Steinbeis-Transferzentrum Angewandte und Umwelt-Chemie, Reutungen.

ENVIRONMENTAL FATE - BIODEGRADATION	
Test Substance	
Chemical Name	Tall oil fatty acid
CAS #	61790-l 2-3
Remarks	This substance is also referred to as TOFA in the test plan for Tall Oil Fatty Acids and Related Substances.
Method	
Method/Guideline followed	Testing was conducted according to the CO_2 Evolution Test (Modified Sturm Test), EPA guideline number OPPTS 853.110, ***"Ready Biodegradability"***
Test Type (aerobic/anaerobic)	Aerobic
GLP (Y/N)	N
Year (Study Performed)	1994
Contact time	29 days
Inoculum	Activated sludge from the Servern Trent water sewage treatment plant
Test conditions	Inoculum: Activated sludge microorganisms were obtained from the Servern Trent water sewage treatment plant at Belper, Derbyshire. A 1% inoculum was prepared. Concentration of test chemical: The test material was used at a concentration of 20 mg/L. Test Setup: Culture medium was prepared by adding 10 mL of a potassium phosphate solution and 1 mL each of three other solutions (magnesium sulfate, calcium chloride, ferric chloride) to a final volume of 1 liter in purified water. Twenty-four hours prior to study initiation, vessels were filled with 2400 mL of culture medium and 30 mL of inoculum and aerated over night. On day 0 of the study, the test and reference material (sodium benzoate, 10 mg/L) were added and the total volume was increased to 3 liters. The following series of vessels was prepared: culture medium with inoculum; culture medium with inoculum and sodium benzoate; and culture medium with inoculum and test material. The CO_2 absorption bottles were connected to the outlet and were sealed. CO,-free air was bubbled through the solution and they were stirred continuously. All experiments were performed in the dark at 20 to 22°C. Sampling frequency: Samples (2 mL) were collected from the first CO_2 absorber vessel on days 0, 1, 2, 3, 6, 8, 10, 14, 16, 18, 20, 22, 24, 27, 28, and 29, and from the second absorber on days 0 and 29. Controls: Yes. Analysis: Samples from the CO_2 absorbers were injected into the inorganic carbon channel of the total carbon analyzer for direct analysis of evolved CO_2. The analyses were conducted in triplicate.
Degradation % after time	74% after 28 days (test article); 80% after 28 days (sodium benzoate)
Conclusions	The test article was degraded 74% after 28 days and sodium

	benzoate was degraded 80% after 28 days. Under the conditions of the OECD guidelines, the test article cannot be considered to be readily biodegradable.
Data Quality	Reliable without restrictions- Klimisch Code 1 b
Reference	Sewell, I.G. 1994. Assessment of ready biodegradability using the CO_2 evolution test (modified Sturm test). Project No. 508/28. SafePharm Laboratories Ltd., Derby, England.

ENVIRONMENTAL FATE - BIODEGRADATION	
Test Substance	
Chemical Name	Tall oil fatty acids, low boiling
CAS #	65997-03-2
Remarks	This substance is also referred to as tall oil heads in the test plan for Tall Oil Fatty Acids and Related Substances.
Method	
Method/Guideline followed	Testing was conducted according to OECD Test Method 301 D, ***"Ready Biodegradability: Closed Bottle Test"***
Test Type (aerobic/anaerobic)	Aerobic
GLP (Y/N)	Y
Year (Study Performed)	1993
Contact time	28 days
Inoculum	Secondary effluent from Rungsted Treatment plant
Test conditions	Inoculum: Secondary effluent was collected from Rungsted Treatment plant. Concentration of test chemical: A stock solution of the test material (2 g/L) was prepared in demineralized water by ultra sonication for 5 minutes. Test Setup: Test medium was prepared by adding 1 mL each of four solutions (potassium phosphate, magnesium sulfate, calcium chloride, ferric chloride) to 1 liter of demineralized water, which was aerated to an initial oxygen concentration of 9 mg O_2/L and inoculated with 1 drop of secondary effluent per liter. The test article was added at 2.4 mg/L to a part of the inoculated test medium, equivalent to a chemical oxygen demand of 4.94 mg O_2/L. Sodium benzoate, the reference compound, was added at 2 mg/L to another part of the inoculated medium (to assess the activity of the inoculum), equivalent to a theoretical oxygen demand of 3.34 mg O_2/L. Both the test and reference articles were added to a third part of the inoculated medium (to assess possible inhibitory effects of the test article), at a theoretical oxygen demand of 8.28 mg O_2/L. Blank controls were prepared using the inoculated medium without test or reference materials. After the samples were prepared, the medium was transferred to calibrated respirometric bottles (BOD bottles), and placed in the dark at 20°C. The study was performed in triplicate. Sampling frequency: Samples were collected for BOD analysis on days 0, 7, 14, 21, and 28. Controls: Yes. Method of calculating oxygen demand: Oxygen demand was calculated as the difference between the measured oxygen concentrations at time t and the start of the test. Biological oxygen demand was calculated by subtracting the oxygen demand for the blank controls from the oxygen demand in the bottles containing test and reference compounds.

Results Degradation % over time	33% after 7 days and 41% after 28 days (test article); 63% after 7 days and 77% after 28 days (sodium benzoate)
Conclusions	The biological oxygen demand for tall oil heads was 33 and 41% of the theoretical oxygen demand after 7 and 28 days, respectively. These results indicate that the test material contains readily biodegradable and recalcitrant compounds. Tall oil heads did not inhibit the respiratory activity of the inoculum.
Data Quality	Reliable without restrictions- Klimisch Code la
Reference	Madsen, T. 1993. Biodegradation of tall oil heads, GLP Study No. 308067/474. Water Quality Institute, Horshplm, Denmark:

ENVIRONMENTAL FATE – BIODEGRADATION	
Test Substance	
Chemical Name	Fatty acids, Cl6 - Cl8 and Cl8 unsaturated, branched and linear
CAS #	68955-98-6
Remarks	This substance is also referred to as monomer acid in the test plan for Tall Oil Fatty Acids and Related Substances.
Method	
Method/Guideline followed	Testing was conducted according to the CO_2 Evolution Test (Modified Sturm Test), EPA guideline number OPPTS 853.110, ***"Ready Biodegradability"***
Test Type (aerobic/anaerobic)	Aerobic
GLP (Y/N)	N
Year (Study Performed)	1994
Contact time	29 days
Inoculum	Activated sludge from the Severn Trent water sewage treatment plant
Test conditions	Inoculum: Activated sludge microorganisms were obtained from the Severn Trent water sewage treatment plant at Belper, Derbyshire. A 1% inoculum was prepared. Concentration of test chemical: The test material was used at a concentration of 20 mg/L. Test Setup: Culture medium was prepared by adding 10 mL of a potassium phosphate solution and 1 mL each of three other solutions (magnesium sulfate, calcium chloride, ferric chloride) to a final volume of 1 liter in purified water. Twenty-four hours prior to study initiation, vessels were filled with 2400 mL of culture medium and 30 mL of inoculum and aerated over night. On day 0 of the study, the test and reference material (sodium benzoate, 10 mg/L) were added and the total volume was increased to 3 liters. The following series of vessels was prepared: culture medium with inoculum; culture medium with inoculum and sodium benzoate; and culture medium with inoculum and test material. The CO_2 absorption bottles were connected to the outlet and were sealed. CO_2-free air was bubbled through the solution and they were stirred continuously. All experiments were performed in the dark at 21 to 22°C. Sampling frequency: Samples (2 mL) were collected from the first CO_2 absorber vessel on days 0, 1, 2, 3, 6, 8, 10, 12, 14, 16, 20, 22, 24, 27, 28, and 29, and from the second absorber on days 0 and 29. Controls: Yes. Analysis: Samples from the CO_2 absorbers were injected into the inorganic carbon channel of the total carbon analyzer for direct analysis of evolved CO_2. The analyses were conducted in triplicate.
Results	
Degradation % after time	67% after 28 days (test article); 87% after 28 days (sodium benzoate)

Conclusions	The test article was degraded 67% after 28 days. Under the conditions of the OECD guidelines, it cannot be considered to be readily biodegradable.
Data Quality	Reliable without restrictions- Klimisch Code 1 b
Reference	Sewell, I.G. 1994. Assessment of ready biodegradability using the CO2 evolution test (modified Sturm test). Project No. 508/23. SafePharm Laboratories Ltd., Derby, England.

ENVIRONMENTAL FATE – BIODEGRADATION	
Test Substance	
Chemical Name	Tall oil fatty acids, potassium salt
CAS #	61790-44-l
Remarks	This substance is referred to as tall oil fatty acids, potassium salt, in the test plan for Tall Oil Fatty Acids and Related Substances.
Method	
Method/Guideline followed	Testing was conducted according to a modified OECD test for ready biodegradability, EPA guideline number OPPTS 853.110, ***"Ready Biodegradability"***
Test Type (aerobic/anaerobic)	Aerobic
GLP (Y/N)	Y
Year (Study Performed)	1991
Contact time	28 days
lnoculum	Activated sludge from Bergen County sewage treatment plant
Test conditions	Inoculum: Activated sludge from Bergen County sewage treatment plant was mixed with soil extract and surface water to prepare the inoculum. Concentration of test chemical: The test article was tested at a concentration of 20 to 25 ppm. Test Setup: OECD test medium was used. Aniline was the reference material and was tested at a concentration of 20 to 25 ppm. The experiments were performed in the dark at 20 to 25°C. Sampling frequency: Samples were collected for analysis on days 0, 7, 14, 21, and 28. Controls: Yes. Method of calculating degradation: The mean initial concentration of soluble organic carbon (SOC) in the controls is subtracted from the initial concentration in the test sample. From this is subtracted, the mean initial concentration of SOC in the test and control samples at time t. This value is divided by the mean initial concentration of SOC in the controls subtracted from the initial concentration in the test sample.
Results	
Degradation % after time	79% after 28 days (test article); 97% after 28 days (aniline)
Conclusions	The test material degraded 79% and is considered to be readily biodegradable as defined by OECD.
Data Quality	Reliable without restrictions- Klimisch Code 1 b
Reference	Drozdowki, D. 1991. Modified OECD test for ready biodegradability of [product name deleted] tall oil fatty acid potassium salt. Report No. 063383-l. United States Testing Company, Inc., Hoboken, New Jersey.

ACUTE TOXICITY – ORAL	
Test substance	
Chemical Name	Tall oil fatty acid
CAS #	61790-l 2-3
Remarks	This substance is also referred to as TOFA in the test plan for Tall Oil Fatty Acids and Related Substances.
Method	
Method/Guideline followed	Test procedure was consistent with OECD Test Method 401, ***"Acute Oral Toxicity"***
GLP (Y/N)	Y
Year (Study Performed)	1983
Species	Rat
Strain	Sprague-Dawley
Route of administration	Oral
Dose levels	10,000 mg/kg
Sex and number/group	5 male and 5 female rats
Frequency of treatment	Single oral gavage
Duration of test	14 day observation post-treatment
Control group (Y/N)	N
Result	
Acute Oral LD_{50}	>10,000 mg/kg
Detailed Summary	Sprague-Dawley rats (n = 5/sex) received a single oral (gavage) dose of 10,000 mg/kg of fatty acid, tall oil (CAS #61790-12-3) and were observed for 14 days. Parameters evaluated included clinical signs, mortality, body weight, and gross pathology. None of the animals died. One hour post-dosing, piloerection was observed in one male and abnormal stance was observed in one male and one female. By four hours, these effects had resolved. No body weight effects were observed. Gross necropsy revealed no treatment-related effects, The acute oral LD_{50} was greater than 10,000 mg/kg.
Data Quality	Valid without restriction – Klimisch Code 1 a
Reference	Mallory, V.T. 1983. Acute oral toxicity study in rats: fatty acid [product name deleted]. Study No. PH 402-AC-009-83. Pharmakon Research International, Inc., Waverly, Pennsylvania.

REPEAT DOSE TOXICITY	
Test substance	
Chemical Name	Tall oil fatty acid
CAS #	61790-12-3
Remarks	This substance is also referred to as TOFA in the test plan for Fall Oil Fatty Acids and Related Substances.
Method	
Method/Guideline followed	Test procedure was similar to OECD Test Method *407, "Repeat Dose 28-Day Oral Toxicity Study in Rodents,"* but failed to collect data on several parameters (hematology, clinical chemistry, histopathology) and was only conducted in male animals.
Year	1969
GLP (Y/N)	N (pre-GLP)
Species	Rat
Strain	Sprague-Dawley
Sex	Male
Route of Administration	Oral, diet
Exuosure Period	28 days
Frequency of Treatment	Daily
Post-exposure observation period	None
Dose Levels	0, 15, 30, and 60% of total calories
Control group (Y/N)	Y
Results	
NOAEL:	15%
Detailed Summary	Male Sprague-Dawley rats (n = 10/group) were fed diets containing tall oil acid distillate (CAS #61790-12-3) as 0, 15, 30 or 60% of the total calories for four weeks. Parameters evaluated included mortality, body weight, and food consumption. One animal treated with 15% died (day of death not specified) and all animals treated with 60% died within four days of dose initiation. It is unlikely that this single death was a treatment related effect since similar mortality did not occur at 30%. No effect on growth rate was reported at 15%, but a significant decrease in growth was reported at 30%.
Data Quality	Not assignable – Klimisch Code 4b
Reference	Seppanen 1969 as cited in: Anon. 1989. Final report on the safety assessment of tall oil acid. J. Amer. Coll. Toxicol. 8:769-776.

REPEAT DOSE TOXICITY	
Test substance	
Chemical Name	Tall oil fatty acid
CAS #	61790-l 2-3
Remarks	This substance is also referred to as TOFA in the test plan for Tall Oil Fatty Acids and Related Substances.
Method	
Method/Guideline followed	Test procedure is consistent with OECD Test Method 407, *"Repeat Dose 28-Day Oral Toxicity Study in Rodents"*
Year	1969
GLP (Y/N)	N (pre-GLP)
Species	Rat
Strain	Charles River
Sex	Male, female
Route of Administration	Oral, diet
Exposure Period	90 days
Frequency of Treatment	Daily
Post-exposure observation period	None
Dose Levels	5, 10, and 25% (approximately equivalent to 2500, 5000, and 12,500 mg/kg/day)
Control group (Y/N)	Y
Results	
NOEL:	5%, approximately 2500 mg/kg/day
De tailed Summary	Tall oil fatty acid was administered to Charles River rats (n = 10/sex/group) in the diet at concentrations 0, 5, 10, or 25% for 90 days. The approximate doses were 0, 2,500, 5,000, or 12,500 mg/kg/day, based on standard conversion factors provided by WHO (1990). Parameters evaluated included clinical signs, mortality, body weight, body weight gain, food consumption, hematology, clinical chemistry, urinalysis, gross pathology, organ weights (liver, kidneys, spleen, gonads, heart, adrenal glands, thyroid gland, brain), and microscopic pathology (esophagus, stomach, small intestine, cecum, colon, liver, kidneys, spleen, pancreas, urinary bladder, pituitary gland, adrenal gland, testes, seminal vesicle, ovary, bone marrow, thyroid gland, parathyroid gland, salivary gland, prostate gland, heart, aorta, lung, lymph node, skeletal muscle, peripheral nerve, bone, spinal cord, uterus, trachea, eye, optic nerve, brain). Two control rats died during blood sampling. No other deaths occurred and no clinical signs were observed. Body weight and body weight gain were not affected by treatment, but food consumption was slightly decreased at 10 and 25%. No changes in hematology, clinical chemistry or urinalysis parameters occurred at any dose. At gross pathology, no treatment-related effects were noted at any dose. No consistent organ weight changes and no histopathological effects were reported at any dose. Based on these data, the NOEL was 5% (approximately 2,500 mg/kg/day).
Data Quality	Valid without restriction - Klimisch Code 1 b
References	Fancher, O.E. 1969. Ninety-day subacute oral toxicity of [trade name deleted; tall oil fatty acid] in albino rats. IBT No. B7067. Industrial Bio-Test Laboratories, Inc., Northbrook, Illinois.

	World Health Organization (WHO). 1990. Principles for the Toxicological Assessment of Pesticide Residues in Food.

IN VITRO GENETIC TOXICITY	
Test substance	
Chemical Name	Tall oil fatty acid
CAS #	61790-l 2-3
Remarks	This substance is also referred to as TOFA in the test plan for Tall Oil Fatty Acids and Related Substances.
Method	
Method/Guideline followed	Test was consistent with OECD Test Method 471, *"Bacterial Reverse Mutation Test"*
Year	1984
GLP (Y/N)	Y
System of testing	*S. typhimurium* strains TA98, TA100, TA1535, TA1537, TA1538
Concentration	0, 100, 333, 1000, 3333, 10000 μg/plate
Metabolic activation	With and without addition of S-9 fraction from Aroclor 1254-treated Sprague-Dawley rats.
Results	Non-mutagenic
Detailed Summary	Tall oil fatty acid was tested against S. *typhimurium* strains TA98, TA100, TA1535, TA1537 and TA1538 for mutagenic activity. The test article was tested at concentrations of 100, 333, 1000, 3333 and 10,000 μg/plate with and without metabolic activation. Positive controls not requiring metabolic activation included sodium azide, 9-aminoacridine and 2-nitrofluorene; the positive control requiring metabolic activation was 2-aminoanthracene. No increases in mutation frequency were reported at any concentration of tall oil fatty acid with or without metabolic activation. Tall oil fatty acid was not mutagenic in this assay.
Data Quality	Valid without restriction – Klimisch Code la
Reference	Godek, E.G. 1983. Ames Salmonella/microsome plate test: fatty acid [trade name deleted]. Study No. PH 301 D-AC-018-83. Pharmakon Research International, Inc., Waverly, Pennsylvania.

REPRODUCTION AND DEVELOPMENTAL TOXICITY	
Test substance	
Chemical Name	Tall oil fatty acid
CAS #	61790-l 2-3
Remarks	This substance is also referred to as TOFA in the test plan for Tall Oil Fatty Acids and Related Substances.
Method	
Method/Guideline followed	Test procedure was consistent with OECD Test Method 416, *"Two-Generation Reproduction Toxicity Study"* with one exception: the initial treatment period was decreased (three weeks versus ten weeks).
Year	1975
GLP (Y/N)	N
Species	Rat
Strain	Sprague-Dawley
Sex	Male and female
Route of Administration	Oral, diet
Frequency of Treatment	Daily
Dose	5 and 10% (approximately equivalent to 2500 and 5000 mg/kg/day)
Control group (Y/N)	Y
Pre-mating exposure period for males	20 days (parental generation)
Pre-mating exposure period for females	20 days (parental generation)
Results	
NOEL	10%, approximately 5000 mglkglday, for reproductive and systemic toxicity
Detailed Summarv	Sprague-Dawley rats (n = 30 females/group and 15 males/group) were administered tall oil fatty acid (CAS #61790-1 2-3) in the diet at concentrations of 0, 5 or 10%. The approximate doses were 0, 2,500, or 5,000 mg/kg/day, based on standard conversion factors provided by WHO (1990). The parental (F_0) generation began treatment at 80 days of age and were mated at 100 days of age. Treatment continued through the weaning of the first generation (F_1). After weaning, 20 F_1 males and 20 F_1 females per group were maintained on the parental diet, At 100 days of age, these rats were mated and allowed to deliver pups (F_2). Parameters evaluated included F_1 reproductive parameters, F_1 fertility, viability, lactation, and gestation indices, hematology, serum chemistry, urinalysis, and microscopic pathology of the F_2 pups (brain, pituitary gland, spinal cord, eye, sub-maxillary gland, thyroid, lungs, heart, liver, kidneys, spleen, adrenals, pancreas, stomach, intestines, lymph nodes, bladder, gonads, skin, bone, bone marrow, nerve, muscle). Treatment did not affect the number of liveborn or stillborn F_1 litters and pups, or F_1 weaning weight. No treatment-related changes in fertility, viability, lactation, or gestation indices were measured. Hematology, clinical chemistry and urinalysis parameters were similarly unchanged, and gross and microscopic pathology revealed no treatment-related effects. Tall oil fatty acid had no effect on the reproductive or developmental capabilities of rats at doses as high as 10% (approximately 5,000 mg/kg/day).

Data Quality	Valid without restriction – Klimisch Code 1 b
References	Tegeris, AS. 1975. Sub-acute reproduction in the rat on tall oil fatty acid [trade name deleted]. Report No. 75-106. Pharmacopathics Research Laboratories, Inc., Laurel, Maryland. World Health Organization (WHO). 1990. Principles for the Toxicological Assessment of Pesticide Residues in Food.

REPRODUCTION AND DEVELOPMENTAL TOXICITY	
Test substance	
Chemical Name	Tall oil fatty acid
CAS #	61790-l 2-3
Remarks	This substance is also referred to as **TOFA** in the test plan for Tall Oil Fatty Acids and Related Substances.
Method	
Method/Guideline followed	Test procedure was consistent with OECD Test Method 416, *"Two-Generation Reproduction Toxicity Study"* with one exception: the initial treatment period was decreased (three weeks versus ten weeks).
Year	1977
GLP (Y/N)	N
Species	Rat
Strain	Sprague-Dawley
Sex	Male and female
Route of Administration	Oral, diet
Frequency of Treatment	Daily
Dose	5 and 10% (approximately equivalent to 2500 and 5000 mg/kg/day)
Control group (Y/N)	Y
Pre-mating exposure period for males	20 days (parental generation)
Pre-mating exposure period for females	20 days (parental generation)
Results	
NOEL	10%, approximately 5000 mg/kg/day, for reproductive and systemic toxicity
Detailed Summary	Sprague-Dawley rats (n = 30 females/group and 15 males/group) were administered tall oil fatty acid (CAS #61790-12-3) in the diet at concentrations of 0, 5 or 10%. The approximate doses were 0, 2,500, or 5,000 mg/kg/day, based on standard conversion factors provided by WHO (1990). The parental (F_0) generation began treatment at 80 days of age and were mated at 100 days of age. Treatment continued through the weaning of the first generation (F_1). After weaning, 20 F_1 males and 20 F_1 females per group were maintained on the parental diet. At 100 days of age, these rats were mated and were allowed to deliver pups (F_2). The F_2 generation survived to weaning. Parameters evaluated included F_1 reproductive parameters, F_1 fertility, viability, lactation, and gestation indices, hematology, serum chemistry, urinalysis, organ weights for F_1 animals (thyroids, heart, liver, adrenals, kidneys, gonads), gross pathology of F_1 and F_2 animals, and microscopic pathology of the F_2 pups (brain, pituitary gland, spinal cord, eye, sub-maxillary gland, thyroid, lungs, heart, liver, kidneys, spleen, adrenals, pancreas, stomach, intestines, lymph nodes, bladder, gonads, skin, bone, bone marrow, nerve, muscle). There were no treatment effects on reproductive performance, the number of liveborn or stillborn F_1 litters and pups, or weaning weight of the F_1 pups. No treatment-related changes in fertility, viability, lactation, or gestation indices were measured. Hematology, clinical chemistry and urinalysis parameters were

	similarly unchanged, organ weights were unchanged, and gross and microscopic pathology revealed no treatment-related effects. Tall oil fatty acid had no effect on the reproductive or developmental capabilities of rats at doses as high as 10% (approximately 5,000 mg/kg/day).
Data Quality	Valid without restriction - Klimisch Code 1 b
References	Tegeris, A.S. 1977. Tall oil fatty acid: two-generation reproduction study in the rat. Report No. 77-l 24. Pharmacopathics Research Laboratories, Inc., Laurel, Maryland. World Health Organization (WHO). 1990. Principles for the Toxicological Assessment of Pesticide Residues in Food.