201-15703

HIGH PRODUCTION VOLUME (HPV)
CHEMICAL CHALLENGE PROGRAM

FINAL SUBMISSION

for

ROSIN ADDUCTS AND ADDUCT SALTS

CAS No. 65997-04-8
CAS No. 8050-28-0
CAS No. 68554-16-5
CAS No. 68201-59-2
CAS No. 68649-83-2
CAS No. 85409-27-4

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Submitted to the US EPA

November 2004

By

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

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Final Submission for Rosin Adducts and Adduct Salts

Final Submission for Rosin Adducts and Adduct Salts

Summary

As part of the High Production Volume (HPV) Program, the Pine Chemicals Association, Inc. (PCA) has sponsored six HPV chemicals. This final submission addresses the following six chemicals, known collectively as Rosin Adducts and Adduct Salts:

CAS No. 65997-04-8, Rosin, fumarated
CAS No. 8050-28-0, Rosin, maleated
CAS No. 68554-16-5, Rosin, maleated/fumarated
CAS No. 68201-59-2, Rosin, fumarated, sodium salt
CAS No. 68649-83-2, Rosin, fumarated, potassium salt
CAS No. 85409-27-4, Rosin, maleated, potassium salt

This summary encompasses data previously described in the Test Plan for these substances as well as newly acquired data. The totality of the data shows that these chemicals are all non-toxic.

All of the members of this group of substances are closely related to rosin, which is a naturally occurring substance found in trees, predominantly pine trees. Rosin is composed primarily of resin acids, a class of tricyclic carboxylic acids, but also contains minor amounts of dimerized rosin, fatty acids and unsaponifiable matter.

The six substances in this subgroup of rosins are all composed of rosin that has been chemically reacted with either fumaric acid or maleic anhydride. Because of the complex nature of their composition, rosin adducts and the rosin adduct salts are considered to be “Class 2” substances.

The rosin adducts are typically utilized as chemical intermediates which, after undergoing further reactions, have numerous uses. For example, the rosin adducts (i.e., non salts) may undergo reactions such as esterification and polymerization and then can be used in the production of a wide variety of derivatives that go into printing inks and surface coatings. The rosin adducts may also be used to form sodium and potassium adduct salts which are used for sizing paper to improve the final finish of the paper and to provide water resistance.

There were essentially no available SIDS data on rosin adducts or adduct salts. Where applicable, PCA conducted physical/chemical property and environmental fate testing on all of the substances in the group. With respect to toxicological testing, PCA elected to treat this group of chemicals as a category for purposes of the HPV program. Therefore, a representative of the category was used for the required ecotoxicity and mammalian toxicity testing.

Rosin, fumarated (CAS# 65997-04-8) was selected as the representative substance in this category for ecotoxicity and mammalian toxicity testing. All of the substances in this category are very similar in chemical composition being either fumarated or maleated adducts of rosin or rosin adduct salts. In addition, the fumarated rosin adduct is the most chemically and thermodynamically stable of the rosin adducts.

The totality of the SIDS data for the substances in this category is briefly summarized below and in Tables 1-3. As shown in these summaries, rosin adducts and adduct salts are all non-toxic in both mammalian and aquatic test systems. These data are described and discussed in the main document. Detailed Robust Summaries of all relevant data are appended to this document.

Physical/Chemical Properties

Physical and chemical properties were determined where appropriate; however, many of these endpoints are either inappropriate or cannot be measured for these compounds:

- Melting or boiling points were not determined because these substances will either will not give a sharp melting point when heated or will decompose before they melt or boil.
- Under ambient conditions, the vapor pressure of these substances is essentially zero and experimental measurement is not possible.
- Water solubility and partition coefficients are summarized in Table 1. It should be noted that although all of the non-salt substances in this category are essentially insoluble in water, considerable effort was undertaken to accurately determine water solubility.
- With respect to the partition coefficient (K_{ow}), the approved method (OECD 117) yields a range of values rather than a single value representative of the mixture as summarized in Table 1. The range of values reflects the partition coefficients of the individual constituents of these complex mixtures.

The details on these test results are provided in the Robust Summaries.

Table 1. Summary of Physical/Chemical and Environmental Fate Data*

Chemical	Required SIDS Endpoints		
	Partition Coefficient	**Water Solubility (mg/l)**	**Percent Biodegradation At 28 Days**
Rosin, fumarated	4.4 – 7.0	9.0	15
Rosin, maleated	1.5 – 7.6	1.38	0.34
Rosin, maleated/fumarated	1.5 – 6.6	0.58	18.92
Rosin, fumarated, sodium salt	1.5 – 6.6	Miscible	48
Rosin, fumarated, potassium salt	3.2 – 6.6	Miscible	50.5
Rosin, maleated, potassium salt	1.4 – 7.9	Miscible	59.2

*No testing was conducted for melting point, boiling point, vapor pressure, hydrolysis, photodegradation, and transport and distribution between environmental compartments as explained in summary document.

Environmental Fate

The SIDS environmental fate endpoints were determined where appropriate; however, many of these endpoints are either inapplicable or cannot be measured for these compounds.

- Photodegradation was not relevant, since the vapor pressure of these compounds is essentially zero and they could not enter the atmosphere.
- Hydrolysis in water was not determined for any of the compounds in this category because all have low water solubility and also lack a functional group that would be susceptible to hydrolysis.
- Transport and distribution between environmental compartments (i.e., fugacity) was not determined due to the inability to provide usable inputs to the required model.
- Biodegradation data are summarized in Table 1 and show that only the rosin adduct salts are somewhat biodegradable in the environment.

The details on these test results are provided in the Robust Summaries.

Ecotoxicity

Fumarated rosin was tested for acute toxicity to fish, daphnia and algae at the maximum measured water solubility. These data are summarized in Table 2 and show that none of the compounds in this category are toxic to algae, daphnia or fish. The details of these test results are provided in the Robust Summaries.

Table 2. Summary of Ecotoxicity Data

Chemical Name	Required SIDS Endpoint		
	Acute Fish 96 hr $NOEL_r$	Acute Daphnia 48 hr $NOEL_r$	Acute Algae 72 hr $NOEL_r$
Rosin, fumarated	1000 mg/l	1000 mg/l	1000 mg/l
Rosin, maleated	C	C	C
Rosin, maleated/fumarated	C	C	C
Rosin, fumarated, sodium salt	C	C	C
Rosin, fumarated, potassium salt	C	C	C
Rosin, maleated, potassium salt	C	C	C

C = Indicates category read-down from available data
$NOEL_r$ = no observed effect loading rate

Mammalian Toxicity

Data on acute toxicity, repeat dose toxicity, genotoxicity, reproductive and developmental effects for fumarated rosin were generated. In addition, an acute toxicity test on rosin, maleated was also conducted. These mammalian toxicity data are summarized in Table 3 and demonstrate that rosin, fumarated is non-toxic. Based on the category approach, results for the test substance (augmented by the acute toxicity results on rosin, maleated) also represent other members of the category. The details of these test results are provided in the Robust Summaries.

Table 3. Summary of Mammalian Toxicity Data

Chemical Name	Required SIDS Endpoints				
	Acute Oral	Repeat Dose	In vitro genetox (Mutation)	In vitro genetox (Chrom. Ab.)[a]	Repro/ Develop
Rosin, fumarated	LD_{50} > 2000 mg/kg	NOEL 91 mg/kg/day	+S9 Neg. -S9 Neg.	+S9 Neg. -S9 Neg.	NOEL 260 mg/kg/day
Rosin, maleated	LD_{50} > 2000 mg/kg	C	C	C	C
Rosin, maleated/fumarated	C	C	C	C	C
Rosin, fumarated, sodium salt	C	C	C	C	C
Rosin, fumarated, potassium salt	C	C	C	C	C
Rosin, maleated, sodium salt	C	C	C	C	C

C = Indicates category read-down from available data.
a = see main document for additional explanation.

Overall Hazard Evaluation and Potential Exposure

For potential human health effects, the totality of the SIDS data demonstrates that rosin, fumarated is non-toxic. Accordingly, based on the category approach, it can be inferred that all of the substances in this group are also non-toxic.

Rosin, fumarated has no acute oral toxicity (i.e., LD_{50} > 2,000 mg/kg), and repeat dose toxicity data demonstrate a no observed effect level (NOEL) of approximately 91 mg/kg/day and a NOEL of approximately 260 mg/kg/day for reproductive/developmental effects. The lack of acute oral toxicity (i.e., LD_{50} > 5,000 mg/kg) for rosin, maleated, is confirmatory of the lack of acute toxicity of the substances in this category.

Consequently, no adverse health consequences would be associated with exposure to any of the rosin adducts or adduct salts. For potential ecotoxicological effects, the data on rosin, fumarated demonstrate that all of the substances in this category are non-toxic to aquatic organisms with the $NOEL_r$ of 1000 mg/l for fish, daphnia and algae.

With respect to potential exposure to the substances in this category, all are consumed almost entirely in the production of other chemical intermediates. Rosin is reacted in a variety of ways to form salts, adducts, esters, dimers and other reaction products which find application in the production of printing inks, adhesives (primarily hot melt packaging adhesives), paper size, and coatings. These uses would be considered non-dispersive in that the rosin derived chemical is reacted or otherwise contained within the article in which it is being used. It is estimated that grater than 80% of the various rosin derivatives are used in the type of applications described above. As such inhalation exposure or volatization to air is minimal due to a lack of vapor pressure for these substances. Exposure in the listed applications is generally limited to dermal contact during the processing, finishing and shipping of the products of which they become a part.

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
Crompton Corporation
Eastman Chemical Co. (including the former Hercules Inc. Resins Division)
Georgia-Pacific Resins Inc.
Hercules 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 Westvaco (includes the former Westvaco)
Packaging Corporation of America
Plasmine Technology, Inc.
Raisio Chemicals
Rayonier
Riverwood International
Smurfit – Stone Container Corporation
Weyerhaeuser Co.

The PCA HPV Task Force filed multiple test plans covering various chemicals. Not all members of the Task Force produce the substances covered by this final submission.

I. Description of Rosin Adducts and Adduct Salts

The Pine Chemicals Association, Inc. (PCA) has sponsored six HPV chemicals known collectively as Rosin Adducts and Adduct Salts. The Test Plan for this group of substances was posted on EPA's HPV website on October 12, 2001, with comments from the EPA and the Physicians Committee for Responsible Medicine (PCRM), posted on March 26, 2002, and February 21, 2002, respectively. After reviewing these comments, PCA prepared a response which was subsequently posted on EPA's HPV website on October 17, 2002.

This group of substances consists of the following:

CAS No. 65997-04-8, Rosin, fumarated
CAS No. 8050-28-0, Rosin, maleated
CAS No. 68554-16-5, Rosin, maleated/fumarated
CAS No. 68201-59-2, Rosin, fumarated, sodium salt
CAS No. 68649-83-2, Rosin, fumarated, potassium salt
CAS No. 85409-27-4, Rosin, maleated, potassium salt

All of the members of this group are either fumarated or maleated adducts of rosin (or their salts). Rosin is a naturally occurring substance found in trees, predominantly pine trees. Rosin is composed primarily of resin acids, a class of tricyclic carboxylic acids, but also contains minor amounts of dimerized rosin, fatty acids and unsaponifiable matter. Six rosins and rosin salts are addressed in another Final Submission.

A. Composition

Overall, all of the rosin adducts are similar in chemical composition, as all the members of this category are derived from rosin and either fumaric acid or maleic anhydride. (The composition of rosin was described in the PCA's test plan for Rosins and Rosin Salts and the reader is referred to that plan for detailed information.) The sodium and potassium rosin adduct salts are simply the rosin adducts that have been reacted with the appropriate base, either sodium hydroxide or potassium hydroxide. These materials are then dispersed in water for commercial applications.

The reaction between a representative rosin and maleic anhydride is shown schematically in Figure 1. As complex mixtures, rosin adducts and adduct salts are all considered Class 2 substances.[1]

1 As defined in the TSCA Inventory, *"In terms of composition, some chemical substances are single compounds composed of molecules with particular atoms arranged in a definite known structure. For purposes of this discussion, such substances will be denoted Class 1 substances. Many commercial chemical substances are not in this class. They may have variable compositions or be composed of a complex combination of different molecules. These substances will be denoted Class 2 substances."*

Rosin adducts are made by heating rosin and the adducting reactant together at a temperature of about 200^{o} C. However, the rosin is not completely converted to the adduct form. The commercial adduct consists of a mixture of rosin adducts and rosin with the final ratio a function of the expected use of the product. Because adducts are always prepared with an excess of rosin, the commercial products will not contain any free fumaric acid or maleic anhydride (Zinkel and Russell 1989).

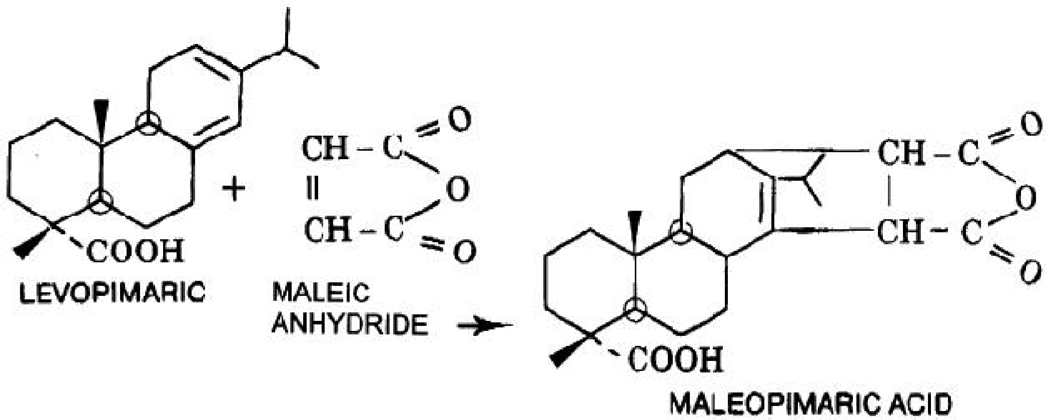

Figure 1. Schematic illustration of the reaction between a representative rosin and maleic anhydride to form a maleated rosin adduct. This reaction, known as a Diels-Alder reaction, requires that both reactants contain double bonds. The reaction product formed between rosin and fumaric acid would be identical to that shown in Figure 1 except that the anhydride group would be open and the resulting carboxyl groups would be in a trans configuration compared to a cis configuration for maleic adducts. That ring would also open when the maleic adduct is converted to a salt.

B. Commercial Uses of Rosin Adducts and Adduct Salts

Fumaric acid or maleic anhydride are commonly added to rosin to increase its softening point, stability, and overall functionality. The rosin adducts are typically utilized as chemical intermediates which undergo further reactions (e.g., esterification and neutralization) to form derivatives that go into printing inks and surface coatings. The sodium and potassium rosin adduct salts are used in paper sizing to improve the final finish of the paper and to provide water resistance. Fortified size (the name given to size containing the adducted material) offers greater efficiencies in the sizing process over unmodified rosin size. A schematic of the production and commercial uses of rosin adducts is shown below in Figure 2.

C. Complexity of Analytical Methodology

All of the substances in this category are Class 2 substances. This, combined with the fact that rosin adducts are essentially insoluble in water and decompose on heating at high temperature, creates a variety of analytical challenges. Gas chromatography of methylated derivatives is the accepted method for the analysis of the members of this category. Because the solubility of rosin, fumarated is very low (approximately 10 ppm) the reliability of the standard analytical method was verified at such low concentrations.

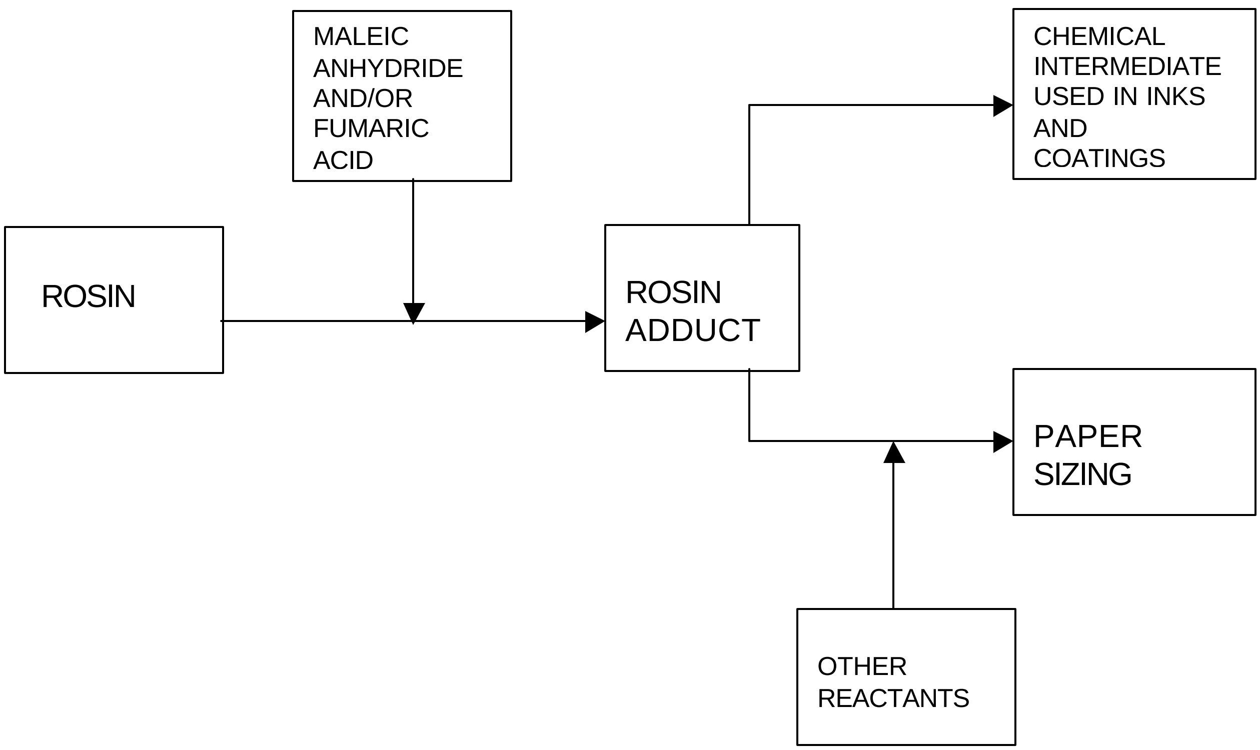

Figure 2. Schematic of rosin adduct production and end use applications

II. Rationale for Selection of Representative Compound for Testing

Rosin, fumarated (CAS# 65997-04-8) was selected as the representative substance in this category for testing for the applicable SIDS ecotoxicity and mammalian toxicity tests. Relevant physical/chemical properties and environmental fate endpoints were determined for all six members of this category.

Based on an understanding of the chemistry involved in the production of fumarated or maleated adducts of rosin, the selection of fumarated rosin as the most representative substance to be tested was based on the following factors.

- All of the substances in this category are very similar in chemical composition being either fumarated or maleated adducts of rosin or rosin salts.
- The fumarated rosin adduct is the most chemically and thermodynamically stable of the adducts.
- These chemicals meet the "family approach" criterion listed by EPA for grouping related chemicals into a category when they are acids or acid salts. The rosin adduct salts are quickly converted into the free adducts when they are neutralized by acid or by dilution, as would be the case 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 fumarated rosin is the appropriate representative test material from this category.

In their comments on the *Test Plan for Rosin Adducts and Adduct Salts,* EPA, while agreeing that the grouping was generally well supported, questioned the justification of fumarated rosin as the representative compound for this category. The concern was that maleated rosin might be more biologically active than fumarated rosin -- the representative test substance. However, at the temperature where rosin/fumaric acid adduction occurs, isomerization and dehydration of a fraction of the fumaric acid to maleic anhydride invariably takes place. This results in a portion of the adduct being rosin/maleic anhydride as demonstrated on the gas chromatogram below (see Fig. 3). The chromatogram clearly shows that approximately 10-20% of the test substance is the rosin/maleic anhydride reaction product. Therefore, any potential effects of the maleic anhydride adduct will be included in the testing of the fumaric acid adduct. Furthermore, testing the fumaric acid adduct is equivalent to testing the maleic anhydride adduct because it is likely that the anhydride adduct will be readily hydrolyzed to the maleic acid adduct in an aqueous media. Since the maleic acid adduct and the fumaric acid adduct are cis-trans isomers, the hypothetical reactivity of the two adducts to proteins or other macromolecules should be equivalent. After carefully considering the EPA comments, PCA concluded that this category should remain as originally proposed with fumarated rosin as the material most representative of the category. Nonetheless, PCA did undertake an additional acute test (OECD 425, the up-down procedure) on maleated rosin (CAS # 68425-08-1) in order to demonstrate that the testing on fumarated rosin represents maleated rosin. The finding of identical LD_{50}'s of >2000 mg/kg for both substances confirmed this judgment.

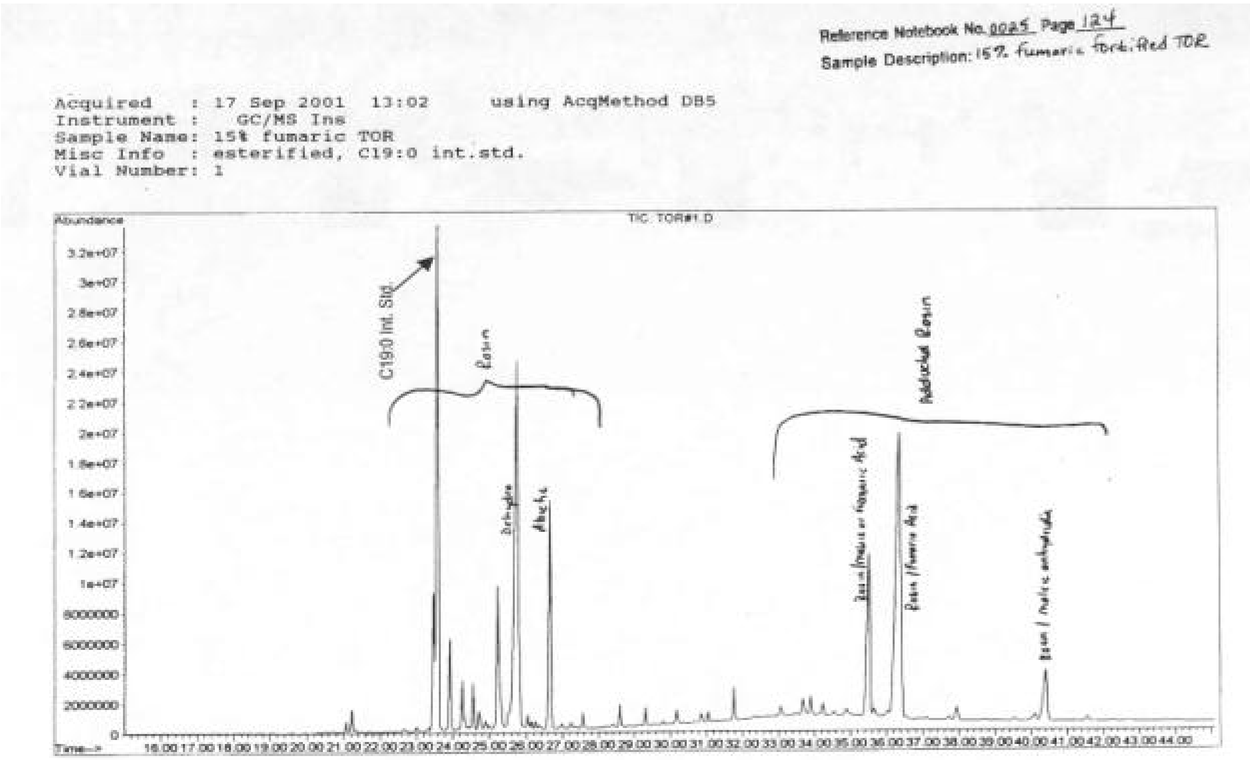

Figure 3. Chromatogram of 15% fumaric fortified tall oil rosin (TOR)

EPA also requested that PCA provide information on the range of adduct to rosin ratios for commercially available products and for the substance to be tested. Their concern was that variations in the ratios of rosin adducts to rosin in the product might have an effect on physicochemical properties, as well as on ecotoxicity and health effects. However, the range of adduct to rosin varies widely depending on the intended end use of the final product thus precluding a summary of fixed ratios. For example, the level of adduct in a rosin based ink resin can vary from about 1 to 15%. Rosin based paper sizes are generally in the range of 3 to 5%. The particular sample of fumarated rosin selected as the test substance is a material having about 15% adduct to ensure that testing was conducted on a typical product, high in adduct and relatively low in rosin.[2]

2 See Final Submission for Rosins and Rosin Salts

III. Summary of Data

Where applicable, physical/chemical property and environmental fate testing was conducted on all of the substances in the group. With respect to toxicological testing, fumarated rosin was selected as a representative of the category and used for the required ecotoxicity and mammalian toxicity testing. Table 4 summarizes the results from all of the testing conducted on the substances in this category.

A. Physicochemical Data

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

Some of these measures are inapplicable given the nature of the materials. Moreover, Class 2 substances are composed of a complex mixture of substances and are often difficult to characterize. Rosin adducts and adduct salts are not only Class 2 substances, but also are derived from natural sources. Therefore, their composition is variable and cannot be represented by a single chemical structural diagram. Due to this "complex mixture" characteristic of rosin adducts and salts, some physical property measurements, such as partition coefficient, do not give single definitive results because the methodology used to determine these properties will actually fractionate or partition the substance into various components. Consequently, some results are likely to be erroneous, difficult to interpret, or meaningless.

1. Melting Point

Due to their complex nature, none of the members of this category have a well-defined melting point. These substances soften when heated and so have softening points rather than a true melting point. The softening point of these compounds can cover a wide range depending on the level of adducting reactant in the substance and the type of reactant. Therefore, these substances do not have specific melting points. The adduct salts decompose on heating, and so melting point has no significance for these materials. Consequently, the melting point of these substances was not measured.

2. Boiling Point

All of the members of this category are produced by high temperature reactions and are non-volatile solids at ambient temperatures. A boiling point under ambient conditions has no significance because these materials will thermally decompose before they boil. Accordingly, measurement of this property was inappropriate for all the substances in this category.

Table 4
Summary of Data
Rosin Adducts and Adduct Salts*

Chemical and CAS#	Required SID Endpoints										
	Partition Coef.	**Water Sol. Mg/l**	**Biodeg. % @ 28 days**	**Acute Fish $NOEL_r$**	**Acute Daphnia $NOEL_r$**	**Acute Algae $NOEL_r$**	**Acute Oral LD_{50}**	**Repeat Dose NOEL**	**Genetox Mutation (*Salmonella*)**	**Genetox (Chrom. Ab.)**	**Repro/ Develop. NOEL**
Rosin, fumarated 65997-04-8	4.4 – 7.0	9.0	15	1000 mg/l	1000 mg/l	1000 mg/l	> 2000 mg/kg	91 mg/kg/day	Neg. ± S9	Not clastogenic ±S9; slight polyploidy at overtly toxic concentra-tion	260 mg/kg/day
Rosin, maleated 8050-28-0	1.5 - 7.6	1.38	0.34	C	C	C	> 2000 mg/kg	C	C	C	C
Rosin, maleated/ fumarated 68554-16-5	1.5 - 6.6	0.58	19	C	C	C	C	C	C	C	C
Rosin, fumarated, sodium salt 68201-59-2	1.5 - 6.6	Miscible in H_2O	48	C	C	C	C	C	C	C	C
Rosin, fumarated, potassium salt 68649-83-2	3.2 - 6.6	Miscible in H_2O	51	C	C	C	C	C	C	C	C
Rosin, maleated, potassium salt 85409-27-4	1.4 - 7.9	Miscible in H_2O	59	C	C	C	C	C	C	C	C

C= category read-down from data on rosin, fumarated; ***No testing was conducted for melting point, boiling point, vapor pressure, hydrolysis, photodegradation and transport and distribution between environmental compartments as explained in the text.

3. Vapor Pressure

Vapor pressures for the rosin adducts (which are solids at ambient temperatures) are effectively zero, and their experimental measurement is inappropriate. In addition, when rosin adduct salts are dissolved or dispersed in water, their solutions or dispersions 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 the six compounds in this category was determined using OECD (105).

Table 5

Chemical	Water Solubility (mg/l)
Rosin, fumarated	9.0
Rosin, maleated	1.38
Rosin, maleated/fumarated	0.58
Rosin, fumarated, sodium salt	Miscible in H_2O
Rosin, fumarated, potassium salt	Miscible in H_2O
Rosin, maleated, potassium salt	Miscible in H_2O

All of these data are presented in detail in the Robust Summaries.

5. Partition Coefficient

The partition coefficients (i.e., K_{ow}) for all of the compounds in this category were determined. Because all of these substances are Class 2 mixtures, the procedure (OECD 107) to determine the K_{ow} yields a range of K_{ow} values rather than a single value representative of the mixture. Thus, the results reflect the partition coefficients of the components rather than the mixture. The partition coefficient data are shown below in Table 6.

Table 6

Chemical	Partition Coefficient (K_{ow})
Rosin, fumarated	4.4 – 7.0
Rosin, maleated	1.5 – 7.6
Rosin, fumarated/maleated	1.5 – 6.6
Rosin, fumarated, sodium salt	1.5 – 6.6
Rosin, fumarated, potassium salt	3.2 – 6.6
Rosin, maleated, potassium salt	1.4 – 7.9

These data are presented in detail in the Robust Summaries.

B. Environmental Fate Data

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

1. Biodegradation

Biodegradability 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 as reflected in the different tests shown in Table 7. One of the chemicals in this category (rosin, fumarated) had existing data on the biodegradation endpoint. Biodegradation for the other five substances in this category was determined. For the adduct salts OECD method 302B was used and for the non-salts OECD method 301B was used. The biodegradation data are shown in Table 7

Table 7

Chemical	Percent Biodegradation At 28 Days	Test Method
Rosin, fumarated	15	OECD 301D
Rosin, maleated	0.34	OECD 301B
Rosin, fumarated/maleated	18.92	OECD 301B
Rosin, fumarated, sodium salt	48	OECD 302B
Rosin, fumarated, potassium salt	50.5	OECD 302B
Rosin, maleated, potassium salt	59.2	OECD 302B

All of these data are presented in greater detail in the Robust Summaries.

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 functional group suitable to be displaced, then the organic compound is considered to be resistant to hydrolysis. None of the substances in this category contains an organic functional group that might be susceptible to this physical degradative mechanism. The maleated rosin adduct will hydrolyze by addition into the acid form, but does not undergo degradation. Therefore, hydrolysis need not be measured.

In addition, low water solubility often limits the ability to determine hydrolysis as a function of pH. The three non-salt rosin adducts 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 rosin adduct salts, in an aqueous medium they hydrolyze (ionize) immediately, but form stable species. Consequently, it is also unnecessary to measure this endpoint for the salts of the rosin adducts.

In commenting on the *Test Plan for Rosin Adducts,* EPA agreed that PCA's approach to physicochemical and environmental fate data *was "acceptable for purposes of the HPV Challenge Program."* Nonetheless, because of the above statement that maleated rosin adduct would hydrolyze by addition into the acid form, EPA requested hydrolysis data on the maleated rosin adduct. After consideration of EPA's suggestion, PCA agreed to conduct a hydrolysis test (OECD 111) on the maleated rosin adduct, if possible. However, the guidelines for conducting this test require a water solubility of at least 10 ppm. Because the water solubility of the maleated rosin adduct is < 10 ppm precluded the conduct of the hydrolysis test on this compound.

3. Photodegradation

Due to their lack of any vapor pressure under ambient conditions, there is essentially 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 was not determined for any of the substances in this category.

4. Transport and Distribution between Environmental Compartments

The transport and distribution between environmental compartments (fugacity) is intended to estimate the ability of a chemical to move or partition in the environment. The determination of this property requires the use of various models. One of the most frequently referenced models is the level III model from the Canadian Environment Modeling Centre at Trent University. Even the simplest of these models requires estimates of solubility, vapor pressure and octanol/water partition coefficient to estimate fugacity for a single component. For complex class 2 substances such as rosin adducts and adduct salts, estimates of any one of these physical parameters for the various known components could span a range of more that a order of magnitude. When combining three or more parameters of equally variable ranges to derive estimates for different environmental media, the variability in the estimate for any given medium could grow geometrically to three or more orders of magnitude. This suggests that any estimates based on arbitrarily selected individual components would be essentially useless for any practical purpose. Add to this the additional fact that there is variability in the chemical composition of these substances and the possible permutations become unmanageable. Consequently, for complex mixtures such as rosin adducts and adduct salts, the mathematical models which rely upon estimates for individual components are of no practical use in predicting environmental fate. Therefore, due to the inability to provide usable inputs to the required model, no determination of transportation and distribution between environmental compartments was undertaken for rosin adducts or adduct salts.

C. Ecotoxicity Data

The basic ecotoxicity data that are part of the HPV Program include acute toxicity to fish, daphnia and algae. While there are some existing data on these endpoints for one of the substances in this category, the inconsistencies in how water samples were prepared for testing these endpoints render these data inadequate. Consequently, acute toxicity to fish, daphnia and algae was tested for fumarated rosin under conditions that maximize the solubility under the specific test exposure conditions, but reduce exposure to insoluble fractions, which may cause nonspecific toxicological effects. 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, was investigated to determine whether they influence toxicological effects. The results of preliminary tests were used to select the most appropriate test conditions for the definitive test for each species.

In its comments on the *Test Plan for Rosin Adducts and Adduct Salts*, EPA suggested that PCA consider a 21-day chronic daphnid reproduction test using a flow-through method with measured concentrations. After considering this suggestion, it was determined not to undertake a 21-day chronic daphnid reproduction test. The methodology for preparing the water for the ecotoxicity testing of fumarated rosin was identical to that used to determine the solubility of this substance. This procedure was adopted in order to ensure that ecotoxicity testing was conducted at the limit of actual water solubility. Given the extremely low solubility of the material (i.e., < 10 ppm), the recommendation for a 21-day test using a flow-through method would be impractical due to the amount of water that would be required and the difficulty in performing the necessary serial analytical measurements. Finally, where there is a risk of emulsions forming inherently (as is likely with these substances), flow through testing in not possible and is not recommended in the OECD (2000) Guidance Document 23 (*Aquatic Toxicity Testing of Difficult Substances and Mixtures*).

EPA also noted that *"insufficient information was provided to explain why the testing of fumarated rosin will adequately describe the aquatic toxicity of the maleated rosin adduct given the latter's ability to hydrolyze to the corresponding diacid."* As described above, the fact that the fumarated adduct contains a substantial amount of the rosin/maleic anhydride reaction product should effectively address this issue.

The ecotoxicity data are summarized in Table 8 below and demonstrate that fumarated rosin is non-toxic to fish, daphnia and algae.

Table 8

Chemical	**Fish 96 hr. *$NOEL_r$**	**Daphnia 48 hr. $NOEL_r$**	**Algae 72 hr. $NOEL_r$**
Rosin, fumarated	1000 mg/l	1000 mg/l	1000 mg/l

*$NOEL_r$ = No Observed Effect Loading Rate

These data are presented in greater detail in the Robust Summaries.

D. Human Health Effects Data

As noted above, EPA suggested that the choice of fumarated rosin as the test substance was not fully supported in the Test Plan. In particular, the Agency was concerned that the *"acylating ability* [of maleated rosin] *allows it to react with proteins and other biomolecules"* which could make this substance more biologically active than the fumarated rosin. However, as explained in greater detail above, testing the fumaric acid adduct is essentially equivalent to testing the maleic acid adduct as any dissolved anhydride will be readily hydrolyzed to the free maleic acid adduct in an aqueous media. The hypothetical reactivity of the maleic acid adduct (an isomer of the fumaric acid adduct) to proteins should be equivalent to the fumaric acid adduct. Nonetheless, in order to address these concerns, an additional acute toxicity test (OECD 425, the up-down procedure) on maleated rosin was conducted to demonstrate the similarity of acute toxicity of the two substances.

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 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 Acute Oral Toxicity Data

Fumarated rosin is non-toxic following acute oral exposure with an acute oral LD_{50} value > 2000 mg/kg. To address the concerns raised by EPA as noted above, maleated rosin was also tested for acute oral toxicity and determined to have an LD_{50} value > 2000 mg/kg. These data are presented in greater detail in the Robust Summaries.

2. Repeat Dose Toxicity

Subchronic repeat 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 doses used in acute toxicity 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 Repeat Dose Toxicity Data

A repeat dose toxicity study using OECD method 422 was conducted on fumarated rosin in conjunction with testing for reproductive and developmental effects. This method uses fewer animals than testing for each endpoint in separate tests.

Fumarated rosin was administered to four groups of 10 male and 10 female Sprague-Dawley rats in the diet at concentrations of 0, 1000, 3000 and 10000 ppm. The males were treated for 2 weeks prior to mating, through mating for a total of 4 weeks of treatment. The females were treated for 2 weeks prior to mating, through mating, gestation and until at least Day 4 of lactation. The animals were monitored for clinical signs, body weight, food consumption, mating and litter performance.

Blood samples were initially taken from 5 males and 5 females per group for laboratory investigations. Males were again sampled during week 5 and females on day 6 or 7 of lactation. All animals were submitted for necropsy, which included weighing major organs. Histopathology was conducted on tissues from 5 males from control and high dose groups, and 6 females from control and 10 females from the high dose group.

At 10000 ppm, the mean number of implants per pregnancy was slightly decreased with a subsequent reduction in litter size and litter weight. None of these effects were significantly different from controls. There were no obvious effects of treatment on mating performance, duration of gestation, litter size and pup weight in animals treated at 1000 and 3000 ppm. At 3000 and 10000 ppm, there was a decrease in mean body weight gain and food consumption in both sexes. There were no obvious effects on body weight gain or food consumption in animals treated at 1000 ppm.

Under the conditions of this study, maternal toxicity was exhibited at levels of 3000 and 10000 ppm, but there were no clear effects of toxicity at 1000 ppm. Therefore the parental No Observed Effect Level (NOEL) was considered to be 1000 ppm (91 mg/kg) while for reproductive parameters the NOEL was considered to be 3000 ppm (260 mg/kg). These data are presented in greater detail in the Robust Summaries.

3. Genotoxicity – In vitro

Genetic testing is conducted to determine the effects of substances on genetic material (i.e., DNA and chromosomes). Genetic mutations are commonly measured in bacterial and mammalian cells, and the HPV program calls for completing both types of tests. Fumarated rosin was tested for genotoxicity in bacteria (OECD 471) and *in vitro* in mammalian cells (OECD 473). The genotoxicity data are summarized in Table 9 below and demonstrate that fumarated rosin is non-genotoxic in bacterial cells and non-clastogenic in mammalian cells. However, in mammalian cells, fumarated rosin induced polyploidy (i.e., a cell containing multiples of the normal number of chromosomes) only at overtly toxic concentrations.

Table 9

Chemical	**Ames *Salmonella***		**Chromosomal Aberration**	
	+S9	**-S9**	**+S9**	**-S9**
Rosin, fumarated	Neg.	Neg.	Neg.	Neg.

These data are presented in greater detail in the Robust Summaries.

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 repeat dose study (OECD 421 or OECD 422, respectively).

Summary of Reproductive and Developmental Toxicity Data

Fumarated rosin was tested for reproductive and developmental toxicity using OECD method 422, in conjunction with testing for repeat dose toxicity. Combining the testing in a single protocol requires the use of fewer animals. The results of this test are summarized above under repeat dose toxicity. As noted in that summary, fumarated rosin at doses of 3000 and 10000 ppm resulted in maternal toxicity as evidenced by decreased mean body weight gain and food consumption in both sexes. However, only at a dose of 10000 ppm was there a slight decrease in the mean number of implants per pregnancy with a subsequent reduction in litter size and litter weight. These findings were likely secondary to maternal food consumption and body weight effects. The No Observed Effect Level (NOEL) for reproductive/developmental effects was 3000 ppm (260 mg/kg/day). These data are presented in greater detail in the Robust Summaries.

IV. Category Justification: Validation of Rosin, Fumarated as Representative of Other Category Members for SIDS Endpoints

All of the rosin adducts or adduct salts are similar in chemical composition since all the substances in this category are derived from rosin and either fumaric acid or maleic anhydride. The sodium and potassium rosin adduct salts are simply the rosin adducts that have been reacted with the appropriate base, either sodium hydroxide or potassium hydroxide and then dispersed in water.

Rosin adducts are made by heating rosin and the adducting reactant together. Because the rosin is not completely converted to the adduct form, the resulting adduct consists of a mixture of rosin adducts and rosin with the final ratio a function of the expected use of the product. Because adducts are always prepared with an excess of rosin, no free fumaric acid or maleic anhydride is contained in commercial products. In addition, fumarated rosin also contains a substantial proportion of the maleated rosin adduct. This is due to the fact that at the temperature where rosin/fumaric acid adduction occurs, isomerization and dehydration of a fraction of the fumaric acid to maleic anhydride invariably takes place. This results in approximately 10-20% of the fumarated rosin adduct being rosin/maleic anhydride.

Therefore, any potential effects due to maleic anhydride adduct are included in the testing of the fumaric acid adduct. Thus, testing the fumaric acid adduct is essentially equivalent to testing the maleic anhydride adduct because it is likely that the anhydride adduct will be readily hydrolyzed to the maleic acid adduct in an aqueous media (i.e., the maleic acid adduct and the fumaric acid adduct are cis-trans isomers). An additional acute toxicity test on maleated rosin was conducted in order to demonstrate that the testing on fumarated rosin represents both substances. The finding of identical LD_{50}'s of >2000 mg/kg for both substances confirmed this judgment. In summary, based on adequate toxicity data and a detailed understanding of the composition of the six substances in this category, the data on rosin, fumarated (augmented by acute toxicity data on rosin, maleated) can be reliably extrapolated to the entire category thereby validating the composition of the category.

V. Hazard Characterization of Rosin Adducts and Adduct Salts

For potential human health effects, the totality of the SIDS data demonstrates that fumarated rosin is non-toxic. Because all of the chemicals in this group are closely related to rosin, fumarated, as well as the fact that all members of this group are qualitatively similar in chemical composition, based on the category approach, it can be inferred that all of the substances in this group are also non-toxic.

Fumarated rosin has no acute oral toxicity (i.e., LD_{50} > 2,000 mg/kg), and repeat dose toxicity data demonstrate a no observed effect level (NOEL) of approximately 91 mg/kg/day. This was based on reduced food consumption and body weight at the two highest doses used. There was no evidence of reproductive or developmental toxicity in the screening test (OECD 422) conducted in conjunction with the repeat dose toxicity study with a NOEL of 260 mg/kg/day; the only finding of note was a decrease in implantation sites with subsequent decreased litter size and weight at a dose of 735 mg/kg/day, which was likely due to reduced maternal food intake and body weight deficits. The lack of acute oral toxicity (i.e., LD_{50} > 2000 mg/kg) for maleated rosin is confirmatory of the lack of acute toxicity of the substances in this category. *In vitro* genotoxicity test results show no evidence of mutagenicity in *Salmonella* (i.e., Ames test) or chromosomal aberrations in Chinese hamster ovary (CHO) cells for fumarated rosin. A slight increase in the number of polyploidy cells was evident only at concentrations of fumarated rosin that were overtly toxic to the cells in the absence of metabolic activation. Consequently, no adverse health consequences would be associated with any anticipated exposures to rosin adducts or adduct salts.

With respect to potential ecotoxicological effects, the totality of SIDS data on fumarated rosin, the representative substance in this category, demonstrate that the substances in this category are non-toxic to aquatic organisms including fish, daphnia and algae. The No Observed Effect Loading Rate ($NOEL_r$) for fumarated rosin on fish, daphnia and alga was 1000 mg/l.

VI. Potential Exposure to Rosin Adducts and Adduct Salts

This brief summary provides an overview of market end uses and potential exposure to products derived from tall oil, a major feed stock to the pine chemicals industry with emphasis on rosin adducts and adduct salts. This information along with hazard data developed as part of the High Production Volume Chemical Testing Program is useful in evaluating the potential risks (if any) that might be associated with various uses of rosin adducts and adduct salts.

During the process of pulping coniferous trees to make paper, sodium salts of chemicals occurring naturally in the trees are produced as a co-product. When acidulated, this soap becomes tall oil. Typically, tall oil is a mixture of 25–35% rosin acids and 45–55% fatty acids with the balance being neutral compounds. Tall oil can be further processed or separated into its major components by a process of high temperature low pressure distillation. The recovery and distillation of tall oil began on a commercial scale in the mid twentieth century. As the pulp and paper industry has expanded globally so has the processing of tall oil, and the production of tall oil derivatives. At the present time there are 10 companies operating a total of 19 tall oil distillation plants in 10 countries.

Rosin derived from tall oil is consumed almost entirely in the production of other chemical intermediates. Depending on specific needs, rosin is reacted in a variety of ways to form salts, adducts, esters, dimers and other reaction products which find application in the production of printing inks, adhesives (primarily hot melt packaging adhesives), paper size, and coatings. These uses would be considered non-dispersive in that the rosin derived chemical is reacted or otherwise contained within the article in which it is being used. It is estimated that greater than 80% of the various rosin derivatives including adducts and their salts are used in the above type of applications where exposure is limited to contact with the article in which the rosin product is contained. As such inhalation exposure or volatization to air is minimal. Exposure in the listed applications is generally limited to dermal contact during the processing, finishing and shipping of the products of which they become a part

Human exposure is limited by the fact that most tall oil chemicals, including rosin adducts and salts are industrial intermediates consumed in the production of other chemicals As such there is little, if any, potential for exposure of the general consumer population. Environmental exposure is limited by the fact that the chemical processes used in the tall oil industry are essentially closed system processes where temperature and pressure are carefully controlled.

Environmental releases from tall oil processing plants are limited to (1) treated waste water discharge, and (2) ambient emissions following treatment with scrubbers or thermal oxidizers. Waste water can be generated from operation of the plant pressure control system or from minor spills and leaks associated with the process and/or handling of chemical products and routine housekeeping activities. In all cases the waste water is collected, the stream is treated to remove any free oil, and is then discharged into a larger biological waste treatment facility (either municipal treatment system or the treatment system of the paper mill). Any air emissions generated from the pressure control system or from the storage and transfer of various streams, are generally collected and treated in chemical scrubbers or thermal oxidizers.

The entire array of tall oil based chemicals and their related processing steps are best depicted by a “family tree” or flow diagram rather than a listing of discrete independent chemicals. Such a diagram demonstrates how various “parent” chemicals are consumed in the production of down stream chemicals. Consequently, it is inappropriate to sum production volumes. Figure 4 is a representation of the “family tree” for tall oil products and the relationship between these products. Based on industry data approximately 95% of tall oil is consumed during the production of other downstream products.

Table 10 illustrates general use categories and potential exposures to tall oil and related substances. Of the various tall oil products, it is estimated that greater than 95% are consumed as intermediates in the production of the wide array of products derived from tall oil. Volatilization to air and hence inhalation exposure would be minimal due to the essential lack of a vapor pressure for these substances. Exposure in all of these industrial applications is generally limited to dermal contact during manufacture of the numerous products derived from tall oil and related substances, including rosin adducts and adduct salts. The only other potential exposure to any of the substances in this category occurs during their production from activities such as changing reaction vessels, sampling for quality control, transferring material from one work area to another, loading and unloading bulk containers, changing filters, and cleaning equipment. The lack of water solubility of rosin adducts demonstrates that they are not bioavailable to aquatic organisms; this is confirmed by the lack of ecotoxicity to fish, daphnia, and algae.

Figure 4
U.S. TALL OIL INDUSTRY

PRODUCTION & MARKET DISTRIBUTION
POUNDS/YEAR (000)

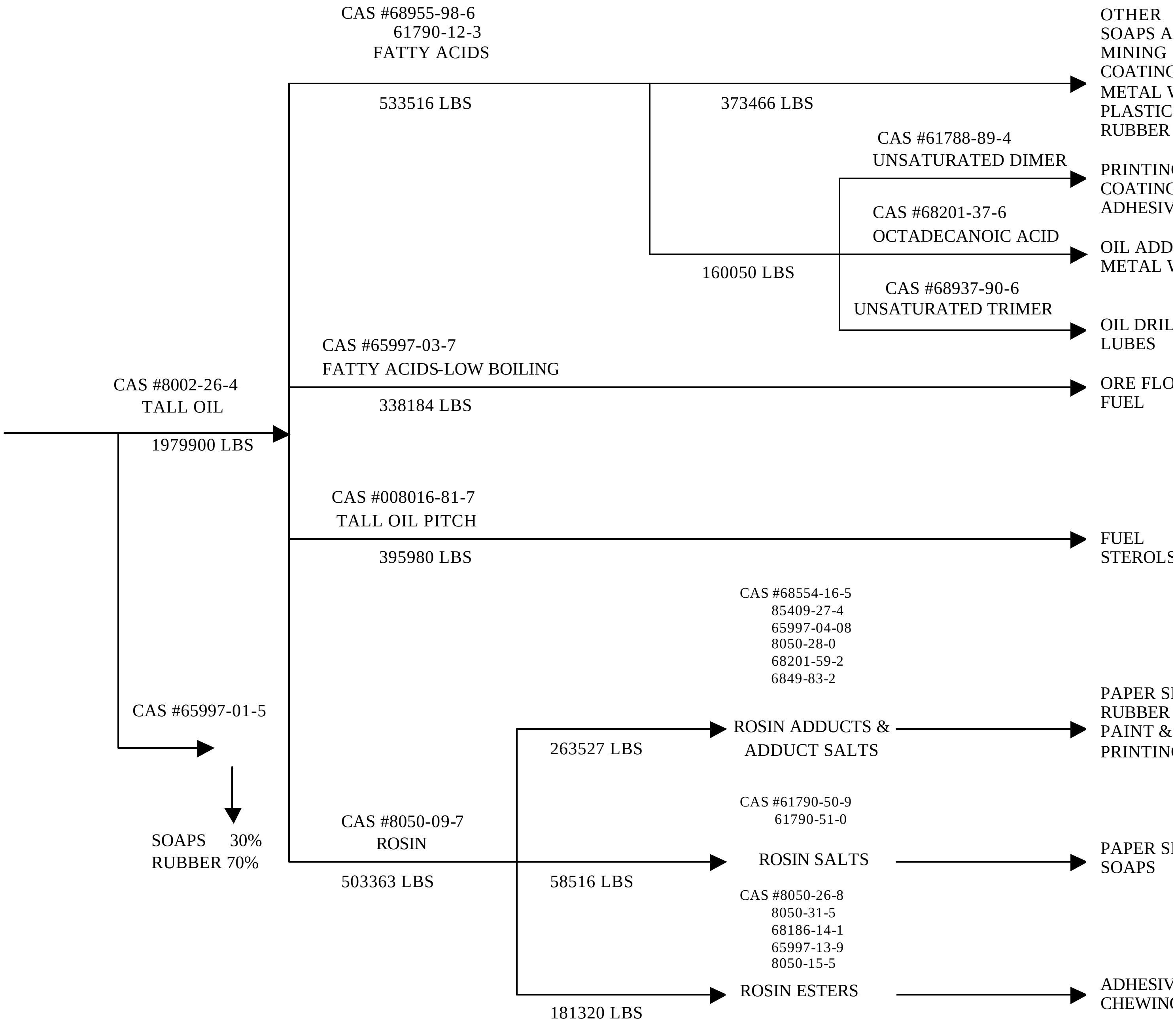

Table 10

Distribution, Application and Potential Occupational Exposure to Rosin Adducts and Adduct Salts

Substance	CAS #	Primary Function	Use Category	Major End Use Application	%
Rosin, fumarated Rosin, maleated Rosin, maleated/fumarated Rosin, fumarated, sodium salt Rosin, fumarated, potassium salt Rosin, maleated, potassium salt	65997-04-8 8050-28-0 68554-16-5 68201-59-2 68649-83-2 85409-27-4	Chemical intermediate	Industrial; site limited	Paper sizing Rubber Paints & coatings Printing inks	19 15 6 60

References

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