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Group 25 - Succinimide Dispersants

October 9, 2002

HIGH PRODUCTION VOLUME (HPV)

CHALLENGE PROGRAM

TEST PLAN

For

SUCCINIMIDE DISPERSANTS

**Prepared by
The American Chemistry Council
Petroleum Additives Panel
Health, Environmental, and Regulatory Task Group**

October 9, 2002

**LIST OF MEMBER COMPANIES IN THE
HEALTH, ENVIRONMENTAL AND REGULATORY TASK GROUP**

**The Health, Environmental, and Regulatory Task Group (HERTG) of the American
Chemistry Council Petroleum Additives Panel includes the following member companies:**

B.P. PLC

Chevron Oronite Company, LLC

Crompton Corporation

Ethyl Corporation

ExxonMobil Chemical Company

Ferro Corporation

Infineum

The Lubrizol Corporation

Rhein Chemie Corporation

Rhodia, Inc.

EXECUTIVE SUMMARY

The American Chemistry Council Petroleum Additives Panel Health, Environmental, and Regulatory Task Group (HERTG), and its member companies, hereby submit for review and public comment their test plan for the “*Succinimide dispersant*” category of chemicals under the United States Environmental Protection Agency High Production Volume (HPV) Chemical Challenge Program. This report should be read in its entirety in order to obtain an understanding of the chemical category and proposed testing.

Succinimide Dispersant Category. Relying on several factors specified in the EPA guidance document on “Development of Chemical Categories in the HPV Challenge Program,” in which use of chemical categories is encouraged, the following two closely related chemicals constitute a chemical category:

- 2,5-Pyrrolidinedione, 1-[2-[[2-[[2-[(2-aminoethyl)amino]ethyl]amino]ethyl]amino] ethyl]-, monopolyisobutenyl derivatives – (CAS # 67762-72-5), referred to as “mono alkenyl succinimide derivative”.
- Amines, polyethylenepoly-, reaction products with succinic anhydride polyisobutenyl derivatives – (CAS # 84605-20-9), referred to as “bis alkenyl succinimide derivative”.

Structural Similarity. A key factor supporting the classification of these chemicals as a category is their structural similarity. All substances in this category consist of a polyisobutylene succinic anhydride structure with polyethylene polyamine substituent groups.

Similarity of Physicochemical Properties. The similarity of the *physicochemical properties* of these substances parallels their structural similarity. All are dark colored viscous liquids intended for use as components in finished lubricating oils. The use of these substances in finished lubricants requires that they be stable under high temperatures (>100°C). Their low volatility is due to their low vapor pressure, high viscosity, and relatively high molecular weights. The existing information for these substances indicates that they have low water solubility.

Fate and Transport Characteristics. Members of this category have been shown to be poorly biodegradable. Since the members of this category have low water solubility, hydrolysis testing is technically unfeasible. Furthermore, members of the category are resistant to hydrolysis because they lack hydrolyzable moieties. This makes hydrolysis modeling unnecessary. Photodegradation is not expected to cause significant physical degradation of succinimide dispersants. However, computer-modeled data will be developed to adequately characterize the potential atmospheric oxidation potential for members of this category. These substances are not expected to partition into water or into air if released into the environment due to their low water solubility and low vapor pressure, and computer-modeled environmental partitioning data indicates that these substances will partition into soil and sediment.

Toxicological Similarity. Review of existing published and unpublished test data for succinimide dispersants shows the *aquatic and mammalian toxicity* of the two substances within this category are similar and are of a low concern.

Aquatic Toxicology. Data on acute fish toxicity, acute invertebrate toxicity, and alga toxicity were reviewed, and the findings indicate little to no toxicity when appropriate test methods are used. Therefore, the category has been adequately tested for acute aquatic toxicity, and no additional testing is necessary.

Mammalian Toxicology - Acute. Data on acute mammalian toxicity were reviewed, and the findings indicate a low concern for acute toxicity. Data are available for both members of the category indicating that the category has been well tested for acute mammalian effects. Therefore, no additional acute mammalian toxicity testing is necessary.

Mammalian Toxicology - Mutagenicity. Data from bacterial reverse mutation assays and *in vitro* and *in vivo* chromosome aberration studies were reviewed. Data are available for both members of the category, and the findings indicate a low concern for mutagenicity. Therefore, the category has been adequately tested for mutagenicity, and no additional mutagenicity testing is necessary.

Mammalian Toxicology - Subchronic Toxicity. Data from repeated-dose toxicity studies were reviewed. No signs of toxicity were observed following repeated oral or dermal exposure. Data are available for both members of the category. Therefore, the category has been adequately tested for repeated-dose toxicity, and no additional testing is necessary.

Mammalian Toxicology - Reproductive and Developmental Toxicity. Data from a reproductive/developmental toxicity screening study were reviewed. No signs of reproductive or developmental toxicity were observed following repeated oral exposure. These findings can be bridged to the other member of the category. Therefore, the category has been adequately tested for reproductive and developmental toxicity, and no additional testing is necessary.

Conclusion. Based upon the data reviewed for this test plan, the individual physicochemical, environmental fate, and toxicological properties of the proposed succinimide dispersant category members are similar and/or follow a regular, predictable pattern based on structural similarity and can be grouped together.

Test Plan. The test plan for the succinimide dispersant category indicates that no further testing or computer modeling is required. As this test plan was developed, careful consideration was given to the number of animals that would be required for tests included in the proposed plan and conditions to which the animals might be exposed. In consideration of the concerns of some non-governmental organizations about animal welfare, the use of animals in this proposed test plan has been minimized.

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1.0 INTRODUCTION

In March 1999, the American Chemistry Council (formerly the Chemical Manufacturers Association) Petroleum Additives Panel Health, Environmental, and Regulatory Task Group (HERTG), and its participating member companies committed to address certain chemicals listed under the Environmental Protection Agency (EPA) High Production Volume (HPV) Chemical Challenge Program. This test plan follows up on that commitment.

Specifically, this test plan sets forth how the HERTG intends to address physico-chemical, environmental, aquatic and health effects testing information for the following substances:

- 2,5-Pyrrolidinedione, 1-[2-[[2-[[2-(2-aminoethyl)amino]ethyl]amino]ethyl]amino] ethyl]-, monopolyisobutenyl derivatives – (CAS # 67762-72-5), referred to as “mono alkenyl succinimide derivative”.
- Amines, polyethylenepoly-, reaction products with succinic anhydride polyisobutenyl derivatives – (CAS # 84605-20-9), referred to as “bis alkenyl succinimide derivative”.

An analysis of the available data on these chemicals supports the designation of the succinimide dispersants as a “chemical category” as provided in the EPA guidance document entitled, “Development of Chemical Categories in the HPV Challenge Program”. This document provides the basis for that determination, indicates the findings of the data review process, and sets forth a proposed testing plan to satisfy parts of the required test battery for endpoints without data that would be considered adequate under the program.

EPA guidance on the HPV Chemical Challenge Program indicates that the primary purpose of the program is to encourage “the chemical industry . . . to voluntarily compile a Screening Information Data Set (SIDS) on all chemicals on the US HPV list.” (EPA, “Development of Chemical Categories in the HPV Challenge Program,” p. 1) At the same time, EPA recognizes that the “large number of chemicals to be tested [about 2800 HPV chemicals] makes it important to reduce the number of tests to be conducted, *where this is scientifically justifiable.*” (*Id.*, p. 1) [emphasis added] The next part of the guidance explains where this would be scientifically justifiable:

One approach is to test closely related chemicals as a group, or category, rather than test them as individual chemicals. In the category approach, *not every chemical needs to be tested for every SIDS endpoint.* However, *the test data finally compiled* for the category must prove adequate to support a screening level hazard-assessment of the category and its members. That is, the *final data set* must allow one to estimate the hazard for the untested endpoints, *ideally* by interpolation between and among the category members. In certain cases, where toxicity is low and no upward trend is expected, extrapolation to the higher category members may be acceptable. (*Id.*, p. 1) [emphasis added].

EPA guidance goes on to state, “The use of categories is encouraged in the Challenge Program and will have a number of benefits.” (*Id.*, p. 1) Among the benefits identified in the guidance for the use of categories are “a reduction in testing will result in fewer animals used to test a category of chemicals as opposed to doing each test on each individual chemical,” and “there will be . . . economic savings since less testing may be needed for chemicals considered as a category.” (*Id.*, p. 1) That guidance also states that categories “accomplish the goal of the Challenge Program – to obtain screening level hazard information – through the strategic application of testing to the category.” (*Id.*, p. 2)

A similarly stated intent “to reduce the number of tests to be conducted, *where this is scientifically justifiable*” was articulated by the Agency in its draft guidance document titled, “The Use of Structure Activity Relationships (SAR) in the High Production Volume Chemicals Challenge Program.” [emphasis added].

The EPA “Chemical Categories” guidance sets forth a definition of what constitutes a “chemical category, for the purposes of the Challenge Program”. Specifically, that definition states that a chemical category under the HPV Challenge Program “is a group of chemicals whose physicochemical and toxicological properties *are likely to be similar or follow a regular pattern as a result of structural similarity.*” (*Op. Cit.*, p. 2) [emphasis added].

According to the guidance, what is important is that the “structural similarities [among members of the group] *may create a predictable pattern in any or all of the following parameters: physicochemical properties, environmental fate and effects, and human health effects.*” (*Id.*, p. 2) [emphasis added]. Thus, it is not necessary for the chemicals in a category to be similar in all respects. Nor must there be conclusive proof that the chemicals in the postulated category will behave identically across all relevant parameters. All that is required for an acceptable category under the HPV Challenge Program is that there be a *likelihood* of similarity of physicochemical and toxicological properties or a *likelihood* that the chemicals will in some pertinent respect follow a regular pattern as a result of their structural similarity.

In identifying the succinimide dispersant category, the six-step process set out in the EPA guidance on category development was followed. As the information below indicates, the succinimide dispersant chemicals clearly satisfy the standards established in that guidance for use of a chemical category:

Step 1: group structurally similar chemicals into a putative category

Step 2: gather relevant published and unpublished literature for each member of the category

Step 3: evaluate the compiled data for adequacy in accordance with the EPA guidance documentation

Step 4: construct matrices of SIDS endpoints versus category members arranged so as to indicate the structural progression of the category (in this case, by increasing molecular weight)

Step 5: evaluate the data to determine whether there is a correlation between category members for each SIDS endpoint

Step 6: make available to EPA, and to the public for review, this test plan including the foregoing category definition and rationale and the following data assessment with the proposed testing scheme for the succinimide dispersants.

2.0 CHEMISTRY OF SUCCINIMIDE DISPERSANTS

2.1 DESCRIPTION

Succinimide dispersants consist of a polyisobutylene hydrocarbon chain connected to a polyethylene polyamine substituent group by a succinic anhydride linking group. The polyisobutylene portion of the molecule is a saturated branched hydrocarbon of that may vary from 950 to 2500 daltons in molecular

weight. The polyethylene polyamine substituent group may vary from diethylenetriamine to a “heavy polyamine”, which contains from 5 to 10 ethylene amine groups. The chemical names and CAS numbers for the members of the succinimide dispersant category are presented in Table 1 and the chemical structures in Table 2.

These substances are prepared by reacting polyisobutylene succinic anhydride with a polyethylene polyamine in highly refined lubricating base oil. Thus the “active ingredients” are never isolated during the life cycle of these substances. This is done for two reasons: 1) the kinetics of the chemical reactions used in the manufacturing process are optimized when highly refined lubricating base oils are used as the reaction solvent, and 2) lubricant additives diluted in highly refined lubricating base oils are required to control viscosities during blending with other additives or with additional highly refined lubricating base oil to make finished lubricants. To meet the required viscosities for these substances, the concentration of highly refined lubricating base oil ranges from 25 wt% to 35 wt%.

There are two structural variables that influence the molecular weight of the category members and consequently their bioavailability and toxicity: the polyethylene polyamine and the isobutylene substituents. As mentioned above, the polyethylene polyamine substituent group may vary from diethylenetriamine (102 daltons in molecular weight) to a “heavy polyamine” (231 to 446 daltons in molecular weight). Although the distribution frequency of the number of ethylene amine groups in heavy polyamine ranges from 5 to 10, the relative proportions of each distribution frequency are expected to be similar to meet industry performance requirements. However, the structural variable that has the greatest impact on the molecular weight of these molecules is the molecular weight of the polyisobutylene group. The carbon chain length of the 950 dalton polyisobutylene is approximately C68, and the carbon chain length of the 2200 dalton polyisobutylene is approximately C160. Linking more than one polyisobutylene succinic anhydride group to the polyethylene polyamine to form a “bis” molecule essentially doubles the molecular weight. As the alkyl carbon chain increases and molecular weight increases, bioavailability is expected to decrease. In addition, as the alkyl carbon chain length increases, water solubility is expected to decrease. Thus, aquatic toxicity is expected to decrease with increasing alkyl carbon chain length. Consequently, the members of this category are arrayed by increasing molecular weight, which is primarily dependent on polyisobutylene carbon chain length, and, to a lesser extent, on the number of ethylene amine groups in the polyethylene polyamine.

2.2 PHYSICOCHEMICAL PROPERTIES

The physicochemical properties of the members of the succinimide dispersant category are presented in Table 3. Succinimide dispersants, as manufactured and distributed in commerce in highly-refined lubricating base oil, are dark brown viscous liquids. These substances exist in the absence of base oil as idealized structures only. Attempts to “de-oil” succinimide dispersants result in substances that are solid materials that do not retain their original chemical structure and physico-chemical properties that are critical for performance. Therefore, the measured physico-chemical properties presented in Table 3 are derived from a mixture of the succinimide dispersant in highly refined lubricating base oils, and the modeled physico-chemical data are based on the idealized structure.

2.2.1 Molecular Weight

The members of the category range in molecular weight from 1134 to 3160 daltons. The two structural variables that influence the molecular weight of the category members have been

discussed above. Due to the influence of molecular weight on water solubility and bioavailability, the members of the category are arrayed in order of increasing molecular weight in Tables 3-9.

2.2.2 Specific Gravity

Available specific gravity data are presented in Table 3. The specific gravity of the members of the category as manufactured in highly refined lubricating base oil is approximately 0.91 @ 60°F.

2.2.3 Melting Point and Boiling Point

Succinimide dispersants, as manufactured in highly refined lubricating base oils, are liquid at ambient temperature. The use of these substances in finished lubricants requires that they be thermally and chemically stable under high temperatures (>100°C). Typically, the petroleum base stocks in these substances boil at temperatures above 300°C. Modeling data for the theoretical “de-oiled” substances indicates that the boiling point is 841.5°C to 1271.5°C.

2.2.4 Vapor Pressure and Viscosity

As mentioned above, attempts to “de-oil” succinimide dispersants result in substances that are solid materials. Thus, the vapor pressure of the succinimide dispersants as manufactured in highly refined lubricating base oil can be estimated from the vapor pressure of the base oil in which they are manufactured. Typically, highly refined lubricating base oils have a low vapor pressure, < 10¹⁰ Pa @ 25°C (Table 3). In addition, the viscosity of these substances is also dependent on that of the highly refined lubricating base oil used in their manufacture. Measured viscosities range from 1100 to 1330 cSt @ 40°C (Table 3). Thus, the low volatility of the members of the succinimide dispersants category is due to their low vapor pressure, high viscosity, and high relative molecular weights.

2.2.5 Water Solubility and Octanol-Water Partition Coefficients

The water solubility of a representative succinimide dispersant, mono alkenyl succinimide derivative (CAS # 67762-72-5), was measured at 0.125 mg/L. This value indicates that succinimide dispersant are generally regarded to be insoluble in water. A log P value of 6.7 was also determined for this derivative (Table 3).

3.0 USES OF SUCCINIMIDE DISPERSANTS

Succinimide dispersants are used to formulate finished lubricating oils including all types of automotive and diesel engine crankcase oils, air and water-cooled two-cycle engine oils, natural gas engine oils, marine trunk piston engine oils, and medium-speed railroad diesel engine oils. They are used as ashless dispersants to inhibit colloidal particle-to-particle aggregation by an adsorbed film mechanism, and they solubilize oil-insoluble liquids. Succinimide dispersants are generally sold to finished oil blenders in additive packages, where the concentration ranges from 5 to 50 wt.%. These additive packages are then blended into finished oils where the typical concentration of succinimide dispersant ranges from 0.5 to 10 wt.% in the finished oil.

Succinimide dispersants in this category are manufactured at plants owned by members of the HERTG and blended into additive packages at plants owned by members of the HERTG and their customers. Finished lubricants are blended at facilities owned by HERTG's customers. Additive packages are shipped to customers in bulk in ships, isocontainers, railroad tank cars, tank trucks or in 55-gallon steel drums. The bulk additive packages are stored in bulk storage tanks at the customer blending sites. Finished oils are blended by pumping the lubricating oil blend stocks and the additive package from their storage tanks through computer controlled valves that meter the precise delivery of the components into a blending tank. After blending, the finished lubricant products are sold in bulk and shipped in tank trucks to large industrial users, such as manufacturing facilities and facilities that service truck fleets and passenger motor vehicles. Finished lubricants are also packaged into 55-gallon drums, 5-gallon pails, and one-gallon and one-quart containers for sale to smaller industrial users. Sales of lubricants in one-gallon and one-quart containers to consumers at service stations or retail specialty stores also occur.

Based on these uses, the potentially exposed populations include (1) workers involved in the manufacture of succinimide dispersants, blending them into additive packages, and blending the additive packages into finished lubricants; (2) quality assurance workers who sample and analyze these products to ensure that they meet specifications; (3) workers involved in the transfer and transport of succinimide dispersants, additive packages or finished lubricants that contain them; (4) mechanics who may come into contact with both fresh and used lubricants while working on engines or equipment; (5) gasoline station attendants and consumers who may periodically add lubricating oil to automotive crankcases; and (6) consumers who may change their own automotive engine oil. The most likely route of exposure for these substances is skin and eye contact. Manufacturing, quality assurance, and transportation workers will likely have access to engineering controls and wear protective clothing to eliminate exposure. Mechanics wear protective clothing, but often work without gloves or eye protection. Gasoline station attendants and consumers often work without gloves or other protective equipment. The most likely source of environmental exposure is accidental spills at manufacturing sites and during transport.

4.0 EVALUATION OF AVAILABLE PUBLIC AND COMPANY DATA

4.1 Environmental Fate Data

4.1.1 Physicochemical Properties Relevant to Environmental Fate

In order to understand the environmental fate of a substance, one must understand how that substance can potentially partition among environmental compartments (i.e., air, soil, sediment, suspended sediment, water, and biota). The physicochemical properties of a substance influence the way in which a substance will degrade. The important environmental degradation pathways include biodegradation, hydrolysis, and photodegradation. Biodegradation is a measure of the potential of a compound to be degraded by microorganisms. 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. Photodegradation is the degradation of a chemical compound as a result of absorption of solar radiation.

The physicochemical properties of the parent substance will influence the way in which these substances may partition among environmental compartments. Substances characterized by a low vapor pressure do not partition into air to any great extent. Similarly, substances that are characterized by low water solubility do not partition extensively into water. Substances that do not partition into air and water to any great extent tend to partition into soil and sediments.

4.1.2 Biodegradability

4.1.2.1 Test Methodologies

Chemical biodegradation involves a series of microbially-mediated reactions that may require many kinds of microorganisms acting together to degrade the parent substance. There are several standard test methods, which measure primary degradation (i.e., loss of parent chemical) or ultimate degradation (i.e., complete utilization of the substance to produce carbon dioxide, water, mineral salts, and microbial biomass). Primary degradation can be determined analytically by measuring dissolved organic carbon (DOC) for water-soluble chemicals, infrared absorbance, or by a chemical-specific detection method. Ultimate degradation (also called mineralization) can be determined by measuring oxygen consumption or carbon dioxide evolution relative to the theoretical levels that can be achieved based on an elemental analysis of the chemical under investigation.

4.1.2.2 Summary of Available Data

Biodegradation data for the succinimide dispersant category are summarized in Table 4. One member of the category have been adequately tested.

The Modified Sturm Test (OECD Guideline 301B, *CO₂ Evolution Test*) was used to evaluate the biodegradability of bis alkenyl succinimide derivative (CAS # 84605-20-9). After the 28-day test, the extent of biodegradation was 16% based on carbon dioxide evolution.

4.1.2.3 Data Assessment and Test Plan for Biodegradability

One biodegradation test has been conducted on one of the two members of the succinimide dispersant category, and the results indicate that this substance is poorly biodegraded.

Adequate biodegradation data exist for one of the two substances in the succinimide dispersant category. These data will be bridged to both category members due to the presence of predominantly branched polyisobutylene chains in these substances, thereby characterizing the biodegradability of the entire category.

4.1.3 Hydrolysis

4.1.3.1 Test Methodologies

The potential for a substance to hydrolyze in water is assessed as a function of pH (OECD Guideline 111, *Hydrolysis as a Function of pH¹*). When an organic molecule undergoes hydrolysis, a nucleophile (water or hydroxide ion) attacks an electrophile and

¹ Organization for Economic Cooperation and Development (OECD) (1993) OECD Guidelines for Testing of Chemicals. OECD. Paris, France.

displaces a leaving group (e.g., halogen, phenoxide).² Potentially hydrolyzable groups include alkyl halides, amides, carbamates, carboxylic acid esters and lactones, epoxides, phosphate esters, and sulfonic acid esters³. The lack of a suitable leaving group renders compounds resistant to hydrolysis.

4.1.3.2 Summary of Available Data

There are no published or unpublished hydrolysis studies for members of the succinimide dispersant.

4.1.3.3 Data Assessment and Test Plan for Hydrolysis

Although these substances contain amide functional groups that are susceptible to hydrolytic degradative mechanisms³, testing these substances for hydrolysis as a function of pH is not needed to adequately evaluate this endpoint. A technical discussion will be developed as a robust summary that characterizes the potential for succinimide dispersants in this category to undergo hydrolysis. Therefore, no hydrolysis testing is proposed for the HPV Challenge Program (Table 4).

4.1.4 Photodegradation

4.1.4.1 Test Methodologies

Photodegradation can occur as a result of direct and indirect mechanisms. A prerequisite for direct photodegradation is the ability of one or more bonds within a chemical to absorb ultraviolet (UV)/visible light in the 290 to 750 nm range. Light wavelengths longer than 750 nm do not contain sufficient energy to break chemical bonds, and wavelengths below 290 nm are shielded from the earth by the stratospheric ozone layer. In comparison, indirect photodegradation also requires light energy as well as a series of chemical reactions that include a reaction of the parent molecule with hydroxyl radicals.

Direct photochemical degradation occurs through the absorbance of solar radiation by a chemical substance. If the absorbed energy is high enough, then the resultant excited state of the chemical may lead to its transformation. Simple chemical structures can be examined to determine whether a chemical has the potential for direct photolysis in water. First order reaction rates can be calculated for some chemicals that have a potential for direct photolysis using the procedures of Zepp and Cline (1977). [Zepp, R. G., and D. M. Cline. 1977. Rates of Direct Photolysis in the Aqueous Environment. *Environ. Sci. Technol.* 11:359.366.]

To develop information that characterizes the potential of the members in this category to undergo direct photochemical degradation, the existing substance chemical composition has been evaluated and a subset of chemicals has been selected that adequately represent substances in this category.

Although substances in this category have a low potential to volatilize to air where they can react with hydroxyl radicals (OH⁻), photodegradation can be estimated using models

² W. Lyman et al. (1990) *Handbook of Chemical Estimation Methods*. Chapter 8.

³ W.J. Lyman, W.F. Reehl, and D.H. Rosenblatt. (1982) *Handbook of Chemical Property Estimation Methods*. McGraw-Hill Book Co. New York, NY, USA.

accepted by the US EPA. An estimation method accepted by the US EPA includes the calculation of atmospheric oxidation potential (AOP) to characterize this fate property.

The computer program AOPWIN (atmospheric oxidation program for Microsoft Windows) (EPIWIN, 1999) is used by the US EPA OPPTS (Office of Pollution Prevention and Toxic Substances). This program calculates a chemical half-life based on an overall OH- reaction rate constant, a 12-hr day, and a given OH- concentration.

4.1.4.2 Summary of Available Data

The atmospheric oxidation potential of the selected chemical structures for members of the succinimide dispersant category is presented in Table 2 of Appendix I. The modeling data indicates that the members of this category have a very low potential to photodegrade.

4.1.4.3 Data Assessment and Test Plan for Photodegradation

Modeling data indicate that members of the Succinimide Dispersant category do not undergo photodegradation in the environment. The potential for category members to undergo direct photodegradation has been adequately evaluated, and no further testing is required.

4.1.5 Fugacity Modeling

4.1.5.1 Modeling Methodologies

Fugacity-based multimedia fate modeling compares the relative distribution of chemicals among environmental compartments. A widely used model for this approach is the EQC model⁴.

There are multiple levels of the EQC model. In the document, "Determining the Adequacy of Existing Data", EPA states that it accepts Level I fugacity modeling to estimate transport/distribution values. The EQC Level I model utilizes input of basic chemical properties, including molecular weight, vapor pressure, and water solubility to calculate percent distribution within a standardized environment. EQC Level III model uses these parameters to evaluate chemical distribution based on emission rates into air, water, and soil, as well as degradation rates in air, water, soil, and sediment.

4.1.5.2 Summary of Available Data

Fugacity-based multimedia fate modeling data for members of the succinimide dispersant category are presented in Table 3 of Appendix I. All of the members of this category have low vapor pressure and low water solubility, and the modeling data indicate that they will partition into soil and sediment.

4.1.5.3 Test Plan for Fugacity

The relative distribution of substances within this category among environmental compartments has been evaluated using the Level I model. Data developed using a Level I model indicate that the members of the Succinimide Dispersant category partition into

⁴. Mackay, D., A. Di Guardo, S. Paterson, and C. E. Cowan. 1996. Evaluating the Environmental Fate of a Variety of Types of Chemicals Using the EQC Model. Environ.

soil and sediment. Based on this assessment, the fugacity of the members of the category has been adequately evaluated, and no further work is required.

4.2. ECOTOXICOLOGY DATA

4.2.1 Aquatic Ecotoxicity Testing

4.2.1.1 Test Methodologies

Acute aquatic ecotoxicity tests are usually conducted with three species that represent three trophic levels in the aquatic environment: fish, invertebrates, and algae. The fish acute toxicity test (OECD Guideline 203, *Fish, Acute Toxicity Test*) establishes the lethality of a substance to a fish during a 96-hour exposure period. The acute invertebrate test (OECD Guideline 202, *Daphnia sp., Acute Immobilization Test and Reproduction Test*) establishes the lethality of a substance to an invertebrate, typically a daphnid (*Daphnia magna*), during a 48-hour exposure period. The alga growth inhibition test (OECD Guideline 201, *Alga, Growth Inhibition Test*) establishes the potential of a substance to inhibit alga growth, typically using the freshwater unicellular green algae, *Pseudokirchneriella subcapitata* (formerly called *Selenastrum capricornutum*), during a 96-hour exposure period.

Three test methodologies are commonly used to conduct aquatic toxicity tests; i.e., flow-through, static, and static renewal tests.

In *flow-through tests*, organisms are continually exposed to fresh chemical concentrations in each treatment level in the incoming water and there is greater assurance than with other test methods that the exposure levels and water quality remains constant throughout the test. Although flow-through testing is the preferred method, it is only applicable for chemicals that have adequate water solubility for testing.

In *static tests*, organisms are exposed in the test medium that is not replaced for the duration of the study. There is less assurance that the test concentrations will remain constant because test material can be adsorbed onto test chambers, degraded, volatilized, or otherwise changed during the test. Nevertheless, due to limitations of other test systems for non-volatile materials, the static test has been widely used, especially for testing organisms such as algae and *Daphnia*.

The *static-renewal test* is similar to a static test because it is conducted in still water, but the test solutions and control water are renewed periodically, usually every 24 hours. Daily test solution renewal provides a greater likelihood that the exposure concentrations will remain stable throughout the test. This is the preferred method for conducting aquatic toxicity tests for compounds such as the succinimide dispersants on fish. Daily renewals cannot be done in the algae test, and usually not in *Daphnia* tests, because the process of separation and replenishment would cause a discontinuity in the alga growth rate and it can stress, coat, or entrap *Daphnia* in any surface film during renewals. OECD considers the use of static test for *Daphnia* and algae, and the use of static renewal test for fish to be appropriate for testing poorly soluble chemicals like the succinimide dispersants provided

that test solution preparation uses water accommodated fraction or water soluble fraction methods.⁷

4.2.1.2 Test Solution Preparation

Succinimide dispersants are poorly water-soluble substances, and it is not possible to prepare exposure solutions for aquatic toxicity testing by direct addition of measured quantities of test material to water. Two methods⁶ are used to prepare solutions of poorly water-soluble materials for aquatic toxicity testing:

- *Water accommodated fraction (WAF)* – This is a method in which the test solution contains only that fraction of the test material (organic phase) which is retained in the aqueous phase after a period of stirring long enough to reach equilibrium, followed by a sufficient time (1-4 hours) for phase separation. The WAF (aqueous phase) will contain soluble components of the test material at levels that will be dependent on the test material loading (the amount of material added to the aqueous medium). The resulting WAF is used in the aquatic toxicity test. Ideally, a WAF consists of a water-soluble extract of test material, but it can also include a stable micro-emulsion or contain small amounts of suspended matter.
- *Water soluble fraction (WSF)* – This is a method in which a WAF is either filtered, centrifuged, or allowed to settle for a greater length of time (24 hours) than with the WAF method to remove suspended matter from the aqueous phase before being used in the aquatic toxicity test.

4.2.1.3 Reporting Toxicity Results

In both WAF and WSF tests, test material concentrations are expressed as loading rates (i.e., defined as the weight of test material added per unit volume of test medium during WAF or WSF preparation)⁷. For fish tests, endpoints can be expressed as median lethal loading rate (LL_{50}) when lethal effects occur to 50% of the test population or in cases where no lethal effects are observed at all loadings tested, LL_0 . In both cases, results can be expressed in mg/L and in studies where no lethality is observed, the result is expressed as LL_0 = the highest loading rate tested. For invertebrate and alga tests, endpoints are expressed as median effective loading rate (EL_{50}) or EL_0 in mg/L as discussed above.

Loading rates allow poorly water-soluble complex substances such as the succinimide dispersants to be compared to more readily soluble substances and /or pure chemicals on an equal basis. To allow comparison, the toxicity value is expressed as the amount of test material added per unit volume of water when preparing the WAF or WSF.

If test material exposure levels are analytically measured in the test, the endpoints can also be expressed as median lethal concentration (LC_{50}) or median effective concentration

⁵ Organization for Economic Cooperation and Development (OECD) (2000). Guidance Document on Aquatic Toxicity Testing of Difficult Substances and Mixtures. OECD Environmental Health and Safety Publications, Series on Testing and Assessment No.23, Paris, France.

⁶ American Society for Testing and Materials (1998) D6081-98, Standard Practice for Aquatic Toxicity Testing of Lubricants: Sample Preparation and Results Interpretation.

⁷ Organization for Economic Cooperation and Development (OECD) (1999) Draft Guidance document on Aquatic Toxicity Testing of Difficult Substances. OECD, France.

(EC₅₀) in mg/L. EC/LC₅₀s are often not reported because it is very difficult to accurately measure test material exposure levels that can be below 1.0 mg/L.

NOTE: In this test plan, these results are reported as loading rates (EL/LL), to reflect the current reporting practices for the WAF method used in the tests. In the robust summaries, these data are presented as concentrations (EC/LC) as originally reported even though the test methods employed WAF preparation of test solutions without measurement of test material concentration.

4.2.2 Aquatic Toxicity of the Succinimide Dispersants

In general, the toxicity of a substance to an organism is limited by mechanisms of uptake and movement to target organs. Characteristics such as smaller molecular size and a lesser degree of ionization increase the ability of a substance to passively cross biological membranes. However, the soluble fraction of a compound in water represents the chemical fraction responsible for toxicity to aquatic organisms. Therefore, aquatic toxicity can be limited by the water solubility of a substance.

Data and preliminary modeling information indicates that all members of the succinimide dispersant category have low water solubility. The low water solubility suggests that the acute aquatic toxicity of these substances should be low due to limited bioavailability to aquatic organisms. However, the length of the alkyl side chains on these substances will influence their relative water solubility, and, hence, their relative toxicity.

4.2.2.1 Summary of Available Data

Acute aquatic ecotoxicity data for the succinimide dispersant category are summarized in Table 5. Both members of the category have been tested for acute aquatic toxicity in fish, daphnia and algae. A low order of toxicity was observed in all tests.

4.2.2.1.1 Fish Acute Toxicity

Both substances in the category were evaluated for acute toxicity to fish. The maximum test material loading rate was 1000 mg/L, and no mortality was observed in the studies. Overall, the LL₅₀ for both substances from both studies were greater than 1000 mg/L, indicating a relatively low order of toxicity to fish.

4.2.2.1.2 Invertebrate Acute Toxicity

Both substances in the category were evaluated for acute toxicity to daphnids. The maximum test material loading rate was 1000 mg/L. Overall, the EL₅₀ for the two substances were greater than 1000 mg/L, indicating a relatively low order of toxicity to daphnids.

4.2.2.1.3 Alga Toxicity

Both substances in the category were evaluated for algal growth inhibition. The maximum test material loading rate was 1000 mg/L. Overall, the EL₅₀ for these substances was greater than 100 mg/L indicating a relatively low order of toxicity to algae.

4.2.2.2 Data Assessment and Test Plan for Acute Aquatic Ecotoxicity

In total, six adequate acute aquatic ecotoxicity studies have been conducted for the succinimide dispersant category. These studies involved all three trophic levels of aquatic

organisms and evaluated the acute aquatic ecotoxicity of both members of the category. The data demonstrate a low order of acute aquatic ecotoxicity. The similarity in the low order of toxicity for these substances is consistent with their similar chemical structure and physicochemical properties and supports the scientific justification of these twelve substances as a category within the HPV Challenge Program.

Adequate data for all three trophic levels exist for both substances in the category. Therefore, no additional testing is necessary.

4.3 MAMMALIAN TOXICOLOGY DATA

4.3.1 Physicochemical Properties Relevant to Mammalian Toxicity

Physicochemical properties of chemicals are useful for predicting the routes by which exposure may occur, and in some cases, the mechanism and extent of toxicological responses. The physicochemical properties of the succinimide dispersants that are presented in Table 3 show these substances are relatively high molecular weight, liquid substances with moderately high octanol/water partition coefficients and low water solubilities. These characteristics indicate that the succinimide dispersants are lipophilic, and thus, capable of passive diffusion across biological membranes. It would be predicted that upon oral exposure these chemical substances would be absorbed by the gastrointestinal tract. However, the structural and physical properties such as comparatively high molecular weight, the presence of long-chain alkyl moieties and poor water solubility is expected to impede the rate and extent of absorption of succinimide dispersants from dermal surfaces. In addition to the general considerations discussed above, the succinimide dispersants are high boiling point, low vapor pressure, high viscosity liquid components. As a result, these substances have a low propensity to form vapors or aerosols, and thus, unintentional exposure via inhalation is uncommon.

4.3.2 Acute Mammalian Toxicity of Succinimide Dispersants

4.3.2.1 Acute Toxicity Test Methodology

Acute toxicity studies investigate the effect(s) of a single exposure to a relatively high dose of a substance. Potential routes of exposure for acute toxicity assays include oral, dermal, and inhalation. Oral toxicity assays are conducted by administering test material to fasted animals (typically rats or mice) in a single gavage dose. Acute dermal toxicity tests are conducted by administering test material to the shaved skin on the back of the test animal (typically rats or rabbits) and allowing the test material to stay in contact with the skin application site for a specific duration (usually 24 hours). Acute inhalation toxicity assays are conducted by exposing test animals (typically rats) in a controlled atmosphere to a fixed air concentration of the test substance for a specific duration (typically 4 hours). The test material is either generated as a vapor or intentionally aerosolized into respirable particles, then metered into the exposure air at the desired concentration. Preferably, inhalation toxicity studies are conducted using either nose-only or head-only exposure to minimize potential confounding effects resulting from whole-body exposure. Whole body exposure may lead to over-prediction of inhalation toxicity hazard by increasing the body-burden of the test material through skin absorption or ingestion of test material as a consequence of grooming both during and after the inhalation exposure period.

Historically, lethality is a primary end-point of concern in acute toxicity studies, and the traditional index of oral and dermal potency is the median lethal dose that causes mortality in 50 percent of the test animals (LD₅₀). In acute inhalation studies, the traditional measurement of potency is the median lethal concentration of the test material in air that causes mortality in 50 percent of the test animals (LC₅₀). In addition to lethality, acute toxicity studies also provide insights regarding potential systemic toxicity through careful observation and recording of clinical signs and symptoms of toxicity as well as through detailed examination of tissues and organ systems.

Typically, acute oral and dermal toxicity studies are conducted using a limit dose of 5000 and 2000 mg/kg body weight, respectively, and acute inhalation toxicity studies are conducted using a limit dose of 5 mg/L for 4 hours (according to OECD and EPA testing guidelines). Prior to 1990, some acute dermal toxicity studies may have used a limit dose of 5000 mg/kg. Recently, harmonized EPA testing guidelines (August 1998) have set the limit dose for both oral and dermal acute toxicity studies at 2000 mg/kg body weight, while the recommended limit concentration for acute inhalation studies has been set at 2 mg/L for 4 hours. The limit dose test method minimizes the number of animals tested by exposing a single group of animals to a large dose (the limit dose) of the test substance. A test substance that shows little or no effects at the limit dose is considered essentially nontoxic, and no further testing is needed. If compound-related mortality is observed at the limit dose, then further testing may be necessary.

4.3.2.2 Summary of Available Data

Acute toxicity data for the succinimide dispersant category is summarized in Table 6. Both members of the category have been tested by the oral and dermal route of administration and demonstrate a low order of acute toxicity.

4.3.2.2.1 Acute Oral Toxicity

Both substances in the succinimide dispersant category have been adequately tested for acute oral toxicity. The acute oral LD₅₀ for these studies in rats is greater than 5000 mg/kg (limit tests). Clinical signs observed following treatment included diarrhea and dark staining of the anal area. There were no significant necropsy findings. Overall, the acute oral LD₅₀ for these substances was greater than 5000 mg/kg indicative of a relatively low order of lethal toxicity.

4.3.2.2.2 Acute Dermal Toxicity

Both substances in the succinimide dispersant category have been adequately tested for acute dermal toxicity. The acute dermal LD₅₀ for these studies in rabbits and rats were greater than 2000 mg/kg (limit tests). Dermal application of the test materials to the skin of rabbits for 24 hours typically produced slight to well-defined erythema, which persisted through the first 7 days of the study and was characterized microscopically as dermatitis, hyperkeratosis, and acanthosis. Clinical signs in rabbits included reduced weight gain. There were no remarkable findings in rats. There were no remarkable macroscopic observations at necropsy. Overall, the acute dermal LD₅₀ for these substances were greater than 2000 mg/kg indicative of a relatively low order of lethal toxicity.

4.3.2.3 Data Assessment and Test Plan for Acute Mammalian Toxicity

In total, four adequate acute toxicity studies have been conducted for both members of the succinimide dispersant category. These studies involved two species of laboratory

animals (rats or rabbits); two routes of exposure (oral and dermal); and evaluated the toxicity of both members of the category. The data consistently demonstrate a low order of acute toxicity. The overall low order of acute toxicity for these substances in combination with their similar chemical structure and physicochemical properties supports the scientific justification of these twelve substances as a category within the HPV Challenge Program.

Based on the results of these studies, the acute toxicity of the category has been evaluated adequately with respect to all acute toxicity endpoints, and no additional acute toxicity testing is proposed for the HPV Challenge Program.

4.3.3 Mutagenicity of the Succinimide Dispersant Category

4.3.3.1 Mutagenicity Test Methodology

Genetic toxicology is concerned with the effects of substances on genetic material (i.e., DNA and chromosomes). Within genetic material, the gene is the simplest functional unit composed of DNA. Mutations are generally non-lethal, heritable changes to genes that may arise spontaneously or because of xenobiotic exposure. Genetic mutations are commonly measured in bacterial and mammalian cells. The simplest test systems measure the occurrence of a base-pair substitution mutation in which a single nucleotide is changed followed by a subsequent change in the complementary nucleotide on the other DNA strand. Frame shift mutations occur following the deletion or insertion of one or more nucleotides, which then changes the "reading frame" for the remainder of the gene or multiple genes. Genetic testing for these types of point mutations is generally accomplished by *in vitro* cellular assays for forward or reverse mutations. A forward mutation occurs when there is a detectable change in native DNA whereas a reverse mutation occurs when a mutated cell is returned to its initial phenotype. Both base-pair substitutions and frame shift mutations are routinely measured in bacterial cells by measuring the ability of a cell to acquire the capability to grow in an environment missing an essential amino acid. In these tests, a large number of cells are examined to demonstrate a significant increase in the frequencies of mutations that occur over the frequency of spontaneous mutations.

Chromosomal aberrations are large scale numerical or structural alterations in eukaryotic chromosomes including deletions (visualized as breaks), translocations (exchanges), non-disjunction (aneuploidy), and mitotic recombination. Chromosomal breakage is the classical end point in chromosomal aberration assays. Substances that induce structural changes in chromosomes, especially chromosome breaks, are referred to as "clastogens." To visualize chromosomes and chromosomal aberrations following *in vitro* or *in vivo* treatment with a substance, cells are arrested in metaphase, treated to swell the chromosomes, fixed, transferred to slides and stained. The first metaphase following treatment is the time at which the greatest number of cells with damaged chromosomes may be observed. The most frequently used test systems investigate changes in mammalian cells (such as Chinese hamster ovary or lung cells; human or rat lymphocytes; or human, rat or mouse bone marrow cells) following either *in vitro* or *in vivo* exposure to the test substance. The micronucleus test is a common *in vivo* assay that measures the frequency of micronuclei formation (i.e., chromosomal fragments) in polychromatic erythrocytes.

4.3.3.2 Summary of Mutagenicity Data

A summary of the mutagenicity information for the succinimide dispersants is presented in Table 7. *In vitro* bacterial gene mutation assays and *in vitro* and *in vivo* chromosomal aberration assays have been conducted for both members of the category. Frequencies of reverse mutations in bacteria were not significantly changed after exposure to the succinimide dispersants. *In vitro* and *in vivo* chromosomal aberration studies indicate that succinimide dispersants are not clastogenic.

4.3.3.2.1 Bacterial Gene Mutation Assay

Both substances in this category have been adequately tested in a bacterial reverse mutation test (OECD Guidelines 471 and/or 472). Both tested substances were negative for mutagenic activity, with and without metabolic activation.

4.3.3.2.2 Mammalian Gene Mutation Assay in Transformed Cells

One substance in this category was tested in an *in vitro* mouse lymphoma cell mutagenicity assay (Guideline 476, *In vitro Mammalian Cell Gene Mutation Test*). The result of this study indicates that, in the absence and presence of hepatic microsome activation, succinimide dispersants are not mutagenic or clastogenic.

4.3.3.2.3 *In vivo* Chromosomal Aberration Assays

One of the substances in this category was tested in an *in vivo* chromosomal aberration assay (OECD Guideline 474, *Mammalian Erythrocyte Micronucleus Test*). The test substance was negative for clastogenicity.

4.3.3.3 Data Assessment and Test Plan for Mutagenicity

Both members of the succinimide dispersant category have been tested for mutagenicity in tests for gene mutations and chromosomal aberrations. The assays included point mutations in bacteria, cultured mammalian cells, and *in vivo* chromosomal aberrations in mice. The findings from all studies were negative for mutagenic potential.

Adequate mutagenicity tests exist for both substances in the succinimide dispersant category. Thus, the genetic toxicity of the category has been evaluated adequately with respect to all mutagenic and clastogenic endpoints, and no additional genetic toxicity testing is proposed for the HPV Challenge Program.

4.3.4 Repeated-dose Toxicity of Succinimide Dispersants

4.3.4.1 Repeated-dose Toxicity Test Methodology

Repeated-dose toxicity studies evaluate the systemic effects of repeated exposure to a chemical over a significant period of the life span of an animal (rats, rabbits, or mice). Chronic repeated-dose toxicity studies are concerned with potential adverse effects upon exposure over the greater part of an organism's life span (e.g., one to two years in rodents). Subchronic repeated-dose studies are also concerned with effects caused by exposure for an extended period, but not one that constitutes a significant portion of the expected life span. Subchronic studies are useful in identifying target organ(s), and they can be used in selecting dose levels for longer-term studies. Typically, the exposure regimen in a subchronic study involves daily exposure (at least 5 consecutive days per week) for a period of at least 28 days or up to 90 days (i.e., 4 to 13 weeks). A recovery

period of two to four weeks (generally included in most study designs) following completion of the dosing or exposure period provides information on whether or not the effects seen during the exposure period are reversible upon cessation of treatment. The dose levels evaluated in repeated-dose toxicity studies are notably lower than the relatively high limit doses used in acute toxicity studies. The NOAEL (no observed adverse effect level), usually expressed in mg/kg/day, defines the dose of test material that produces no significant toxicological effects. If the test material produces toxicity at the lowest dose tested (i.e., there is no defined NOAEL), the lowest dose that produced an adverse effect is defined as the LOAEL (lowest observed adverse effect level). While these studies are designed to assess systemic toxicity, the study protocol can be modified to incorporate evaluation of potential adverse reproductive and/or developmental effects.

Reproductive and developmental toxicity studies generate information on the effects of a test substance on male and female reproductive performance such as gonadal function, mating behavior, conception, and development of the conceptus, parturition, and post-partum development of the offspring. Various study designs exist, but they all involve exposure to both male and female test animals before mating. The rat is most often selected as the test species. The test substance is administered to males and females continuously at several graduated doses for at least two weeks prior to mating and until the animals are sacrificed. The males are treated for at least two more weeks. Male gonadal histopathology is carefully assessed at the end of the study. The females are treated through parturition and early lactation. The adult females and offspring are typically studied until termination on post-natal day 21, or sometimes earlier. In addition to providing data on fertility and reproduction, this study design provides information on potential developmental toxicity following prenatal and limited post-natal exposure to the test substance. An NOAEL or LOAEL is also used to describe the results of these tests, with the exception that these values are derived from effects specific to reproduction or development.

The “toxicity to reproduction” requirement in the HPV Challenge Program can be met by conducting the *Reproduction/Developmental Toxicity Screening Test* (OECD Guideline 421) or by adding this screening test to a repeated-dose study (OECD Guideline 422, *Combined Repeated-Dose Toxicity Study with the Reproductive/Developmental Toxicity Screening Test*). The *One-Generation Reproduction Toxicity Study* (OECD Guideline 415) is a more comprehensive protocol for the study of the effect of a test material on reproduction and development that also meets the OECD SIDS and the HPV Challenge Program requirements.

4.3.4.2 Summary of Repeated-Dose Toxicity Data

A summary of the results from the repeated-dose studies for the succinimide dispersant category is presented in Table 8. Repeated-dose toxicity tests have been performed on both members of the succinimide dispersant category by two routes of administration in rats.

4.3.4.2.1 Systemic Toxicity Tests

Both substances in the succinimide dispersant category have been tested for subchronic toxicity.

Mono alkenyl succinimide derivative (CAS # 67762-72-5) was evaluated in a 28-day repeated-dose dermal toxicity study in rats (methodology consistent with OECD

Guideline 410, *Repeated-Dose Dermal Toxicity: 21/28 Day*). The doses used in this study were 10, 40, and 80% solutions of the test material diluted in mineral oil. Twelve male and female rats were included in each test material and vehicle control groups. The test material was applied at a volume of 1 ml/kg to intact skin (clipped of hair), once per day, five days/week for twenty doses. No wrapping was used, but plastic collars were employed to prevent ingestion of the test material. The daily duration of exposure was 6 hours. There were no remarkable findings in this study for any of the endpoints evaluated. A NOAEL for systemic toxicity of ~800 mg/kg/day was established for this study.

Bis alkenyl succinimide derivative (CAS # 84605-20-9) was evaluated in a 28-day repeated-dose oral toxicity study in rats (OECD Guideline 407, *Repeated-Dose 28-Day Oral Toxicity Study in Rodents*). The test material in corn oil was administered to rats by oral gavage at 100, 500, and 1000 mg/kg/day for 28 consecutive days. Control animals received corn oil. There were no remarkable findings in this study for any of the endpoints evaluated. The NOAEL was established at 1000 mg/kg/day.

4.3.4.2.2 Reproduction and Developmental Toxicity Tests

Bis alkenyl succinimide derivative (CAS # 84605-20-9) was tested for reproduction and developmental toxicity (OECD Guideline 421 *Reproduction/ Developmental Screening Test*). The test material in corn oil was administered to rats by oral gavage at doses of 100, 500, and 1000 mg/kg/day. Male and female rats in each dose group received daily treatment for 28 days prior to, and during, the mating period. In addition, the females were treated during gestation and through day 4 of lactation. Control animals received corn oil. Results. There were no remarkable findings in this study for any of the endpoints evaluated. The NOAEL was established at 1000 mg/kg/day.

4.3.4.3 Data Assessment and Test Plan for Repeated-dose Toxicity

Two repeated-dose toxicity studies have been conducted with the two category members. Neither repeated oral administration nor dermal application caused any adverse effects. In addition, one reproductive and developmental toxicity screening study has been conducted on a member of the category. No adverse effects on reproduction or development were observed in this study. The data indicate the members of the succinimide dispersant category are of low concern for repeated-dose toxicity and reproductive and developmental toxicity. Bridging will be used to fill the data gap for the other substance in the category for reproductive and developmental toxicity.

Both substances in this category have been adequately tested for repeated-dose toxicity. By bridging the existing reproductive and developmental toxicity data to the other substance that lacks this data, the reproductive and developmental toxicity of this category has also been adequately evaluated with respect to all endpoints. Therefore, no additional repeated-dose toxicity or reproductive and developmental toxicity testing is proposed for the HPV Challenge Program for this category.

Table 1. Members of the Succinimide Dispersant Category

CAS Number	Chemical Name	Simplified Chemical Name
67762-72-5	2,5-Pyrrolidinedione, 1-[2-[[2-[[2-(2-aminoethyl)amino]ethyl]amino]ethyl]-, monopolyisobutenyl derivatives	Mono alkenyl succinimide derivative
84605-20-9	Amines, polyethylenepoly-, reaction products with succinic anhydride polyisobutenyl derivatives	Bis alkenyl succinimide derivative

Table 2. Chemical Structures of Succinimide Dispersants

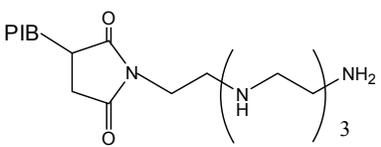
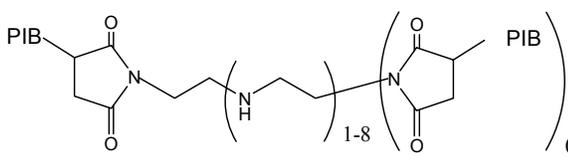
CAS Number	Chemical Structure
67762-72-5	 <p style="text-align: right;">67762-72-5</p> <p style="text-align: center;">PIB= Polyisobutylene 500-2500MW</p>
84605-20-9	 <p style="text-align: right;">84605-20-9</p> <p style="text-align: center;">PIB= Polyisobutylene 500-2500MW</p>

Table 3. Physicochemical Properties of Succinimide Dispersants

CAS Number	Molecular Weight	Specific Gravity ¹ g/ml	Viscosity ² cSt @ 40°C	Melting Point ³ °C	Boiling Point ⁴ °C	Vapor Pressure ⁵ Pa	Water Solubility mg/L	Log Kow
67762-72-5	1134	0.9135	1330	NA	841.5	<1X10 ⁻¹⁰	0.125	6.7
84605-20-9	2859-3160	0.9071	1100	NA	1271.5	<1X10 ⁻¹⁰	NDA ⁶	NDA ⁶

¹ASTM D1298-99, Standard Test Method for Density, Relative Density (Specific Gravity), or API Gravity of Crude Petroleum and Liquid Petroleum Products by Hydrometer Method

²ASTM D 445-97, Standard Test Method for Kinematic Viscosity of Transparent and Opaque Liquids (the Calculation of Dynamic Viscosity)

³Not applicable; substances are viscous liquids at ambient temperatures.

⁴Modeling data for theoretical “de-oiled” substance.

⁵Theoretical “de-oiled” succinimide dispersants are solid. Vapor pressure is estimated from the vapor pressure of the petroleum base stock in which the substance is manufactured.

⁶No data needed; bridging from other members of the category.

Table 4. Evaluation of Environmental Fate Information for Succinimide Dispersants

CAS Number	BIODEGRADABILITY	HYDROLYSIS	PHOTODEGRADATION
	Available Data & Proposed Testing	Available Data & Proposed Testing	Available Data & Proposed Testing
67762-72-5	No testing needed Bridging	No testing needed ¹	Direct photodegradation evaluation AOPWIN Model Estimation
84605-20-9	16% biodegraded after 28 days	No testing needed ¹	Direct photodegradation evaluation AOPWIN Model Estimation

¹ Prepare technical discussion.

Table 5. Evaluation of Aquatic Toxicology of Succinimide Dispersants

CAS Number	ACUTE TOXICITY TO FISH 96-hr LL ₅₀ (mg/L) ¹	ACUTE TOXICITY TO INVERTEBRATES 48-hr EL ₅₀ (mg/L) ¹	TOXICITY TO ALGAE 96-hr EL ₅₀ (mg/L) ¹
	Available Data & Proposed Testing	Available Data & Proposed Testing	Available Data & Proposed Testing
67762-72-5	>1,000 (WAF ² , F)	>1,000 (WAF ³ , D)	>1,000 (WAF ³ , P, R) >1,000 (WAF ³ , P, B)
84605-20-9	>1,000 (WAF ² , T)	>1,000 (WAF ³ , D)	320 (WAF ³ , P, R) 270 (WAF ³ , P, B)

¹Toxicity endpoints are expressed as median lethal loading rates (LL₅₀) for fish and median effective loading rates (EL₅₀) for *Daphnia* and algae. The EL/LL₅₀ is defined as the loading rate that adversely effects 50% of the test organisms exposed to it during a specific time. The greater the EL/LL₅₀ the lower the toxicity.

²WAF = Water accommodated fraction static renewal test.

³WAF = Water accommodated fraction static non-renewal test.

F = fathead minnow, *Pimephales promelas*.

D = freshwater cladoceran, *Daphnia magna*.

P = freshwater algae *Pseudokirchneriella subcapitata* formerly called *Selenastrum capricornutum*.

T = rainbow trout, *Oncorhynchus mykiss* formerly called *Salmo gairdneri*.

R = algae growth rate.

B = algae biomass.

Table 6. Evaluation of Acute Mammalian Toxicology of Succinimide Dispersants

CAS Number	ACUTE ORAL TOXICITY ¹	ACUTE DERMAL TOXICITY ¹
	Available Data & Proposed Testing	Available Data & Proposed Testing
67762-72-5	LD ₅₀ > 5.0 g/kg (rat)	LD ₅₀ > 5.0 g/kg (rabbit)
84605-20-9	LD ₅₀ > 5.0 g/kg (rat)	LD ₅₀ > 2.0 g/kg (rat)

¹¹Toxicity endpoints are expressed as median lethal dose (LD₅₀) for acute oral and dermal toxicity.

Table 7. Evaluation of Mutagenicity of Succinimide Dispersants

CAS Number	GENE MUTATION ASSAY	CHROMOSOMAL ABERRATION ASSAY
	Available Data & Proposed Testing	Available Data & Proposed Testing
67762-72-5	Bacterial Reverse Mutation Assay – Not mutagenic	Mouse Lymphoma Mutagenicity Screen – Not clastogenic
84605-20-9	Bacterial Reverse Mutation Assay – Not mutagenic	Mouse Micronucleus Assay – Not clastogenic

Table 8. Evaluation of Repeated-dose Mammalian Toxicology of Succinimide Dispersants

CAS Number	REPEATED-DOSE TOXICITY	REPRODUCTIVE/DEVELOPMENTAL TOXICITY
	Available Data & Proposed Testing	Available Data & Proposed Testing
67762-72-5	28-day repeated-dose dermal study in rats (OECD 410) NOEL = ~800 mg/kg/day (highest dose tested)	No testing needed Bridging
84605-20-9	4-week repeated-dose oral study in rats (OECD 407) NOEL = 1000 mg/kg/day <u>At 1000 mg/kg/day.</u> <ul style="list-style-type: none"> • No significant effects; <u>At 500 mg/kg/day.</u> <ul style="list-style-type: none"> • No significant effects; <u>At 100 mg/kg/day.</u> <ul style="list-style-type: none"> • No significant effects. 	Reproduction/developmental oral toxicity screening test in rats (OECD 421) NOEL P0 = 1000 mg/kg/day NOEL F1 = 1000 mg/kg/day <u>At 1000 mg/kg/day.</u> <ul style="list-style-type: none"> • No significant effects; <u>At 500 mg/kg/day.</u> <ul style="list-style-type: none"> • No significant effects; <u>At 100 mg/kg/day.</u> <ul style="list-style-type: none"> • No significant effects.

CAS Number	Environmental Fate					Ecotoxicity			Human Health Effects				
	Physical Chem	Photodeg	Hydrolysis	Fugacity	Bio-deg	Acute Fish Toxicity	Acute Invert Toxicity	Algal Toxicity	Acute Toxicity	Point Mutations	Chrom Effects	Sub-chronic	Repro / Develop
67762-72-5	C	C	D	C	B	A	A	A	A	A	A	A	B
84605-20-9	C	C	D	C	A	A	A	A	A	A	A	A	A

- A Adequate data available
- B Bridging data from another category member
- C Computer modeling
- D Technical discussion proposed
- T Test

Appendix I. Application of Environmental Fate Modeling to the Succinimide Dispersants Category

This document describes the application and results of computer modeling to estimate the physicochemical properties and environmental distribution of members in a lubricant additives category. Two structures representative of two members of the HERTG (Health, Environmental, and Regulatory Task Group) Category 25, Succinimide Dispersants, were applied to two computer models. The computer model, EPIWIN® (1), was used to estimate the physicochemical properties of the two structures. These calculated properties were used as input data to a Mackay multimedia fate model, which was used to predict their relative environmental distribution.

The US EPA has agreed that computer modeling techniques are an appropriate approach to estimating chemical partitioning and distribution in the environment. Specifically, fugacity based, multimedia fate modeling can be used to compare the relative distribution of chemicals between environmental compartments (i.e., air, soil, water, suspended sediment, sediment, biota). A widely used model for this approach is the EQC model (2). EPA cites the use of this model for this purpose in its document titled *Determining the Adequacy of Existing Data*, which was prepared for the HPV chemical program.

There are three "levels" of the EQC model. In its document, EPA states that it accepts Level I fugacity modeling to estimate transport/distribution values. In the same document EPA states that Level III model data are considered "more realistic and useful for estimating a chemical's fate in the environment on a regional basis". However, the selection and application of any one of the three models should not be done without considering their appropriateness for use with chemical(s) of interest. This includes a basic understanding of selected physicochemical properties of the chemicals to be modeled, as well as the model.

The EQC Level I model requires values for certain basic physicochemical properties of the chemicals to be modeled. The model uses input values including molecular weight, vapor pressure, water solubility, and octanol-water partition coefficient. Another model was needed to estimate these physicochemical properties from the structures of the Category 25 structures. The model used for this purpose was EPIWIN, version 3.04 (1), which is also used by the EPA and which they developed jointly with Syracuse Research Corporation. EPIWIN includes algorithms for estimation of the properties needed for the application of the EQC model.

The succinimide dispersants in Category 25 are related in structure. The structures representing the two CAS numbers in this category are pictured in Table 1. These structures were used to calculate the physical properties, which are shown in Table 2. The data in Table 2 include the basic input values that were used with the EQC model. The results of the EQC model are listed in Table 3.

The structures in Table 1 indicate the position of polyisobutylene (PB) moieties, which have molecular weights of 500 to 2500 daltons. For modeling purposes, physicochemical properties were calculated using PB moieties of 500 daltons. The PB moiety(s) of these substances largely influences the calculated results. The value reported for bioconcentration factor (BCF) does not vary with the molecular weight of the two structures modeled (both give the same value, log BCF of 0.5). This low-modeled value recognizes the low bioaccumulation potential of "super-hydrophobic" substances as a result of low bioavailability.

Environmental distribution modeling was performed using a simple equilibrium distribution model (Mackay Level I Model, version 1.0). The percent distribution results by environmental

Appendix I. Application of Environmental Fate Modeling to the Succinimide Dispersants Category

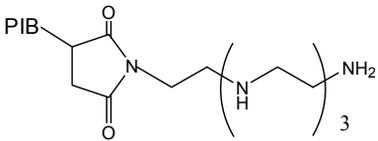
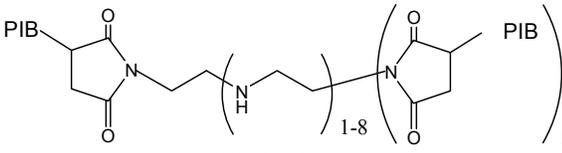
compartment are shown in Table 3. These data suggest that succinimide dispersants have the potential to partition primarily to the soil compartment. They have a much lower potential to partition to sediment. These substances are not calculated to partition to the remaining compartments. The two substances in this category can be characterized as having negligible vapor pressure and water solubility, which is why very low percentages of these substances are calculated to partition to the air and water. Additionally, no appreciable transport through the environment is expected as suggested by the fugacity values for these substances (Table 3).

References

1. EPIWIN. 1999. Estimation Program Interface for Windows, version 3.04. Syracuse Research Corporation, Syracuse, NY, USA.
2. Mackay, D., A. Di Guardo, S. Paterson, and C. Cowan. 1996. Evaluating the Environmental fate of a Variety of Types of Chemicals using the EQC Model. *Environ. Toxicol. Chem.* 15:1627-1637.

Appendix I. Application of Environmental Fate Modeling to the Succinimide Dispersants Category

Table 1. Chemical Structures of Succinimide Dispersants

CAS Number	Chemical Structure*
67762-72-5	 <p style="text-align: center;">PIB= Polyisobutylene 500-2500MW</p> <p style="text-align: right; margin-right: 50px;">67762-72-5</p>
84605-20-9	 <p style="text-align: center;">PIB= Polyisobutylene 500-2500MW</p> <p style="text-align: right; margin-right: 50px;">84605-20-9</p>

Appendix I. Application of Environmental Fate Modeling to the Succinimide Dispersants Category

Table 2. Physical Properties of Representative Structures from Succinimide Dispersants as Modeled by EPIWIN

CAS Number	Molecular Weight	Log K _{ow}	Water Solubility (mg/L)	Vapor Pressure (Pa)	Log K _{oc}	Log Bioconcentration Factor	Melting Point (°C)	Boiling Point (°C)	Atmospheric Oxidation	
									OH ⁻ Rate Constant (cm ³ /molec-sec)	Half-life (hrs)
67762-72-5*	776.3	13.8	1.8E-11	6.1E-19	12.0	0.5	349.8	841.5	368.9E-12	0.3
84605-20-9**	1277.2	31.8	3.1E-30	3.3E-31	21.4	0.5	349.8	1271.5	214.8E-12	0.6

* The chemical structure used to model data included a PB moiety (Table1) of approximately 500 daltons or a total carbon number of C48.

** The chemical structure used to model data included PB moieties (Table1) of approximately 500 daltons each or a total carbon number of C48.

Table 3. Environmental Distribution of Representative Structures from Succinimide Dispersants as Modeled by EQC Level I

CAS Number	Air (%)	Water (%)	Soil (%)	Sediment (%)	Suspended Sediment (%)	Biota (%)	Fugacity (μPa)
67762-72-5*	0.00	0.00	97.75	2.17	0.07	0.01	2.8e-16
84605-20-9**	0.00	0.00	97.75	2.17	0.07	0.01	9.4e-28

* The chemical structure used to model data included a PB moiety (Table1) of approximately 500 daltons or a total carbon number of C48.

** The chemical structure used to model data included PB moieties (Table1) of approximately 500 daltons each or a total carbon number of C48.