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Substituted p-Phenylenediamines Category Justification and Testing Rationale

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CAS Nos. 101-96-2, 3081-14-9, 3081-01-4, 15233-47-3, and 68953-84-4
(+ SIDS Chemicals 101-72-4 and 793-24-8 for data purposes)
Rubber and Plastic Additives Panel
American Chemistry Council
December 2001

List of Member Companies in the Rubber and Plastic Additives Panel

The Rubber and Plastic Additives Panel of the American Chemistry Council include the following member companies: Bayer Corporation, Ciba Specialty Chemicals Corporation, Crompton Corporation, Flexsys America L.P., The Goodyear Tire & Rubber Company, The Lubrizol Corporation, Noveon, Inc., R.T. Vanderbilt Company, Inc., and UOP, LLC.

Executive Summary

The American Chemistry Council's Rubber and Plastic Additives Panel (RAPA), and its member companies, hereby submit for review and public comment their test plan for the Substituted p-Phenylene diamines category of chemicals under the Environmental Protection Agency's High Production Volume (HPV) Challenge Program.

As discussed in the report that follows, Substituted p-Phenylenediamines (PPD), which are used as antidegradants in rubber, fuel additives, or in monomer distillation, are defined as phenylenediamines with various substitutions. These uses require stability at high temperatures, low biodegradation and very low water solubility and low vapor pressure. In consideration of animal welfare concerns to minimize the use of animals in the testing of chemicals, the Panel has conducted a thorough literature search for all available data, published and unpublished. It has also performed an analysis of the adequacy of the existing data. Further, it developed a scientifically supportable category of related chemicals and used structure-activity relationship information to address certain data requirements. Existing data for members of this category indicate that they are of moderate to high toxicity in the aquatic environment, and of low concern for mammalian toxicity. No testing is proposed for the chemicals that constitute the Substituted p-Phenylenediamines category for the purposes of the HPV Program.

Substituted p-Phenylenediamines category

Relying on several factors specified in EPA's guidance document on "Development of Chemical Categories in the HPV Challenge Program," in which use of chemical categories is encouraged, the following closely related chemicals constitute a chemical category:

Substituted p-Phenylenediamines

Alkylated PPD

p-Phenylenediamine, N,N-di-sec-butyl (101-96-2)
p-Phenylenediamine, N,N-bis(1,4-dimethylpentyl) (3081-14-9)

4-Aminodiphenylamine Derivatives

p-Phenylenediamine, N-Isopropyl-N'-phenyl-, (101-72-4)
p-Phenylenediamine, N-(1,3-dimethylbutyl) N'-phenyl (793-24-8)
1,4-Benzenediamine, N,N'-mixed Ph and toyl derivatives (68953-84-4)
p-Phenylenediamine, N-(1,4-dimethylpentyl) N'-phenyl (3081-01-4)
p-Phenylenediamine, N,(1-methylheptyl)-N'-phenyl, (15233-47-3)

The goal of developing a chemical category is to use interpolation and/or extrapolation to assess chemicals rather than conducting additional testing with specific consideration of animal welfare concerns to minimize the use of animals in the testing of chemicals.

Structural Similarity. A key factor supporting the classification of these chemicals as a category is their structural similarity (see Figure 1). All materials in this category are phenylenediamines with various substituent groups that are always in the *para* position of the aromatic ring. The substituent groups may be all alkyl, all aryl, or mixed alkyl/aryl.

Similarity of Physicochemical Properties. The similarity of the physicochemical properties of these materials parallels their structural similarity. All are highly-colored (dark brown, purple, reddish or black) solids or semi-viscous liquids intended for use as antidegradants in dark-colored or black finished rubber articles or functional fluids. The use of these materials requires that they be stable under high temperatures. Their low volatility is due to their low vapor pressure, semi-viscous or solid form. The existing information for these materials indicates that they have very low water solubility and high flash points.

Fate and Transport Characteristics. Members of this category have been tested and shown not to be readily biodegradable via CO2 evolution, but they are susceptible to both hydrolysis and photodegradation. Additional data collection efforts are not necessary. These materials have been shown not to partition to water or air if released into the environment due to their low water solubility and low vapor pressure; as a result additional computer-modeled environmental partitioning data is not necessary for the members of this category, for the purposes of the HPV Program.

Toxicological Similarity. Review of existing published and unpublished test data for Substituted p-Phenylenediamines shows the aquatic and mammalian toxicity among the materials within this category are similar.

> **Aquatic Toxicology**. Data on acute fish toxicity, acute invertebrate toxicity, and algae toxicity were reviewed. The Substituted p-Phenylenediamines, in general, are very toxic to aquatic organisms. Additional testing is not proposed for these materials for the purposes of the HPV Program.

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

Mammalian Toxicology - Mutagenicity. Data from bacterial reverse mutation assays, *in vitro* and *in vivo* chromosome aberration studies, as well as additional supporting *in vitro* and *in vivo* genetic toxicity studies were reviewed, and the findings indicate a low concern for mutagenicity. Data are available for several members of the category or close structural analogs, and these data can be bridged to the other members of the category. Therefore, the category has been adequately tested for mutagenicity to meet the requirements of the HPV Program; therefore, no additional mutagenicity testing is proposed.

Mammalian Toxicology – Repeated Dose Toxicity. Data from repeated-dose toxicity studies were reviewed and sufficient data are available to satisfy the repeated dose toxicity requirements of this category through bridging to members without test data, such that additional testing is not proposed for these materials for the purposes of the HPV Program.

Mammalian Toxicology - Reproductive and Developmental Toxicity. There are several adequate reproductive/developmental studies for members of the Substituted p-Phenylene diamines category. Again, existing study data and results can be bridged to other category members, such that additional testing is not proposed for the purposes of the HPV Program.

Conclusion. Based upon data reviewed for the HPV program, the physicochemical and toxicological properties of the proposed Substituted p-Phenylenediamines category members are similar and follow a regular pattern as a result of that structural similarity. Therefore, the EPA definition of a chemical category has been met. Further, the availability and results of data for the chemicals that constitute the Substituted p-Phenylenediamines category indicate that no additional testing needs to be conducted for the purposes of the HPV Program.

Introduction

A provision for the use of structure activity relationships (SAR) to reduce testing needs is included under EPA's HPV Program. Specifically, categories may be formed based on structural similarity, through analogy, or through a combination of category and analogy for use with single chemicals. The benefits of using a category approach are numerous and include accelerated release of hazard information to the public (category analysis and testing are proposed to be initiated within the first two years of the HPV Program); reduction in the number of animals used for testing; and an economic savings as a result of a reduced testing program.

The Substituted p-Phenylenediamines that form this category based on structural similarity are:

Alkylated N-PPD
p-Phenylenediamine, N,N-di-sec-butyl (101-96-2)
p-Phenylenediamine, N,N-bis(1,4-dimethylpentyl) (3081-14-9)

4-Aminodiphenylamine Derivatives
p-Phenylenediamine, N-Isopropyl-N'-phenyl-, (101-72-4)
p-Phenylenediamine, N-(1,3-dimethylbutyl) N'-phenyl (793-24-8)
1,4-Benzenediamine, N,N'-mixed Ph and toyl derivatives (68953-84-4)
p-Phenylenediamine, N-(1,4-dimethylpentyl) N'-phenyl (3081-01-4)
p-Phenylenediamine, N,(1-methylheptyl)-N'-phenyl, (15233-47-3)

The category has been arranged into two primary subcategories (Alkylated N-PPD and 4-Aminodiphenylamine Derivatives) for purposes of bridging data to the closest related material. The materials were further arranged in order of molecular weight, so that the smallest material is listed first, and the following materials have increasingly larger molecular weights. Of these, p-Phenylenediamine, N-Isopropyl-N'-phenyl-, (CAS#101-72-4) has been evaluated in the Organization for Economic Co-operation and Development (OECD) Screening Information Data Set (SIDS) program and p-Phenylenediamine, N-(1,3-dimethylbutyl) N'-phenyl (CAS#793-24-8) is currently in the OECD SIDS evaluation process. Data for these two members of the Substituted p-Phenylene diamines category are included in support of the five category members sponsored in the HPV Program.

The development of this category follows current EPA guidance[1].

Background Information: Manufacturing and Commercial Applications

Manufacturing

Substituted p-Phenylenediamines are manufactured batchwise in high-pressure autoclave reactors using a process known as catalytic reduction. In a typical reaction process, the chemical intermediate 4-Aminodiphenylamine (CAS#101-54-2) is reacted with the appropriate ketone and hydrogen gas in the presence of a precious metal catalyst on carbon to form the product, which is then purified via separation, filtration and azeotropic distillation.

Commercial Applications

In the U.S., Substituted p-Phenylenediamines are used primarily as antidegradants in the production of black or dark-colored rubber, as fuel additives and in monomer distillation processes. They are widely used in the manufacture of tires (sidewall, tread and retread, carcass, belt skim, liner, bead filler/chafer, and base tread), moldings, hoses, belts and gaskets for the automotive industry and in other industrial rubber products such as roofing material that are exposed to the elements. Others are used as fuel additives to prevent air oxidation, and a few find usage as “short-stoppers” or polymerization inhibitors in the process of monomer distillation. Substituted p-Phenylenediamines are powerful antioxidants/antiozonants that greatly extend the useful life of

[1] US EPA, Office of Pollution Prevention and Toxics. Development of Chemical Categories, Chemical Right-to-Know Initiative. http://www.epa.gov/opptintr/chemrtk/categuid.htm

rubber articles and functional fluids by delaying the oxidative aging process. These highly-colored, or "staining" antidegradants also help prevent surface cracking due to flex fatigue in dynamic applications. Typical usage level for the Substituted p-Phenylenediamines in these industrial applications ranges from 0.5 – 3%.

FDA Status – The Substituted p-Phenylenediamines are not widely used in food contact applications due to their capability to stain and discolor. However, two chemicals in this category have some limited food-contact applications:

175.105	Components of Adhesives	68953-84-4
177.2600	Rubber Articles	68953-84-4 and 101-72-4

Shipping/Distribution

Substituted p-Phenylenediamines are shipped extensively throughout the world from manufacturing plants located in North and South America, Eastern and Western Europe, China and Japan. These materials are typically shipped by tank car, tank truck, and barge.

Worker/Consumer Exposure

The rubber and plastics additives industry has a long safety record and sophisticated industrial users handle materials. Exposure of workers handling PPD category chemicals is likely to be the highest in the area of material packaging rather than manufacturing. These materials are made as pastilles (pellets), powders, flakes, solids and liquids. Thus, during the transfer operation from the manufacturing process to packaging there is a potential for inhalation exposure (nuisance dust is the primary route of worker exposure) and dermal contact to liquid forms. There should be little, if any, consumer exposure to substituted p-phenylenediamines since these materials will be part of finished articles, and as such unavailable for exposure or release under typical conditions of use.

Development of the Substituted p-Phenylenediamines Category

EPA has described a stepwise process for developing categories. These steps include:

- Grouping a series of like chemicals, including the definition of criteria for the group.
- Gathering data on physicochemical properties, environmental fate and effects, and health effects for each member of the category.
- Evaluating the data for adequacy.
- Constructing a matrix of available and unavailable data.
- Determining whether there is a correlation among category members and data gathered.

Definition of the Substituted p-Phenylenediamines Category

As defined by EPA under the HPV Program, a chemical category 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." The similarities should be based on a common functional group, common precursors or

breakdown products (resulting in structurally similar chemicals) and an incremental and constant change across the category. The goal of developing a chemical category is to use interpolation and/or extrapolation to assess chemicals rather than conducting additional testing with specific consideration of animal welfare concerns to minimize the use of animals in the testing of chemicals.

The materials within the Substituted p-Phenylenediamines category, for the purposes of the HPV Program, are defined as phenylenediamines with alkyl, aryl or mixed alkyl-aryl substitutions, as illustrated in Figure 1.

The category referred to as Substituted p-Phenylenediamines is further categorized into two secondary subcategories; Alkylated N-PPD and 4-Aminodiphenylamine derivatives. The Alkylated N-PPD materials are structurally similar in that both N groups are alkylated, while the 4-Aminodiphenylamine Derivatives materials all contain aryl and alkyl substituted groups. Chemical structures for these materials are provided in Figure 2. The very low water solubility, low vapor pressure, slow biodegradation, low bioaccumulation potential, rapid hydrolysis and photodegradation are similar for the Substituted p-Phenylene Diamines (see Tables 1 and 3). These highly-colored, staining compounds also exhibit high flash points (see Table 1).

Matrix of SIDS Endpoints

In order to construct a matrix of SIDS endpoints for the members of the Substituted p-Phenylenediamines category, the data on physicochemical properties, environmental fate and effects, and health effects for each member of the category must be collected and evaluated for adequacy. The results of these activities are presented in the tables and text below, providing a matrix of available data for the Substituted p-Phenylenediamines materials.

Correlation within the Substituted p-Phenylenediamines Category

The matrix data patterns for physicochemical properties; environmental fate, ecotoxicity; and health effects have been evaluated for the members of the Substituted p-Phenylenediamines category. A description of the results of this evaluation follows.

Correlation of Physicochemical Properties

The physicochemical properties of the members of the Substituted p-Phenylenediamines category are presented in Table 2. These materials may exist as viscous liquids or solids at room temperature, such that melting point or boiling point data may be relevant for varying members of the category. The similarities in the other physicochemical properties of these materials, which are described below, are explained by similarities in their chemical structure, and provide justification of this group of chemicals as a category within the HPV Challenge Program.

The members of this category have a wide range of melting points and boiling points (varying based on the physical state as a liquid or solid). Six members of this category have very low vapor pressures, as indicated in Table 2. Data for six members of this category clearly indicate a lack of water solubility or negligible water solubility. Partition coefficient data are primarily in the range of 3 to 5.

Bridging to other members of the category or use of EPIWIN modeling will be used to fill physicochemical properties data requirements for the purposes of the HPV Program, as illustrated below, and in Table 1.

Alkylated N-PPD: Sufficient data exist for the Alkylated N-PPD materials for the purposes of the HPV Program.

4-Aminodiphenylamine Derivatives: Physicochemical properties data (boiling point and vapor pressure) for p-Phenylenediamine, N-(1,3-dimethylbutyl) N'-phenyl (793-24-8) are provided by EPIWIN modeling. Vapor pressure, boiling point and water solubility data will be bridged from p-Phenylenediamine, N-(1,4-dimethylpentyl) N'-phenyl (3081-01-4) to 1,4-Benzenediamine, N,N'-mixed Ph and toyl derivatives (68953-84-4). Partition coefficient data for p-Phenylenediamine, N-(1,4-dimethylpentyl) N'-phenyl (3081-01-4) will be bridged to p-Phenylenediamine, N,(1-methylheptyl)-N'-phenyl, (15233-47-3). EPIWIN was used to provide melting point and vapor pressure data for p-Phenylenediamine, N,(1-methylheptyl)-N'-phenyl, (15233-47-3).

Correlation of Environmental Fate

The members of this category are generally found to be not readily biodegradable by CO_2 generation, but photodegradation is rapid, as is hydrolysis. Analytical studies of hydrolysis products indicate that the molecule cleaves at the aromatic carbon-nitrogen bond.

The HPV Challenge Program requires that hydrolysis, photodegradation, biodegradation and environmental transport information be presented for each material or bridged to each member of a category. Adequate biodegradation data exist for several of the materials in this category for the purposes of the HPV Program; bridging will be used to fill the remaining biodegradation data requirements as illustrated below. The results presented indicate that these materials are poorly biodegradable, with the exception of p-Phenylenediamine, N-Isopropyl-N'-phenyl-, (101-72-4) and p-Phenylenediamine, N-(1,3-diemthylbutyl) N'-phenyl-, (793-24-8). Hydrolysis data exists for several members of this group, and gas chromatography identification and quantification of hydrolysis products suggests a common breakdown mechanism exists. Photodegradation studies presented for several members of this category are adequate for the purposes of the HPV Program; bridging will be used to fill the remaining photodegradation data requirements as illustrated below. Finally, fugacity modeling has been conducted on six of the seven members of this category, with consistent results showing partitioning to soil and/or sediment. This finding is consistent with the lack of water solubility and low vapor pressure of these materials. Bridging to other members of the category will fill environmental transport data requirements, as illustrated below.

Alkylated N-PPD: The hydrolysis data for p-Phenylenediamine, N,N-bis(1,4-dimethylpentyl) (3081-14-9) will be bridged to p-Phenylenediamine, N,N-di-sec-butyl (101-96-2). Biodegradation and photodegradation data for p-Phenylenediamine, N,N-di-sec-butyl (101-96-2) was modeled using EPIWIN.

4-Aminodiphenylamine Derivatives: Photodegradation, hydrolysis, and environmental transport data will be bridged from p-Phenylenediamine, N-(1,3-dimethylbutyl) N'-phenyl (793-24-8) to 1,4-Benzenediamine, N,N'-mixed Ph and toyl derivatives (68953-84-4). Photodegradation data was modeled using EPIWIN for p-

Phenylenediamine, N-Isopropyl-N'-phenyl-, (101-72-4), p-Phenylenediamine, N-(1,3-dimethylbutyl) N'-phenyl (793-24-8), p-Phenylenediamine, N-(1,4-dimethylpentyl) N'-phenyl (3081-01-4 and p-Phenylenediamine, N,(1-methylheptyl)-N'-phenyl, (15233-47-3).

Biodegradation data for p-Phenylenediamine, N,(1-methylheptyl)-N'-phenyl, (15233-47-3) was modeled using EPIWIN.

Correlation of Ecotoxicity

The HPV Challenge Program requires that an acute aquatic ecotoxicity test in fish, invertebrates, and algae be performed or bridged to each member of a category. Existing data (Table 4) indicate that six members of the Substituted p-Phenylenediamines category have low water solubility. The low water solubility suggests that the acute aquatic toxicity of these materials should be low due to limited bioavailability to aquatic organisms. However, the Substituted p-Phenylenediamines, in general, are very toxic to aquatic organisms. Additional testing is not necessary for these materials for the purposes of the HPV Program.

Alkylated N-PPD: Results of acute aquatic toxicity studies show p-Phenylenediamine, N, N-bis(1,4-dimethylpentyl) (3081-14-9) is harmful to algae, and very toxic to fish and Daphnia. P-Phenylenediamine, N, N-di-sec-butyl (101-96-2) was very toxic to fish and toxic to Daphnia in acute aquatic studies. The algal growth inhibition data for p-Phenylenediamine, N, N-bis(1,4-dimethylpentyl) (3081-14-9) will be bridged to p-Phenylenediamine, N, N-di-sec-butyl (101-96-2).

4-Aminodiphenylamine Derivatives: Aquatic toxicity data exist for four of the five members of this subcategory. The results of aquatic toxicity testing of these materials indicate they are toxic to very toxic to fish, Daphnia, and algae in acute studies.

The acute aquatic toxicity data for p-Phenylenediamine, N-(1,4-dimethylpentyl) N'-phenyl (3081-01-4) will be bridged p-Phenylenediamine, N,(1-methylheptyl)-N'-phenyl, (15233-47-3).

Correlation of Health Effects

Acute Mammalian Toxicity

Acute oral and dermal toxicity data for the Substituted p-Phenylenediamines category are summarized in Table 5. The two materials in the Alkylated N-PPD subcategory of the Substituted p-Phenylene Diamines show a moderate order of acute oral toxicity. The second subcategory, the 4-Aminodiphenylamine derivatives, all have a very low order of toxicity, with LD50 values greater than the limit test of 2000 mg/kg with the exception of p-Phenylenediamine, N-Isopropyl-N'-phenyl-, (101-72-4), with an oral LD50 of 900 mg/kg. Acute dermal toxicity data for all members of the Substituted p-Phenylenediamines category demonstrate a very low order of toxicity with the dermal LD50 values greater than the limit test of 2000 mg/kg.

Adequate acute toxicity studies have been conducted for the Substituted p-Phenylenediamines category. These studies involved at least two routes of exposure (oral and dermal); and evaluated the toxicity of all the members of the category. The data demonstrate a moderate to very low order of acute toxicity. The trend in acute oral

toxicity follows the molecular weight of the materials. That is, there is a general trend toward decreasing acute oral toxicity with increasing molecular weight. The similarity in the order of toxicity for these materials is consistent with their similar chemical structure and physicochemical properties and supports the scientific justification of these materials as a category within the HPV Challenge Program.

The HPV Challenge Program requires that either an acute test be performed or bridged to each member of a category. Adequate acute oral and dermal toxicity tests exist for the Substituted N-Phenylenediamines for the purposes of the HPV Program.

Mutagenicity

A summary of the mutagenicity information for the Substituted p-Phenylenediamines category is presented in Table 6. The weight of evidence for the members of this category indicates these materials are not mutagenic.

Adequate bacterial mutagenicity tests have been conducted for all seven of the Substituted N-Phenylene diamines category to satisfy HPV Challenge requirements. Similarly, adequate *in vitro* chromosome aberration tests or *in vivo* micronucleus tests have been conducted for five of the seven materials in the Substituted N-Phenylenediamines category; additional *in vitro* or *in vivo* mammalian mutagenicity studies are available as supporting information; bridging will be used to fill the remaining data requirement.

Bacterial Gene Mutation Assay

With one exception, mutagenicity was not exhibited by any of the materials in the Substituted p-Phenylenediamines category in the bacterial mutagenicity tests with or without metabolic activation. The single exception was a positive response with 1,4-Benzenediamine, N,N'-mixed Ph and toyl derivatives (68953-84-4).

In vivo Chromosomal Aberration Assays (Mammalian Micronucleus Test)

Three of the seven Substituted p-Phenylenediamine materials have been adequately tested in an *in vivo* chromosomal aberration assay for HPV Challenge requirements. The results were negative for clastogenicity.

In vitro Chromosomal Aberration Assay

Six of the seven Substituted p-Phenylenediamine materials have been adequately tested in an *in vitro* chromosomal aberration assay using Chinese hamster ovary cells to satisfy Program requirements. The results of these studies, performed with and without metabolic activation of the test material, were negative for clastogenicity with the exception of p-Phenylenediamine, N-(1,4-dimethylpentyl) N'-phenyl (3081-01-4).

The Substituted p-Phenylenediamines category has been adequately tested for mutagenicity in tests for gene mutations and chromosomal aberrations for purposes of meeting HPV Challenge requirements. The assays included point mutations in bacterial cells, *in vitro* chromosomal aberrations in mammalian cells, and *in vivo* chromosomal aberrations. The data consistently demonstrate no evidence of genotoxicity for this category of materials. 1,4-Benzenediamine, N,N'-mixed Ph and toyl derivatives (68953-84-4) was positive in the bacterial mutagenicity test, but was negative in both in vitro and in vivo mammalian mutagenicity studies. p-Phenylenediamine, N-(1,4-dimethylpentyl) N'-phenyl (3081-01-4) was positive for clastogenicity in the *in vitro* chromosome aberration test, but was negative in the *in vivo* mouse micronucleus test. This suggests that all

members of the category lack genotoxicity due to their similarity in chemical structures and physicochemical properties. The similarity of results for genotoxicity supports treatment of these materials as a chemical category within the HPV Challenge Program.

The HPV Challenge Program requires that a gene mutation and a chromosomal aberration test be performed or bridged to each member of a category. Bridging will be used to fill the remaining data requirements.

Alkylated N-PPD: Sufficient data exist for the Alkylated N-PPD materials for the purposes of the HPV Program.

4-Aminodiphenylamine Derivatives: Data from *in vivo* mutagenicity testing with p-Phenylenediamine, N-(1,3-dimethylbutyl) N'-phenyl (793-24-8) will be bridged to p-Phenylenediamine, N-Isopropyl-N'-phenyl-, (101-72-4). Mutagenicity test data from p-Phenylenediamine, N-(1,4-dimethylpentyl) N'-phenyl (3081-01-4) will be bridged to p-Phenylenediamine, N,(1-methylheptyl)-N'-phenyl, (15233-47-3).

By bridging these data, the category has been evaluated adequately for genotoxicity for the purposes of the HPV Program, and no additional testing is proposed**.**

Repeat Dose Toxicity

A summary of the repeat dose toxicity data for the Substituted p-Phenylene Diamines category is presented in Table 7.

Alkylated N-PPD: Adequate repeat dose studies are available for both the Alkylated N-PPD materials for the purposes of the HPV Program. P-Phenylenediamine, N, N-bis (1,4-dimethylpentyl) (3081-14-9) was given in the diet to rats at levels of 0, 100, 300, 500, 1000, or 2000 ppm (5/sex/group) for four weeks. Males at 300 ppm and above and females at 1000 ppm and above showed a reduced body weight gain. Alterations in hematology and clinical chemistry parameters were noted at the two highest dose levels. The No Observed Effect Level (NOEL) for males and females was 100 and 300 ppm, respectively. 100 male and female rats (10/sex/dose level) were dosed with p-Phenylenediamine, N, N-di-sec-butyl (101-96-2) in corn oil vehicle at 0, 10, 25, 50, or 100 mg/kg for a period of 28 days. Because the results of this study demonstrated hepatic effects in both sexes and at all treatment levels, a NOEL could not be established.

4-Aminodiphenylamine Derivatives: Adequate repeat dose studies are available for four of the five 4-Aminodiphenylamine Derivatives materials for the purposes of the HPV Program.

Subchronic studies have been conducted with p-Phenylenediamine, N-Isopropyl-N'-phenyl-, (101-72-4). When administered to rats in the diet at levels of 0, 500, 1000, 1750 and 2500 ppm for four weeks, decreases in body weight gains, hematological effects, elevations in total serum protein and increased lever and spleen weight were noted at 1000 ppm and above. The NOEL was identified as 500 ppm. In a 90-day study, p-Phenylenediamine, N-Isopropyl-N'-phenyl-, (101-72-4) was administered to rats in the diet at levels of 0, 180, 360 or 720 ppm. Lower body weight gains were observed in high-dose males; increased absolute and relative liver weights were noted in mid- and high-dose males and all treated females. Increased spleen and kidney weights were observed in high-dose females, and mild anemia was noted in mid- and high-dose animals. There

were no treatment related gross or histopathological changes noted in any group. A NOEL for organ weight changes was not established for females, while a NOEL for males was 180 ppm.

Dietary administration of p-Phenylenediamine, N-(1,4-dimethylpentyl) N'-phenyl (3081-01-4) at 0, 500, 750, 1500 or 3000 ppm to rats for one month resulted in reduced food consumption and decreased weight gain at the three highest doses in both sexes. No gross pathology or other signs of toxicity were noted. The NOEL was identified as 500 ppm in the diet.

Dietary administration of 1,4-Benzenediamine, -mixed Ph and toyl derivatives (68953-84-4) at concentrations of 0, 120, 470 and 1900 ppm (0, 7.5, 30 and 120 mg/kg/day) to rats for 28 days resulted in body weight decreases in high dose female rats and decreased food consumption in high-dose males and mid- and high-dose females. Hematological changes (high dose), liver and kidney weight increases (high-dose male and female, mid-dose females). The No Observed Adverse Effects Level (NOAEL) for this study was established at 7.5 mg/kg. A 21-day gavage range-finding study was also conducted with rats with this material at doses of 0, 0.1, 0.3, 1 and 3 g/kg/day. Lethality was observed at 1 and 3 g/kg/day. Body weight gain loss, liver weight increase and hepatocellular labeling index increase were noted at 0.3 and/or 0.1 g/kg/day.

Santoflex 13 (p-Phenylenediamine, N-(1,3-dimethylbutyl) N'-phenyl (793-24-8)) was administered in feed to groups of 6 week old male and female rats at 0, 250, 1000 or 2500 ppm. Analyses via GC verified feeding levels of 0, 230, 950 and 2300 ppm. All animals survived the length of the study. Signs of toxicity during the study were limited to reduced feed consumption/body weight gain in the high-dose males and females and mid-level males. Anemia, lymphocytopenia and thrombocytosis were present in males and females, primarily at the two highest dose levels. Increases in total bilirubin in males, and total protein, albumin, globulin, calcium and/or cholesterol in both sexes were noted in high and some mid-dose level animals. Increased liver weights were observed at the two highest dose levels. There were no gross or microscopic lesions attributed to consumption of the test material. Females at low dose levels exhibited mild anemia at the interim sampling period, but all recovered by the end of the study. Therefore, the NOEL was considered to be 250 ppm.

Repeat dose data from p-Phenylenediamine, N-(1,4-dimethylpentyl) N'-phenyl (3081-01-4) will be bridged to p-Phenylenediamine, N,(1-methylheptyl)-N'-phenyl, (15233-47-3).

By bridging these data, the category has been evaluated adequately for genotoxicity for the purposes of the HPV Program, and therefore, no additional testing is proposed**.**

Reproductive and Developmental Toxicity A summary of the reproductive and developmental toxicity data for the Substituted p-Phenylenediamines category is presented in Table 7.

Alkylated N-PPD: Adequate reproductive toxicity studies are available for the purposes of the HPV Program for one of the two Alkylated N-PPD materials. P-Phenylenediamine, N, N-bis (1,4-dimethylpentyl) (3081-14-9) was not embryotoxic, fetotoxic or teratogenic when administered by gavage at doses of 0, 25, 75 or 150 mg/kg/day to pregnant rats on gestation days 6-15. Administration of CAS No. 3081-14-9 at dietary concentrations of 0, 30, 100 or 300 ppm to male and female rats for three successive generations produced no adverse effects on mating or fertility indices. Reduced survival of offspring was observed in mid- and high-dose

groups; however, evidence of parental toxicity was also present as indicated by reduced body weight gains of mid- and high-dose groups. The NOEL was 30 ppm. The developmental and reproductive studies with p-Phenylenediamine, N, N-bis (1,4-dimethylpentyl) (3081-14-9 will be bridged to p-Phenylenediamine, N, N-di-sec-butyl (101-96-2).

4-Aminodiphenylamine Derivatives: Adequate reproductive and developmental toxicity studies are available for three of the five 4-Aminodiphenylamine Derivatives materials for the purposes of the HPV Program.

p-Phenylenediamine, N-Isopropyl-N'-phenyl-, (101-72-4) was administered to rats by gavage at dose levels of 0, 12.5, 62.5 or 125 mg/kg/day for gestation days 6-15. The NOEL for maternal toxicity was determined to be 62.5 mg/kg. There were significant skeletal effects at 125 mg/kg and the NOEL for teratogenicity was established at 62.5 mg/kg.

1,4-Benzenediamine, N, N'-mixed Ph and toyl derivatives (68953-84-4) was administered in feed at 0, 120, 400 or 1500 ppm to rats in a two-generation reproductive toxicity study. Dystocia (potentially leading to prolonged gestation and increased perinatal deaths, decreased live births and increased pup weights), and polycystic lesions were observed at all dose levels; a NOAEL was not established in this study. A developmental study was also conducted with 1,4-Benzenediamine, N, N'-mixed Ph and toyl derivatives (68953-84-4) in rats. The test article was administered by gavage at dose levels of 0, 20, 70 and 200 mg/kg/day for gestation days 6-15. The test article produced minimal effects (body weight) to maternal rats at 200 mg/kg during pregnancy; the NOAEL for maternal toxicity was established at 70 mg/kg/day. There were no birth defects observed in fetal animals and the NOAEL for teratogenicity/developmental effects was established at 200 mg/kg/day.

A reproductive oral gavage study was conducted in rats with p-Phenylenediamine, N-(1,3-dimethylbutyl) N'-phenyl (793-24-8); no reproductive effects were observed at the highest concentration tested (1000 ppm). In a rat gavage developmental study, the test article was administered by gavage at dose levels of 0, 50, 100 and 250 mg/kg/day for gestation days 6-15. A NOAEL (teratogenicity /developmental effects) greater than 250 mg/kg/day was determined. The NOEL for maternal toxicity was established at 50 mg/kg/day.

Data from these three studies materials will be bridged to p-Phenylenediamine, N- (1,4-dimethylpentyl) N'-phenyl (3081-01-4) and p-Phenylenediamine, N, (1-methylheptyl)-N'-phenyl, (15233-47-3).

Test Plan

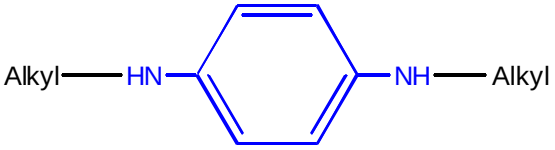
Table 8 provides the category test plan for the Substituted p-Phenylenediamines. All HPV endpoint requirements are fulfilled by existing adequate data, calculated data, or by bridging data based on SAR and the category approach. The chemicals that constitute the Substituted p-Phenylenediamines category require no additional testing for the purposes of the HPV Program.

FIGURES

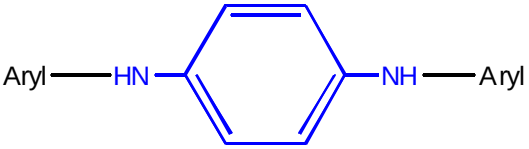
Figure 1. Structural Definition

Phenylenediamine with various aryl or alkyl substitutions in the para position:

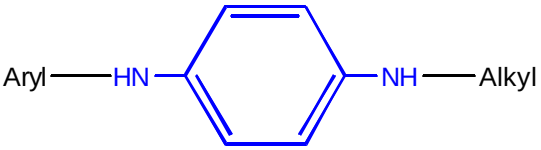
Alkyl-N-Phenyl-N-Alkyl (all Alkyl)
Aryl-N-Phenyl-N-Aryl (All Aryl)
Alkyl-N-Phenyl-N-Aryl (Mixed Alkyl-Aryl)

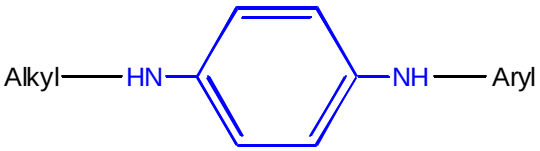


Alkyl-Alkyl Substitutions



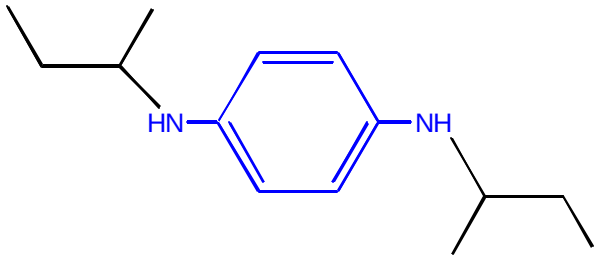
Aryl-Aryl Substitutions



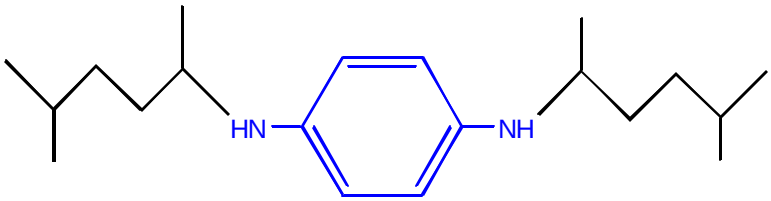


Mixed Alkyl-Aryl Substitutions

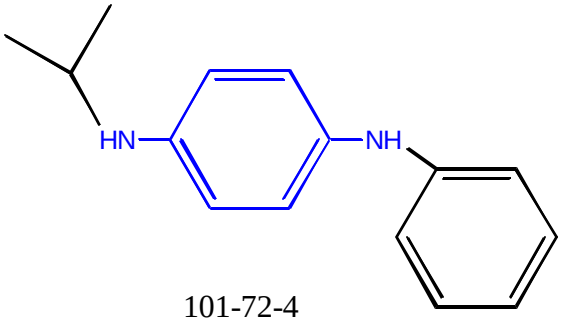
FIGURE 2. Chemical Structures



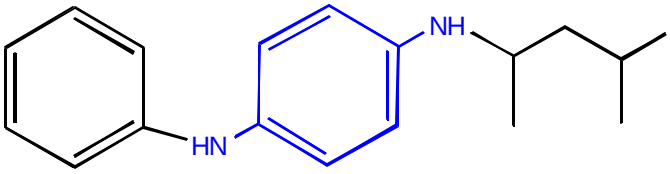
101-96-2
Alkyl-Alkyl



3081-14-9
Alkyl-Alkyl

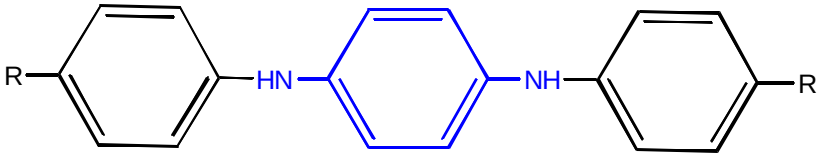


101-72-4
Alkyl-Aryl

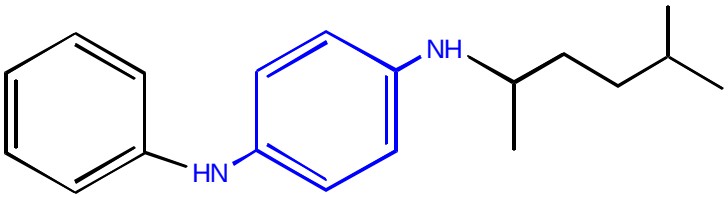


793-24-8
Alkyl-Aryl

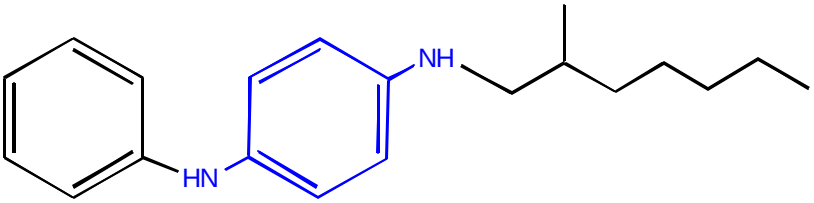
R = H or CH3



68953-84-4
Aryl-Aryl (Mixed)



3081-01-4
Alkyl-Aryl



15233-47-3
Alkyl-Aryl

TABLES

Table 1. Justification of the Substituted p-Phenylenediamines Category using Flash Point, Vapor Pressure, Water Solubility and Biodegradation

Name (CAS No.)/ Molecular weight	Flash Point (^oF)	Vapor Pressure (mm Hg @ 20^oC)	Water Solubility	Bio-degradability
Alkylated N-PPD				
p-Phenylenediamine, N,N-di-sec-butyl (101-96-2)/ 220.4	290	85.3 @ 33C	Insoluble	Not readily biodegradable
p-Phenylenediamine, N,N-bis(1,4-dimethylpentyl) (3081-14-9)/ 304	182	1.1 @ 25C	Very Slight	Not readily biodegradable
4-Aminodiphenylamine derivatives				
p-Phenylenediamine, N-Isopropyl-N'-phenyl-, (101-72-4)/ 226.4	>200 C	3.4E-5 @ 90C	Insoluble	Readily biodegradable
p-Phenylenediamine, N-(1,3-dimethylbutyl) N'-phenyl (793-24-8)/ 268.5	400	4.93E-6 @ 25C (EPIWIN)	Insoluble	Readily biodegradable
1,4-Benzenediamine, N,N'-mixed Ph and toyl derivatives (68953-84-4)/ 274	450	Not determined	Not determined	Not readily biodegradable
p-Phenylenediamine, N-(1,4-dimethylpentyl) N'-phenyl (3081-01-4)/ 282	420	1.25E-10 @25C	Insoluble	Not readily biodegradable
p-Phenylenediamine, N,(1-methylheptyl)-N'-phenyl, (15233-47-3)/ 296	Not determined	4.99E-7 @ 25C (EPIWIN)	Insoluble	Not readily biodegradable

Table 2. Matrix of Available and Adequate Data on Substituted p-Phenylenediamines Category Members Physicochemical Properties

Name (CAS No.)	Melting Point (^oC)	Vapor Pressure (mm Hg @ 20^oC)	Boiling Point (^oC)	Partition Coefficient	Water Solubility
Alkylated N-PPD					
p-Phenylenediamine, N,N-di-sec-butyl (101-96-2)	18	85.3 @ 38 C	98 @ 26.6hPa	3.50	<1 mg/ml @ 20C
p-Phenylenediamine, N,N-bis(1,4-dimethylpentyl) (3081-14-9)	-36	<1.1E-6 @ 25C	183.5 @ 1mm Hg	5.34	21 ppm @ pH5; 0.8 ppm @ pH 9
4-Aminodiphenylamine derivatives					
p-Phenylenediamine, N-Isopropyl-N'-phenyl-, (101-72-4)	75-80	3.4E-3 @90C	161	3.28	15 ppm @25C
p-Phenylenediamine, N-(1,3-dimethylbutyl) N'-phenyl (793-24-8)	45	4.93E-6 @25C (EPIWIN)	369.67 (EPIWIN)	4.7	1 ppm @ 23C
1,4-Benzenediamine, N,N'-mixed Ph and toyl derivatives (68953-84-4)	90-105	Not determined	Not determined	3.4-4.3	Not determined
p-Phenylenediamine, N-(1,4-dimethylpentyl) N'-phenyl (3081-01-4)	32	1.25E-10 @ 25C	231 @3.5 mmHg	5.17	0.67g/l @ 25C
p-Phenylenediamine, N,(1-methylheptyl)-N'-phenyl, (15233-47-3)	145.77 (EPIWIN)	4.99E-7 @ 25C (EPIWIN)	431	Not determined	Insoluble

Table 3. Matrix of Available and Adequate Data on Substituted p-Phenylenediamines Category Members Environmental Fate

Name (CAS No.)	Hydrolysis	Photo-degradation (t1/2 in hours)	Bio-degradation	Environmental Transport
Alkylated N-PPD				
p-Phenylenediamine, N, N-di-sec-butyl (101-96-2)	Not determined	1.095 (EPIWIN)	Not readily biodegradable (EPIWIN)	Primarily to soil
p-Phenylenediamine, N, N-bis(1,4-dimethylpentyl) (3081-14-9)	97%@pH7 after 24 hr	2	50% after 35 days	Primarily to sediment
4-Aminodiphenylamine derivatives				
p-Phenylenediamine, N-Isopropyl-N'-phenyl-, (101-72-4)	99%@pH7 after 24 hr	0.588 (EPIWIN)	98% after 22 hours	Primarily to soil
p-Phenylenediamine, N-(1,3-dimethylbutyl) N'-phenyl (793-24-8)	93%@pH7 after 24 hr	0.567 (EPIWIN)	50 % after 2.9 hours	Primarily to soil
1,4-Benzenediamine, N, N'-mixed Ph and toyl derivatives (68953-84-4)	Not determined	Not determined	0.64% after 28 days	Not determined
p-Phenylenediamine, N-(1,4-dimethylpentyl) N'-phenyl (3081-01-4)	96%@pH7 after 24 hr	0.563 (EPIWIN)	0% @ 35days	Primarily to soil
p-Phenylenediamine, N,(1methylheptyl)-N'-phenyl, (15233-47-3)	Not determined	0.56 (EPIWIN)	Not readily biodegradable (EPIWIN)	Primarily to soil and sediment

Table 4. Matrix of Available and Adequate Data on Substituted p-Phenylenediamines Category Members Ecotoxicity

Name (CAS No.)	Acute Fish 96-hour LC50 (mg/l)	Acute Invertebrate 48-hour EC50 (mg/l)	Algal growth inhibition 96-hour EC50 (mg/l)
Alkylated N-PPD			
p-Phenylenediamine, N,N-di-sec-butyl (101-96-2)	0.13	1.4	Not determined
p-Phenylenediamine, N,N-bis(1,4-dimethylpentyl) (3081-14-9)	0.28	0.37	52
4-Aminodiphenylamine derivatives			
p-Phenylenediamine, N-Isopropyl-N'-phenyl-, (101-72-4)	0.34	1.1	0.5 (cell growth)
p-Phenylenediamine, N-(1,3-dimethylbutyl) N'-phenyl (793-24-8)	0.14-0.4	0.82	0.6
1,4-Benzenediamine, N,N'-mixed Ph and toyl derivatives (68953-84-4)	0.48	1.8	(72-hour EC50) 0.018 (biomass); >0.079 (growth rate)
p-Phenylenediamine, N-(1,4-dimethylpentyl) N'-phenyl (3081-01-4)	0.3-1.1	0.2	0.7
p-Phenylenediamine, N,(1methylheptyl)-N'-phenyl, (15233-47-3)	Not determined	Not determined	Not determined

Table 5. Matrix of Available and Adequate Data on Substituted p-Phenylenediamines Category Members Acute Toxicity

Name (CAS No.)	Acute Oral (mg/kg)	Acute Dermal (mg/kg)
Alkylated N-PPD		
p-Phenylenediamine, N,N-di-sec-butyl (101-96-2)	271	2806
p-Phenylenediamine, N,N-bis(1,4-dimethylpentyl) (3081-14-9)	730	>3160
4-Aminodiphenylamine derivatives		
p-Phenylenediamine, N-Isopropyl-N'-phenyl-, (101-72-4)	900	>7940
p-Phenylenediamine, N-(1,3-dimethylbutyl) N'-phenyl (793-24-8)	>5000	>7940
1,4-Benzenediamine, N,N'-mixed Ph and toyl derivatives (68953-84-4)	>2000	>2000
p-Phenylenediamine, N-(1,4-dimethylpentyl) N'-phenyl (3081-01-4)	>2000	>5010
p-Phenylenediamine, N,(1-methylheptyl)-N'-phenyl, (15233-47-3)	4300	>2000

Table 6. Matrix of Available and Adequate Data on Substituted p-Phenylenediamines Category Members Genotoxicity

Name (CAS No.)	Genotoxicity (*in vitro* - bacterial)	Genotoxicity (*in vitro* - mammalian)	Genotoxicity (*in vivo*)
Alkylated N-PPD			
p-Phenylenediamine, N,N-di-sec-butyl (101-96-2)	Negative	Negative	Not determined
p-Phenylenediamine, N,N-bis(1,4-dimethylpentyl) (3081-14-9)	Negative	Negative	Not determined
4-Aminodiphenylamine derivatives			
p-Phenylenediamine, N-Isopropyl-N'-phenyl-, (101-72-4)	Negative	Negative	Not determined
p-Phenylenediamine, N-(1,3-dimethylbutyl) N'-phenyl (793-24-8)	Negative	Negative	Negative
1,4-Benzenediamine, N,N'-mixed Ph and toyl derivatives (68953-84-4)	Positive	Negative	Negative
p-Phenylenediamine, N-(1,4-dimethylpentyl) N'-phenyl (3081-01-4)	Negative	Weak Positive; Supporting data Negative	Negative
p-Phenylenediamine, N,(1methylheptyl)-N'-phenyl, (15233-47-3)	Negative	Not determined	Not determined

Table 7. Matrix of Available and Adequate Data on Substituted p-Phenylenediamines Category Members Health Effects

Name (CAS No.)	Repeat Dose	Reproductive	Developmental
Alkylated N-PPD			
p-Phenylenediamine, N,N-di-sec-butyl (101-96-2)	28-Day oral gavage with rats. NOEL< 10 mg/kg/day	Not determined	Not determined
p-Phenylenediamine, N,N-bis(1,4-dimethylpentyl) (3081-14-9)	30 day feeding study with rats. NOEL (males) 100 pm; (females) 300 ppm	Three generation rat oral feeding study; NOEL(parental, F1 and F2 offspring) = 30 ppm	Rat gavage: NOEL (teratogenicity) = >150 mg/kg/day; (maternal) = 25 mg/kg/day
4-Aminodiphenylamine derivatives			
p-Phenylenediamine, N-Isopropyl-N'-phenyl-, (101-72-4)	90-day feeding study with rats. NOEL (males) 180 ppm; NOEL not established (females)	Not determined	Rat gavage: NOEL (teratogenicity) = 62.5, (maternal) 62.5 mg/kg/day
p-Phenylenediamine, N-(1,3-dimethylbutyl) N'-phenyl (793-24-8)	90-day oral rat-NOAEL = 250 ppm in feed	Rat gavage – NOEL (parental) >1000 ppm; (F1 offspring) >1000 ppm	Rat gavage: NOAEL (teratogenicity /developmental effects) = 250 mg/kg/day; NOEL (maternal) = 50 mg/kg/day
1,4-Benzenediamine, N,N'-mixed Ph and toyl derivatives (68953-84-4)	28-day rat oral NOAEL = 7.5 mg/kg	Two generation rat oral feeding study – NOEL not identified	Rat gavage: NOAEL (teratogenicity /developmental effects) ≤ 200 mg/kg/day, NOAEL (maternal toxicity 70 mg/kg/day)
p-Phenylenediamine, N-(1,4-dimethylpentyl) N'-phenyl (3081-01-4)	1 month feeding study with rats – NOEL = 500 ppm in diet	Not determined	Not determined
p-Phenylenediamine, N,(1methylheptyl)-N'-phenyl, (15233-47-3)	Not determined	Not determined	Not determined

.

Table 8

Substituted p-Phenylenediamines Category Test Plan

CAS Nos. 101-96-2, 3081-14-9, 101-72-4, 793-24-8, 3081-01-4, 15233-47-3, and 68953-84-4
Rubber and Plastic Additives Panel American Chemistry Council
December 2001

	Physical-Chemical				
CHEMICAL	**Melting Point**	**Boiling Point**	**Vapor Pressure**	**Partition Coefficient**	**Water Solubility**
Alkylated N-PPD					
p-Phenylenediamine, N,N-di-sec-butyl (101-96-2)	A	A	A	A	A
p-Phenylenediamine, N,N-bis(1,4-dimethylpentyl) (3081-14-9)	A	A	A	A	A
4-Aminodiphenylamine derivatives					
p-Phenylenediamine, N-Isopropyl-N'-phenyl-, (101-72-4)	A	A	A	A	A
p-Phenylenediamine, N-(1,3-dimethylbutyl) N'-phenyl (793-24-8)	A	Calc	Calc	A	A
1,4-Benzenediamine, N,N'-mixed Ph and toyl derivatives (68953-84-4)	A	R	R	A	R
p-Phenylenediamine, N-(1,4-dimethylpentyl) N'-phenyl (3081-01-4)	A	A	A	A	A
p-Phenylenediamine, N,(1methylheptyl)-N'-phenyl, (15233-47-3)	R	A	Calc	R	A

Legend	
Symbol	**Description**
R	Endpoint requirement fulfilled using category approach, SAR
Test	Endpoint requirements to be fulfilled with testing
Calc	Endpoint requirement fulfilled based on calculated data
A	Endpoint requirement fulfilled with adequate existing data
NR	Not required per the OECD SIDS guidance
NA	Not applicable due to physical/chemical properties

Table 8 (continued)

	Environmental Fate			
CHEMICAL	**Photo-degradation**	**Hydrolysis**	**Environmental Transport**	**Biodegradation**
Alkylated N-PPD				
p-Phenylenediamine, N,N-di-sec-butyl (101-96-2)	Calc	R	Calc	Calc
p-Phenylenediamine, N,N-bis(1,4-dimethylpentyl) (3081-14-9)	A	A	Calc	A
4-Aminodiphenylamine derivatives				
p-Phenylenediamine, N-Isopropyl-N'-phenyl-, (101-72-4)	Calc	A	Calc	A
p-Phenylenediamine, N-(1,3-dimethylbutyl) N'-phenyl (793-24-8)	Calc	A	Calc	A
1,4-Benzenediamine, N,N'-mixed Ph and toyl derivatives (68953-84-4)	R	R	R	A
p-Phenylenediamine, N-(1,4-dimethylpentyl) N'-phenyl (3081-01-4)	Calc	A	Calc	A
p-Phenylenediamine, N,(1methylheptyl)-N'-phenyl, (15233-47-3)	Calc	R	Calc	Calc

Legend	
Symbol	**Description**
R	Endpoint requirement fulfilled using category approach, SAR
Test	Endpoint requirements to be fulfilled with testing
Calc	Endpoint requirement fulfilled based on calculated data
A	Endpoint requirement fulfilled with adequate existing data
NR	Not required per the OECD SIDS guidance
NA	Not applicable due to physical/chemical properties

Table 8 (continued)

	Ecotoxicity		
CHEMICAL	**Acute Toxicity to Fish**	**Acute Toxicity to Aquatic Plants (e.g., Algae)**	**Acute Toxicity to Aquatic Invertebrates (e.g., Daphnia)**
Alkylated N-PPD			
p-Phenylenediamine, N,N-di-sec-butyl (101-96-2)	A	R	A
p-Phenylenediamine, N,N-bis(1,4-dimethylpentyl) (3081-14-9)	A	A	A
4-Aminodiphenylamine derivatives			
p-Phenylenediamine, N-Isopropyl-N'-phenyl-, (101-72-4)	A	A	A
p-Phenylenediamine, N-(1,3-dimethylbutyl) N'-phenyl (793-24-8)	A	A	A
1,4-Benzenediamine, N,N'-mixed Ph and toyl derivatives (68953-84-4)	A	A	A
p-Phenylenediamine, N-(1,4-dimethylpentyl) N'-phenyl (3081-01-4)	A	A	A
p-Phenylenediamine, N,(1methylheptyl)-N'-phenyl, (15233-47-3)	R	R	R

Legend	
Symbol	**Description**
R	Endpoint requirement fulfilled using category approach, SAR
Test	Endpoint requirements to be fulfilled with testing
Calc	Endpoint requirement fulfilled based on calculated data
A	Endpoint requirement fulfilled with adequate existing data
NR	Not required per the OECD SIDS guidance
NA	Not applicable due to physical/chemical properties

Table 8 (continued)

	Mammalian Toxicity						
CHEMICAL	**Acute Toxicity**	**Genetic Toxicity *In Vitro* (bacterial)**	**Genetic Toxicity *In Vitro* (mammalian)**	**Genetic Toxicity *In Vivo***	**Repeat Dose Toxicity**	**Repro-ductive Toxicity**	**Develop-mental Toxicity**
Alkylated N-PPD							
p-Phenylenediamine, N,N-di-sec-butyl (101-96-2)	A	A	A	NR	A	R	R
p-Phenylenediamine, N,N-bis(1,4-dimethylpentyl) (3081-14-9)	A	A	A	NR	A	A	A
4-Aminodiphenylamine derivatives							
p-Phenylenediamine, N-Isopropyl-N'-phenyl-, (101-72-4)	A	A	A	R	A	R	A
p-Phenylenediamine, N-(1,3-dimethylbutyl) N'-phenyl (793-24-8)	A	A	A	A	A	A	A
1,4-Benzenediamine, N,N'-mixed Ph and toyl derivatives (68953-84-4)	A	A	A	A	A	A	A
p-Phenylenediamine, N-(1,4-dimethylpentyl) N'-phenyl (3081-01-4)	A	A	R	A	A	R	R
p-Phenylenediamine, N,(1methylheptyl)-N'-phenyl, (15233-47-3)	A	A	R	R	R	R	R

Legend	
Symbol	**Description**
R	Endpoint requirement fulfilled using category approach, SAR
Test	Endpoint requirements to be fulfilled with testing
Calc	Endpoint requirement fulfilled based on calculated data
A	Endpoint requirement fulfilled with adequate existing data
NR	Not required per the OECD SIDS guidance
NA	Not applicable due to physical/chemical properties