COURTNEY M. PRICE
Vice President
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American Chemistry Council
Good Chemistry Makes It Possible

December 18, 2001

Via US Mail and e-mail

Christine Todd Whitman, Administrator
U.S. Environmental Protection Agency (EPA)
P.O. Box 1473
Merrifield, VA 22116

Re: Rubber and Plastic Additives (RAPA) Panel, Consortium No.
HPV Chemical Challenge Program Submission
Hindered Phenols Category
Category Justification and Testing Rationale

Dear Governor Whitman:

The RAPA Panel of the American Chemistry Council is pleased to submit the subject documents to EPA's HPV Chemical Challenge Program (Program) as our test plan for a category covering eight of the 39 chemicals RAPA is voluntarily sponsoring in the Program. The RAPA Panel includes 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.

In this submission, please find the *Category Justification and Testing Rationale* for the category *Hindered Phenols*. Eight chemicals in the category are sponsored in the Program, as listed in the following table:

RAPA Panel Hindered Phenols Category Chemicals Sponsored in the US HPV Chemical Challenge Program	
CAS Number	Compound Name
68610-51-5	phenol, isobutylenated methylstyrenated
61788-44-1	phenol, styrenated
96-69-5	4,4'-thiobis-6-(t-butyl-m-cresol)
85-60-9	4,4'-butylidenebis(6-t-butyl-m-cresol)
79-96-9	phenol, 4,4'-(1-methylethylidene)bis[2,(1,1-dimethylethyl)]-
7786-17-6	phenol, 2,2'-methylenebis(4-methyl-6-nonyl)
68610-51-5	phenol, 4-methyl-, reaction products with dicyclopentadiene and isobutylene

RAPA Panel Hindered Phenols Category Chemicals Sponsored for the US HPV Chemical Challenge Program	
CAS Number	Compound Name
27676-62-6	1,3,5-tris(3,5-di-tert-butyl-4-hydroxybenzyl)-1,3,5-triazine-2,4,6(1H,3H,5H)-trione

Data for three additional chemicals in the category, listed in the table below, are used to support the conclusions reached for the category.

RAPA Panel Hindered Phenols Category Additional Chemicals in the Category	
CAS Number	Compound Name
128-37-0	2,6-di-tert-butyl-p-cresol
2082-79-3	(octadecanoxycarbonylether)phenol
6683-19-8	tetrakis-(methylene-(3,5-di-tertbutyl-4-hydrocinnamate)methane

In addition to the *Category Justification and Testing Rationale*, please also find attached robust summaries contained in IUCLID-formatted documents for each of the eight sponsored chemicals and the three supporting chemicals in the category.

This submission is also being sent electronically to the following e-mail addresses:

Oppt.ncic@epa.gov
Chem.rtl@epa.gov

If you require additional information, please contact the RAPA Panel's technical contact, Dr. Anne P. LeHuray at (703) 741-5630 or *anne_lehuray@americanchemistry.com.*

Sincerely yours,

Courtney M. Price
Vice President, CHEMSTAR

Attachments

Cc: C. Auer, EPA/OPPT
B. Leczynski, EPA/OPPT
RAPA Panel (without attachments)
S. Russell, ACC (without attachments)

AR201-13382A

Hindered Phenols
Category Justification and Testing Rationale

CAS Nos.: 68457-74-9, 61788-44-1, 96-69-5, 85-60-9, 79-96-9, 7786-17-6, 68610-51-5 and 27676-62-6
(+ Chemicals 128-37-0, 2082-79-3 and 6683-19-8 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 Hindered Phenols category of chemicals under the Environmental Protection Agency's High Production Volume (HPV) Challenge Program.

Hindered phenols are non-staining, non-discoloring, non-migratory additives for natural rubber, synthetic rubber, adhesives, plastics, textile fibers, cable coatings, flooring, and coated paper as well as natural and synthetic oils. Their sole purpose is to prevent or greatly delay the deterioration caused by air oxidation. The hindered phenols are very cost-effective and efficient antioxidants. Usage levels for most applications are typically within the range of 0.5 to 2%. Due to their low volatility and non-migratory nature, many hindered phenol antioxidants are regulated for use by the Food and Drug Administration (FDA) in a number of food-contact applications as an Indirect Food Additive.

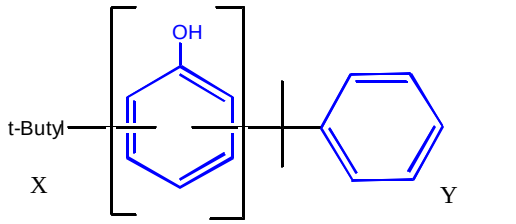
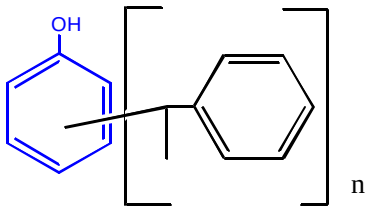
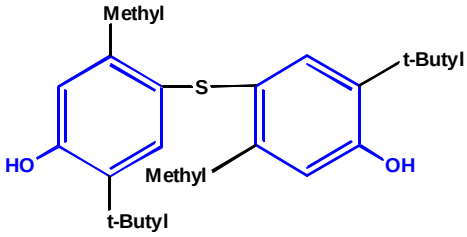
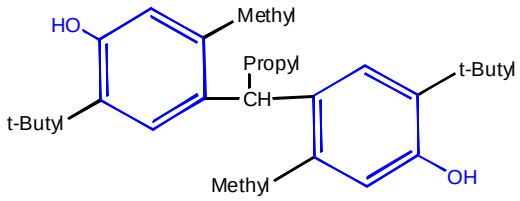
In consideration of animal welfare concerns to minimize the use of animals in the testing of chemicals, the Panel has conducted a thorough literature search for all available data, published and unpublished. It has also performed an analysis of the adequacy of the existing data. Further, it developed a scientifically supportable category of related chemicals and used structure-activity relationship information to fill certain data requirements. It is concluded that there are sufficient data on the members of this category for the purposes of the HPV Program and therefore, no additional testing is recommended.

Hindered Phenols 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.

Relying on several factors specified in EPA's guidance document on "Development of Chemical Categories in the HPV Challenge Program,"[1] in which use of chemical categories is encouraged, the following related chemicals constitute a chemical category.

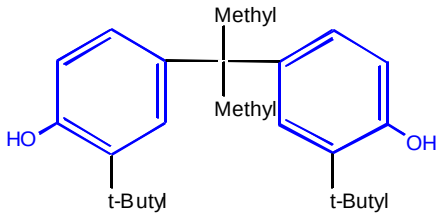
Structural Similarity: The hindered phenols category consists of a group of chemicals in which a molecule of phenol (hydroxybenzene) has relatively large aliphatic and/or aromatic groups positioned adjacent to the hydroxyl group (the 2-, or ortho- position).

Eight substances form the hindered phenols category based on structural similarity:

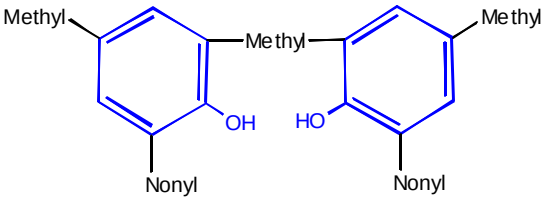
Phenol, isobutylenated methylstyrenated (68457-74-9)  X = 0, 1 or 2 Y = 1, 2 or 3	***Phenol, styrenated (61788-44-1)***  n = 2 or 3
4,4'-Thiobis-6-(t-butyl-m-cresol) (96-69-5)  	***4,4'-Butylidenebis(6-t-butyl-m-cresol) (85-60-9)*** 

[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

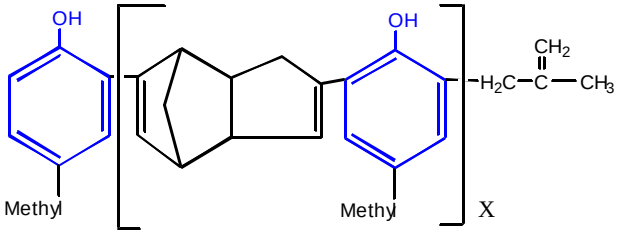
Phenol, 4,4'-(1-methylethylidene)bis [2-(1,1-dimethylethyl)]-, (79-96-9)



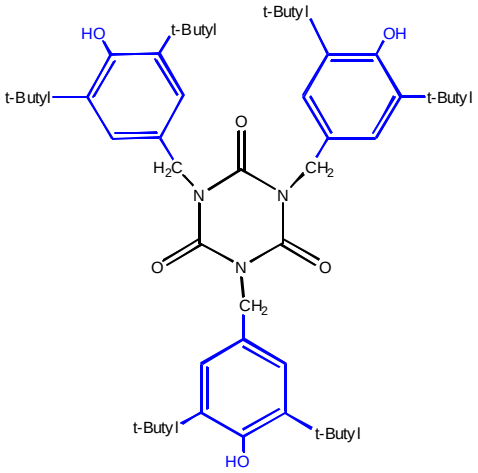
Phenol, 2,2'-methylenebis(4-methyl-6-nonyl) (7786-17-6)



Phenol, 4-methyl-, reaction products with dicyclopentadiene and isobutylene (68610-51-5)

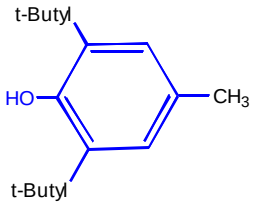


1,3,5-tris(3,5-di-tert-butyl-4-hydroxybenzyl-)-1,3,5-triazine-2,4,6(1H,3H,5H)-trione (27676-62-6)

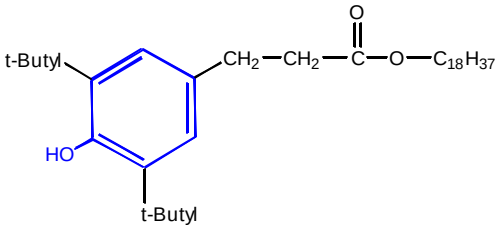


The hindered phenols sponsored in the HPV Program by the RAPA Panel are not a comprehensive list of substances that would fit a hindered phenols category. To better take advantage of the benefits of using a category approach, data for three additional hindered phenols that are not part of the group supported by the RAPA Panel are included in the category justification discussion:

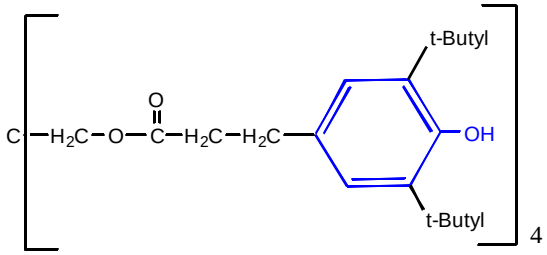
2,6-Di-tert-butyl-p-cresol (BHT) (128-37-0)



***2,6-Di-tert-butyl-4-(octadecanoxycarbonylethyl)phenol* (2082-79-3)**



Tetrakis-(methylene-(3,5-di-tertbutyl-4-hydrocinnamate)methane (6683-19-8)



Similarity of Physiochemical Properties: Hindered phenols are either solids or liquids at room temperature. The vapor pressure of these chemicals is low. Generally, the water solubility for the group chemicals is low and the partition coefficients are high.

Fate and Transport Characteristics. Experimental data show that hindered phenols are not readily biodegradable. With one exception, the low water solubility of these chemicals precludes experimentally obtaining hydrolysis data. Model derived photodegradation indicates that these substances photodegrade rapidly. Fugacity modeling shows that, generally, partitioning would be to soil and sediments rather than air or water. Modeling has been done for all of the substances where the model could be applied and bridging can be done to those substances were the model was not suitable. Additional modeling for the members of this category is not necessary for the purposes of the HPV Program.

Toxicological Similarity. Review of existing published and unpublished test data for the

hindered phenols shows that the aquatic and mammalian toxicity among the substances in this category are similar.

Aquatic Toxicology. Hindered phenols have low water solubility and, therefore, low aquatic toxicity. Experimental data are available on acute fish toxicity, acute invertebrate toxicity, and alga toxicity for the majority of chemicals in this category. Data can be bridged to those substances without experimental data. No additional ecotoxicity toxicity testing is proposed for the purposes of the HPV Program.

Mammalian Toxicology - Acute. Acute oral and dermal toxicity data are available for all but two of the substances in the group. The data show that acute toxicity of these substances is low. The testing for acute toxicity spans five decades. While the majority of studies may not be to current guidelines, tests done according to recent guidelines and under GLP confirm the conclusions of the earlier testing. No additional acute toxicity testing is proposed for the purposes of the HPV Program.

Mammalian Toxicology - Mutagenicity. Data from bacterial reverse mutation assays and *in vitro* and *in vivo* chromosome aberration studies were reviewed. Adequate bacterial gene mutation assays have been conducted with all of the category chemicals except two. Chromosome aberration studies, in vitro and/or in vivo, are available for all but three substances. The mutagenicity data span the range of structures and molecular weights and missing data can be bridged from other members of the group. The weight of evidence for mutagenic potential for this category indicates these substances are not mutagenic. The category has been adequately tested for mutagenicity to meet requirements of the HPV Program, therefore, no additional mutagenicity testing is proposed.

Mammalian Toxicology – Repeated Dose Toxicity. Repeated dose toxicity data of approximately three months (90-day, 12- and 13-week) are available for most of the substances in this group. Data on repeated dose toxicity were not identified for three substances. Reliable chronic toxicity/carcinogenicity studies have been done on two of the group members. Adequate data span the range of structures and molecular weights and missing data can be bridged from other members of the group. Sufficient data are available for meeting the requirements of repeated dose toxicity of the hindered phenols for the purposes of the HPV Program.

Mammalian Toxicology - Reproductive and Developmental Toxicity. For the majority of the hindered phenol chemicals some evaluation of effects on reproduction or reproductive organs is available. Multi-generation reproduction studies are available for three of the substances in this group. Evaluation of effects on reproduction for four of the hindered phenols is provided by histopathological data on male and female reproductive organs from the repeated dose toxicity studies. Developmental toxicity data exist for five of the substances included in this group. Available data for reproductive and developmental toxicity span the range of structures and molecular weights and can be bridged to those group

members where data have not been identified. No additional testing is proposed for the purposes of the HPV Program.

Conclusion. Based on the data reviewed in this document, the physicochemical and toxicological properties of the proposed hindered phenols category are similar and follow a regular pattern as a result of that structural similarity. Therefore, the EPA's definition of a chemical category has been met for the 11 chemicals in the hindered phenols category, and the panel proposes no additional testing 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. They include the 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); a reduction in the number of animals used for testing; and an economic savings as a result of a reduced testing program.

The eight substances that form the hindered phenols category based on structural similarity are:

phenol, isobutylenated methylstyrenated (68457-74-9)
phenol, styrenated (61788-44-1)
4,4'-thiobis-6-(t-butyl-m-cresol) (96-69-5)
4,4'-butylidenebis(6-t-butyl-m-cresol) (85-60-9)
phenol, 4,4'-(1-methylethylidene)bis[2,(1,1-dimethylethyl)]- (79-96-9)
phenol, 2,2'-methylenebis(4-methyl-6-nonyl) (7786-17-6)
phenol, 4-methyl-, reaction products with dicyclopentadiene and isobutylene (68610-51-5)
1,3,5-tris(3,5-di-tert-butyl-4-hydroxybenzyl-)-1,3,5-triazine-2,4,6(1H,3H,5H)-trione (27676-62-6)

The substances identified as hindered phenols committed to by the RAPA Panel are not a comprehensive list of substances that would fit a hindered phenols category. To better take advantage of the benefits of using a category approach, data for three additional hindered phenols that are not part of the group supported by the RAPA Panel are included in the category justification and test plan. Data for these three substances are either publicly available or have been made available to the Panel by a manufacturer. The substances are:

2,6-di-tert-butyl-p-cresol (128-37-0)
(octadecanoxycarbonylether)phenol (2082-79-3)
tetrakis-(methylene-(3,5-di-tertbutyl-4-hydrocinnamate)methane (6683-19-8)

The development of this category follows current EPA guidelines.

Background Information: Manufacturing and Commercial Applications

Manufacturing

A typical manufacturing process for a hindered phenol antioxidant uses a substituted cresol raw material for the phenolic ring portion of the molecule, and an aldehyde raw material for the bridging or connecting group. The batch reaction takes place in an alcoholic solvent and utilizes an acid catalyst. When the reaction is complete, the batch is quenched with water and decanted. Purification steps may include additional water washes/decants before the product is slurried with a hydrocarbon solvent, vacuum filtered, washed with additional solvent, centrifuged and dried.

Commercial Applications

Hindered phenols are non-staining, non-discoloring, non-migratory additives for natural rubber, synthetic rubber, adhesives, plastics, textile fibers, cable coatings, flooring, and coated paper, as well as natural and synthetic oils. Their purpose is to prevent or greatly delay the deterioration caused by air oxidation. Using a hindered phenol antioxidant greatly extends the useful life of a transparent, translucent, white or light-colored article by preventing the formation of surface cracks, brittleness and yellowing. In oils, a hindered phenol antioxidant functions as a stabilizer, extending the useful life of the lubricating fluid by slowing the natural breakdown process and limiting the buildup of tars and residues. The overall mechanism is similar to that of the antioxidant vitamins A and E in the human body – hindered phenol antioxidants serve as free-radical scavengers.

Hindered phenols are cost-effective and efficient antioxidants. Usage levels for most applications are typically within the range of 0.5 to 2%.

Due to their low toxicity, low volatility and non-migratory nature, many hindered phenol antioxidants are regulated for use by the Food and Drug Administration (FDA) in a number of food-contact applications as an Indirect Food Additive:

175.105	Components of Adhesives 85-60-9, 96-69-5, 7786-17-6, 61788-44-1, 68610-51-5, 27676-62-6
175.125	Pressure-Sensitive Adhesives 68610-51-5
175.300	Resinous and Polymeric Coatings 85-60-9
177.1632	Poly(phenyleneterephthalamide) Resins 85-60-9
177.2600	Rubber Articles – Antioxidants 85-60-9, 96-69-5, 7786-17-6, 61788-44-1, 68610-15-5
178.2010	Antioxidants and/or Stabilizers for Polymers 85-60-9, 96-69-5, 7786-17-6, 68610-51-5, 27676-62-6

NOTE: 2,6-di-tert-butyl-p-cresol (128-37-0) (butylated hydroxytoluene or BHT), the prototype molecule for the hindered phenol antioxidants, is Generally Recognized As

Safe (GRAS) by the Food and Drug Administration, and is approved for use as a Direct Food Additive and preservative for numerous food products.

Shipping/Distribution

Hindered phenol antioxidants are manufactured in North America, Europe and Asia by more than a dozen different companies. They are shipped worldwide for use at manufacturing sites engaged in the production of rubber and plastic articles and mechanical goods, food containers and food handling equipment, industrial oils and lubricants, synthetic fabrics and specialized papers.

Worker/Consumer Exposure

The rubber and plastics additives industry has a long safety record and sophisticated industrial users handle these materials. Exposure of workers handling hindered phenol antioxidants materials is likely to be highest in the area of material packaging rather than from chemical manufacturing. These materials are made as powders, flakes, emulsions and liquids. Product forms that minimize dust generation, coupled with the mechanized materials handling systems of the large industrial users, combine to keep exposures to minimum levels. However, during material packout at the manufacturing site and, to a lesser degree during weigh-up activities at the customer site, there is a potential for skin and inhalation exposure (nuisance dust is the primary route of worker exposure) and also dermal contact with liquid forms.

All known sales of the hindered phenol antioxidants are to industrial users only. There are no known consumer uses for these materials as manufactured, so there are no expected direct-to-consumer sales. Only very small amounts are used in the manufacture of rubber and plastics or as oil additives, and the materials themselves become bound in the polymer matrix during the rubber and plastic curing process. For these reasons, consumer exposure to hindered phenol antioxidants is believed to be minimal. Should exposure occur, the most likely route would be skin contact from rubber and plastic articles, or from skin contact with oils.

Development of the Hindered Phenols 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 Hindered Phenols 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.

The substances to be included in this hindered phenols category are:

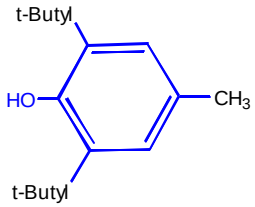
Hindered Phenols

Name	CAS No.
2,6-di-tert-butyl-p-cresol	128-37-0
phenol, isobutylenated methylstyrenated	68457-74-9
phenol, styrenated	61788-44-1
(octadecanoxycarbonylether)phenol	2082-79-3
4,4'-thiobis-6-(t-butyl-m-cresol)	96-69-5
4,4'-butylidenebis(6-t-butyl-m-cresol)	85-60-9
phenol, 4,4'-(1-methylethylidene)bis[2-(1,1-dimethylethyl)]-,	79-96-9
phenol, 2,2'-methylenebis(4-methyl-6-nonyl)	7786-17-6
phenol, 4-methyl-, reaction products with dicyclopentadiene and isobutylene	68610-51-5
tetrakis-(methylene-(3,5-di-tertbutyl-4-hydrocinnamate)methane	6683-19-8
1,3,5-tris(3,5-di-tert-butyl-4-hydroxybenzyl-)-1,3,5-triazine-2,4,6(1H,3H,5H)-trione	27676-62-6

= Non-sponsored chemicals; used for data purposes only

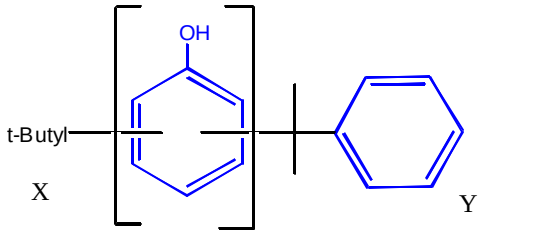
The hindered phenols in this category consist of a group of chemicals in which a molecule of phenol (hydroxybenzene) has multiple substitutions on the aromatic ring with relatively large aliphatic and/or aromatic groups. At least one of the groups is adjacent to the hydroxyl group (the 2-, or ortho- position). Due to the bulky substituent groups, the substances, which may be either room temperature solids or liquids, have limited water solubility, high partition coefficients and are not readily biodegradable.

2,6-di-tert-butyl-p-cresol (128-37-0) (butylated hydroxytoluene or BHT) is hydroxybenzene with aliphatic tertiary butyl groups adjacent to the hydroxyl (OH) group and a methyl group in the 4- or para- position.



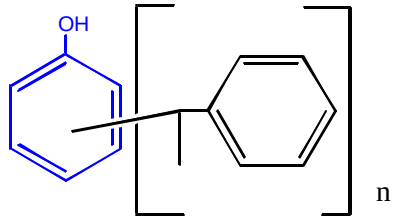
Phenol, isobutylenated methylstyrenated (68457-74-9) is hydroxybenzene with multiple aliphatic and/or aromatic groups on the aromatic ring. At least one group is adjacent to

the hydroxyl group, most often the alpha-methyl styrene. Relative to BHT, one, sometimes both, of the tertiary butyl groups has been replaced with an aromatic alpha-methyl styryl group. The methyl group of BHT is replaced by either a tertiary butyl group or an alpha-methyl styrene.



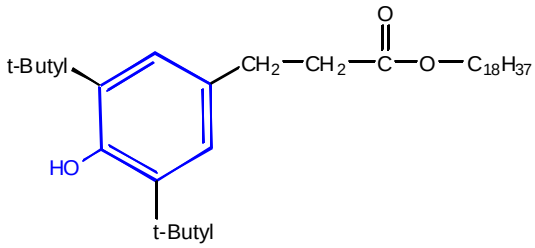
X = 0, 1 or 2 Y = 1, 2 or 3

Phenol, styrenated (61788-44-1) has multiple aromatic styryl groups on the hydroxybenzene. Relative to BHT, the butyl groups adjacent to the hydroxyl (OH) group are replaced with styryl groups and the methyl group may either be absent or replaced with a styryl group.

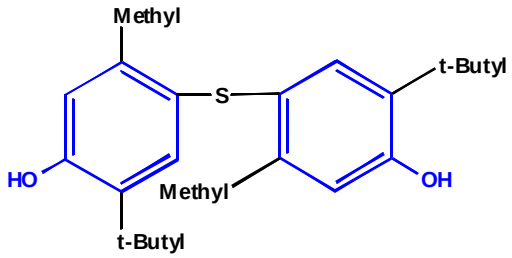


n = 2 or 3

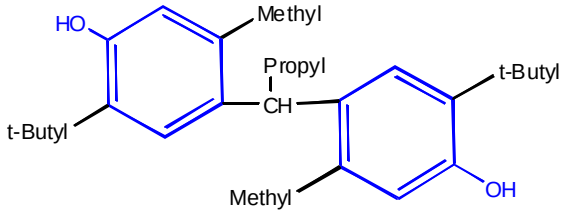
2,6-Di-tert-butyl-4-(octadecanoxycarbonylethyl)phenol **(2082-79-3)**, like BHT, has aliphatic tertiary butyl groups adjacent to the hydroxyl (OH) group, but the methyl group in the 4-position is replaced with an octadecyl (C18) ester group.



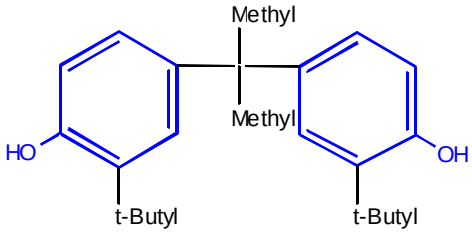
4,4'-Thiobis-6-(t-butyl-m-cresol) (96-69-5) is two identically substituted hydroxybenzene groups linked by a sulfur bridge. Relative to BHT, one butyl group adjacent to the hydroxyl group (OH) is absent, and a sulfur bridge adjacent to the methyl groups links the two hydroxybenzene groups in this configuration.



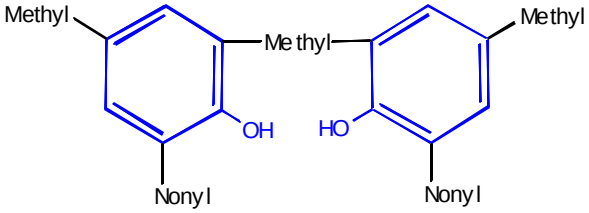
4,4'-Butylidenebis(6-t-butyl-m-cresol) (85-60-9), like 4,4'-thiobis-6-(t-butyl-m-cresol) (96-69-5) is two identically substituted hydroxybenzene groups. In each hydroxybenzene ring one of the aliphatic butyl groups adjacent to the hydroxyl (OH) group is absent and an aliphatic isobutyl group adjacent to the methyl groups links the two rings.



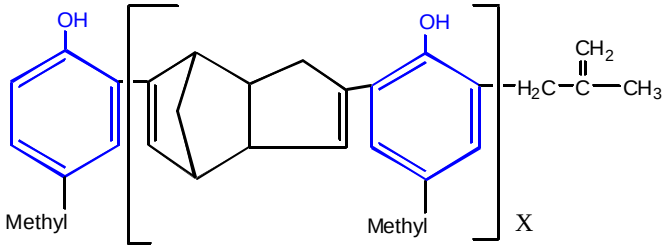
Phenol, 4,4'-(1-methylethylidene)bis[2-(1,1-dimethylethyl)]-, (79-96-9) is two identically substituted hydroxybenzene groups linked by an isopropyl group. Compared to BHT, each hydroxybenzene group lacks one of the tertiary butyl groups adjacent to the hydroxyl group and the isopropyl group linking the two aromatic rings replaces the methyl group.



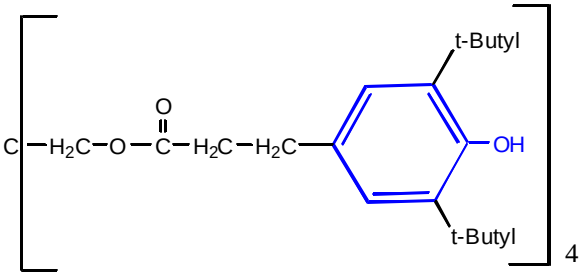
Phenol, 2,2'-methylenebis(4-methyl-6-nonyl) (7786-17-6) is two identically substituted hydroxybenzene groups linked by a methyl group. Compared to BHT, in each hydroxybenzene group, one of the aliphatic butyl groups adjacent to the hydroxyl group (OH) is replaced by an aliphatic nonyl group and the other butyl group is replaced by the methyl group linking the two rings.



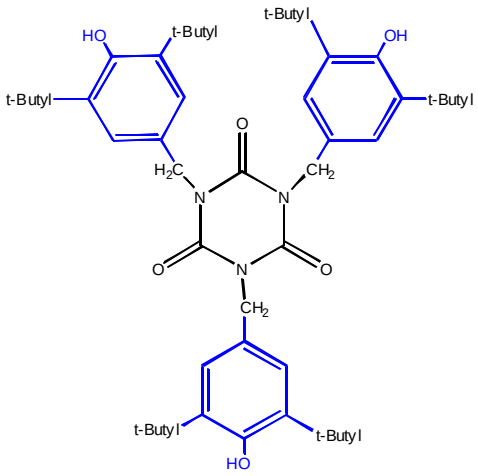
Phenol, 4-methyl-, reaction products with dicyclopentadiene and isobutylene (68610-51-5) is two hydroxybenzene groups which, compared to BHT, have the methyl group in the 4-position, but in place of the butyl group the core hydroxybenzene molecules are linked adjacent to the hydroxyl group by a heterocyclic dicyclopentadiene and/or isobutylene group.



Tetrakis-(methylene-(3,5-di-tertbutyl-4-hydrocinnamate)methane (6683-19-8) is a hindered phenol similar to BHT in that the aliphatic butyl groups remain adjacent to the hydroxyl (OH) group, but the methyl group is absent. In place of the methyl group, four identical molecules in this configuration are linked to a molecule of pentaerythritol by ester groups.



1,3,5-tris(3,5-di-tert-butyl-4-hydroxybenzyl-)-1,3,5-triazine-2,4,6(1H,3H,5H)-trione (27676-62-6) is a hindered phenol consisting of three BHT molecules connected by a triazine trione.



Matrix of SIDS Endpoints

In order to construct a matrix of SIDS endpoints for the hindered phenols 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 hindered phenols substances.

Correlation within the Hindered Phenols Category

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

Correlation of Physicochemical Properties

The physicochemical properties of the members of the hindered phenols category are presented in Table 1. These materials may exist as liquids or solids at room temperature. The similarities in the other physicochemical properties of these materials, which are described below, provide justification of this group of chemicals as a category within the HPV Challenge Program. The vapor pressure of these chemicals is low. Generally, the water solubility for the group chemicals is low and the partition coefficient is high.

Experimentally determined melting and/or boiling point data are available for all, but two, of the hindered phenols. Model calculated melting and boiling points are provided for those two and are generally consistent with the experimentally determined values.

Experimentally determined or model calculated vapor pressures are available for all of the group chemicals. Model calculated vapor pressures are consistent with the experimentally determined values.

Experimentally determined water solubility is reported for eight of the group chemicals. These can be used to extrapolate to the other members of the group. Water solubility data for 4,4'-butylidenebis(6-t-butyl-m-cresol) (85-60-9) can be bridged to phenol, 4,4'-(1-methylethylidene)bis[2-(1,1-dimethylethyl)]-, (79-96-9) and phenol, 2,2'-methylenebis(4-methyl-6-nonyl) (7786-17-6).

Experimentally determined partition coefficients are available for 2,6-di-tert-butyl-p-cresol (128-37-0); phenol, isobutylenated methylstyrenated (68457-74-9); phenol, styrenated (61788-44-1); tetrakis-(methylene-(3,5-di-tertbutyl-4-hydrocinnamate)methane (6683-19-8); and phenol, 4-methyl-, reaction products with dicyclopentadiene, isobutylene (68610-51-5) and 1,3,5-tris(3,5-di-tert-butyl-4-hydroxybenzyl)-1,3,5-triazine-2,4,6(1H,3H,5H)-trione (27676-62-6). Model calculated partition coefficients are available for all of the other substances in this category and are consistent with the experimentally determined values.

Experimental or model calculated physiochemical data are available for all chemicals in the category. The model calculated values are consistent with the experimentally determined data. It is concluded that there are adequate data for physicochemical properties for the hindered phenols for the purposes of the HPV Program.

Correlation of Environmental Fate

Data on environmental fate for the substances in the hindered phenols category are presented in Table 2. The hindered phenols are not readily biodegradable, but have rapid photodegradation. As a result of the low water solubility of these chemicals, hydrolysis data are not available, except for one substance. Fugacity modeling indicates that partitioning would generally be to soil and sediments rather than air or water.

Hydrolysis testing is not possible for the hindered phenols because of low water solubility. Data were available only for 4,4'-thiobis-6-(t-butyl-m-cresol) (96-69-5), indicating that it is not readily hydrolyzed.

Model derived photodegradation half-lives are presented for all of the category substances, except phenol, isobutylenated methylstyrenated (68457-74-9) and phenol, 4-methyl-, reaction products with dicyclopentadiene and isobutylene (68610-51-5). The environmental fate could not be determined with the model for these two substances. The estimate for the photodegradation half-life for phenol, styrenated (61788-44-1) can be bridged to phenol, isobutylenated methylstyrenated (68457-74-9); and for phenol, 4-methyl-, reaction products with dicyclopentadiene and isobutylene (68610-51-5) from tetrakis-(methylene-(3,5-di-tertbutyl-4-hydorcinnamate)methane (6683-19-8).

The hindered phenols are not readily biodegradable. Biodegradation data are available for all but two of the substances. For phenol, 4,4'-(1-methylethylidene)bis[2-(1,1-dimethylethyl)]-, (79-96-9) and phenol, 2,2'-methylenebis(4-methyl-6-nonyl) (7786-17-6) data can be bridged from 4,4'-butylidenebis(6-t-butyl-m-cresol) (85-60-9).

The environmental transport model was not applicable to phenol, isobutylenated methylstyrenated (68457-74-9) and phenol, 4-methyl-, reaction products with dicyclopentadiene and isobutylene (68610-51-5). Information for phenol, styrenated (61788-44-1) can be bridged to phenol, isobutylenated methylstyrenated (68457-74-9) and tetrakis-(methylene-(3,5-di-tertbutyl-4-hydorcinnamate)methane (6683-19-8) can be bridged to phenol, 4-methyl-, reaction products with dicyclopentadiene and isobutylene (68610-51-5).

The available data for environmental fate span the range of structures and molecular weights. It is concluded that there are adequate data to evaluate the environmental fate of this group of hindered phenols for the purposes of the HPV Program.

Correlation of Ecotoxicity

The HPV Challenge Program requires an acute aquatic ecotoxicity test in fish, invertebrates, and algae. The substances in the hindered phenol category have low water solubility and this is reflected in low aquatic toxicity. The data for ecotoxicity are summarized in Table 3.

Acute fish toxicity

Fish 96-hour LC50 data are available for all of the chemicals, except phenol, isobutylenated methylstyrenated (68457-74-9), phenol, 4,4'-(1-methylethylidene)bis[2-(1,1-dimethylethyl)]-, (79-96-9) and phenol, 2,2'-methylenebis(4-methyl-6-nonyl) (7786-17-6). Due to the similarity in structure it would be expected that the aquatic toxicity of phenol, isobutylenated methylstyrenated (68457-74-9), with lower water solubility than phenol, styrenated (61788-44-1), would not have aquatic toxicity greater than phenol, styrenated (61788-44-1). It would be expected that acute fish toxicity of phenol, 4,4'-(1-methylethylidene)bis[2-(1,1-dimethylethyl)]-, (79-96-9) and phenol, 2,2'-methylenebis(4-methyl-6-nonyl) (7786-17-6) would be similar to 4,4'-butylidenebis(6-t-butyl-m-cresol) (85-60-9). It is concluded that there are adequate data to evaluate the acute toxicity to fish for this group of chemicals with limited water solubility for the purposes of the HPV Program.

Acute Invertebrate Toxicity

Acute toxicity data for Daphnia are available for 2,6-di-tert-butyl-p-cresol (128-37-0); (octadecanoxycarbonylether)phenol (2082-79-3); 4,4'-thiobis-6-(t-butyl-m-cresol) (96-69-5); 4,4'-butylidenebis(6-t-butyl-m-cresol) (85-60-9); phenol, 4-methyl-, reaction products with dicyclopentadiene and isobutylene (68610-51-5); tetrakis-(methylene-(3,5-di-tertbutyl-4-hydrocinnamate)methane (6683-19-8); and 1,3,5-tris(3,5-di-tert-butyl-4-hydroxybenzyl)-1,3,5-triazine-2,4,6(1H,3H,5H)-trione (27676-62-6). As with acute fish toxicity, the toxicity in Daphnia is limited by the water solubility of the chemicals. The data for acute invertebrate toxicity span the range of structures and molecular weights. It is concluded that there are adequate data to evaluate the acute toxicity to invertebrates for the purposes of the HPV Program.

Algal Growth Inhibition

Algal growth inhibition tests are available for 2,6-di-tert-butyl-p-cresol (128-37-0); (octadecanoxycarbonylether)phenol (2082-79-3); 4,4'-thiobis-6-(t-butyl-m-cresol) (96-69-5); 4,4'-butylidenebis(6-t--butyl-m-cresol) (85-60-9); phenol, 4-methyl-, reaction products with dicyclopentadiene and isobutylene (68610-51-5); tetrakis-(methylene-(3,5-di-tertbutyl-4-hydrocinnamate)methane (6683-19-8); and 1,3,5-tris(3,5-di-tert-butyl-4-hydroxybenzyl)-1,3,5-triazine-2,4,6(1H,3H,5H)-trione (27676-62-6). The data for algal growth inhibition span the range of structures and molecular weights. It is concluded that there are adequate data to evaluate the acute toxicity to invertebrates for the purposes of the HPV Program.

Correlation of Health Effects

Acute Mammalian Toxicity

The acute toxicity of the hindered phenols category is summarized in Table 4. Acute oral and dermal toxicity data are available for all, but two, of the substances in the group. The data show that the acute toxicity of the hindered phenols is low. The testing for acute toxicity spans five decades. While the majority of studies may not be to current guidelines, tests done according to recent guidelines and under GLP confirm the conclusions of the earlier testing. No additional testing is necessary for the purposes of the HPV Program.

Genotoxicity

A summary of the mutagenicity testing for the hindered phenols category are presented in Table 5. The weight of evidence for mutagenic potential for this category indicates these substances are not mutagenic.

Bacterial Gene Mutation Assays. Adequate bacterial gene mutation assays have been conducted with all of the category chemicals, except phenol, 4,4'-(1-methylethylidene)bis[2-(1,1-dimethylethyl)]-, (79-96-9) and phenol, 2,2'-methylenebis(4-methyl-6-nonyl) (7786-17-6). All assays, with and without metabolic activation, were negative. It is concluded that this group of substances has been adequately tested for gene mutations for the purposes of the HPV Program.

Chromosome Aberration Studies. Chromosome aberration studies, in vitro and/or in vivo, are available for all but three of the hindered phenols in this group. They are phenol, styrenated (61788-44-1)), phenol, 4,4'-(1-methylethylidene)bis[2-(1,1-dimethylethyl)]-, (79-96-9), and (p-cresol, 2,2'-methylenebis[6-nonyl] (7786-17-6). With one exception all tests for chromosome aberrations are negative. It is concluded that this group of chemicals has been adequately tested for clastogenic potential for the purposes of the HPV Program.

In Vitro Chromosome Aberration Studies. In vitro chromosome aberration studies are available for 2,6-di-tert-butyl-p-cresol (128-37-0), 4,4'-butylidenebis(6-t-butyl-m-cresol) (85-60-9), and phenol, 4-methyl-, reaction products with dicyclopentadiene, isobutylene (68610-51-5), and 1,3,5-tris(3,5-di-tert-butyl-4-hydroxybenzyl)-1,3,5-triazine-2,4,6(1H,3H,5H)-trione (27676-62-6). All except 2,6-di-tert-butyl-p-cresol were negative.

In Vivo Chromosome Aberration Studies. In vivo studies evaluating chromosome damage are available for six of the hindered phenols. All in vivo evaluations were negative. Multiple studies have been done with 2,6-di-tert-butyl-p-cresol (128-37-0). Micronucleus tests are available with phenol, isobutylenated methylstyrenated (68457-74-9); 4,4'-thiobis-6-(t-butyl-m-cresol) (96-69-5) and 1,3,5-tris(3,5-di-tert-butyl-4-hydroxybenzyl)-1,3,5-triazine-2,4,6(1H,3H,5H)-trione (27676-62-6). In vivo chromosome aberration studies in Chinese hamsters were negative with (octadecanoxycarbonylether)phenol (2082-79-3) and tetrakis-(methylene-(3,5-di-tertbutyl-4-hydrocinnamate)methane (6683-19-8).

Repeated Dose Toxicity

A summary of the repeated dose toxicity data for the hindered phenols category is presented in Table 6. The summary table is not a comprehensive presentation of all of the repeated dose studies done with the substances in this category. To demonstrate that the substances have been adequately tested for repeated dose toxicity to meet the requirements of the HPV Program, shown in the table are only studies of approximately three months (90-day, 12- and 13-weeks) or longer, unless no data were available and then 28-day studies were used to fill the gap. Three of the category substances are lacking in repeated dose toxicity data. They are (phenol, isobutylenated methylstyrenated (68457-74-9); phenol, 4,4'-(1-methylethylidene)bis[2-(1,1-dimethylethyl)]-, (79-96-9); and phenol, 2,2'-methylenebis(4-methyl-6-nonyl) (7786-17-6). The data for repeated dose toxicity span the range of structures and molecular weights.

The liver was the target organ in rats for all of the substances with subchronic toxicity data in that species, except 1,3,5-tris(3,5-di-tert-butyl-4-hydroxybenzyl)-1,3,5-triazine-2,4,6(1H,3H,5H)-trione (27676-62-6) where no target organ was identified. Other target organs were thyroid in phenol, styrenated (61788-44-1); adrenals in phenol, 4-methyl-, reaction products with dicyclopentadiene and isobutylene (68610-51-5); and kidney and mesenteric lymph nodes in 4,4'-thiobis-6-(t-butyl-m-cresol) (96-69-5). NOAELs in rats ranged from 100 ppm (approximately 5 mg/kg/day) to 10,000 ppm (500 mg/kg/day).

1,3,5-Tris(3,5-di-tert-butyl-4-hydroxybenzyl)-1,3,5-triazine-2,4,6(1H,3H,5H)-trione (27676-62-6) showed no adverse effects in a 90-day study with dogs at doses up to 10,000 ppm in the diet.

Chronic toxicity/carcinogenicity data are available for 2,6-di-tert-butyl-p-cresol (128-37-0); and 4,4'-thiobis-6-(t-butyl-m-cresol) (96-69-5). Liver adenomas were reported for 2,6-di-tert-butyl-p-cresol (128-37-0) and a NOAEL was established for the study at 25

mg/kg/day. 4,4'-Thiobis-6-(t-butyl-m-cresol) (96-69-5) was not carcinogenic in rats or mice, but the kidney was identified as a target organ in female rats.

The data for repeated dose toxicity span the range of structures and molecular weights. It is concluded that there are adequate data to evaluate repeated dose toxicity for the purposes of the HPV Program.

Reproductive and Developmental Toxicity

A summary of the reproductive and developmental toxicity data for the hindered phenols category is presented in Table 7.

Reproductive Toxicity. Multi-generation reproduction studies have been conducted with three of the substances in this group 2,6-di-tert-butyl-p-cresol (128-37-0); (octadecanoxycarbonylether)phenol (2082-79-3); and tetrakis-(methylene-(3,5-di-tertbutyl-4-hydrocinnamate)methane (6683-19-8).

Evaluation of effects on reproduction for the hindered phenols is supplemented by histopathological data on male and female reproductive organs in repeated dose studies. These are 90-day studies with 4,4'-butylidenebis(6-t-butyl-m-cresol) (85-60-9); phenol, 4-methyl-, reaction products with dicyclopentadiene and isobutylene (68610-51-5); and 1,3,5-tris(3,5-di-tert-butyl-4-hydroxybenzyl)-1,3,5-triazine-2,4,6(1H,3H,5H)-trione (27676-62-6). A two-year chronic feeding study provided data for 4,4'-thiobis-6-(t-butyl-m-cresol) (96-69-5). No adverse effects were noted on reproductive organs.

4,4'-Thiobis-6-(t-butyl-m-cresol) (96-69-5) was also tested in an NTP program for screening reproductive toxicants using a postnatal mouse screening test. Increased maternal mortality and decreased pup survival were reported.

No data for the assessment of reproductive toxicity are available for four of the hindered phenol chemicals: phenol isobutylenated methylstyrenated (68457-74-9); phenol, styrenated (61788-44-1); phenol, 4,4'-(1-methylethylidene)bis[2-(1,1-dimethylethyl)]-, (79-96-9); and (p-cresol, 2,2'-methylenebis[6-nonyl] (7786-17-6).

The data on the effects of hindered phenols on reproduction and reproductive organs span the range of structures and molecular weights. While not all of the data for reproductive effects are from reproduction studies, microscopic evaluations of reproductive organs along with other short-term tests for reproductive effects provide adequate data to evaluate the effects of these hindered phenols on reproduction for the purposes of the HPV Program.

Developmental Toxicity. Developmental studies have been conducted in rats, rabbits, and/or mice with 2,6-di-tert-butyl-p-cresol (128-37-0); (octadecanoxycarbonylether)phenol (2082-79-3); 4,4'-thiobis-6-(t-butyl-m-cresol) (96-69-5); phenol, 4-methyl-, reaction products with dicyclopentadiene and isobutylene (68610-51-5); and tetrakis-(methylene-(3,5-di-tertbutyl-4-hydrocinnamate)methane (6683-19-8). The available data span the range of structures and molecular weights and

provide adequate data to evaluate the effects of these hindered phenols on development for the purposes of the HPV Program.

Conclusion

The 11 hindered phenols meet the EPA definition of a chemical category. This group consists of chemicals in which a molecule of phenol (hydroxybenzene) has multiple substitutions on the aromatic ring with relatively large aliphatic and/or aromatic groups. At least one of the groups is adjacent to the hydroxyl group (the 2-, or ortho- position). Due to the bulky substituent groups, the substances have limited water solubility, high partition coefficients and are not readily biodegradable. Therefore, the EPA's definition of a chemical category has been met.

The test plan for the hindered phenols category was developed giving careful consideration to the number of animals that would be required for any tests that are not available for certain members of the category and whether these additional tests would provide useful and relevant information. The test plan is summarized in Table 8. It is concluded that there are sufficient data on the members of this category for the purposes of the HPV Program and therefore, no additional testing is recommended.

Table 1.
Matrix of Available and Adequate Data for the Hindered Phenols Category

Physicochemical Properties

Name (CAS No.)	Molecular Weight	Melting Point ^{0}C	Boiling Point ^{0}C	Vapor Pressure (mm Hg)	Water Solubility (mg/L)	Partition Coefficient
2,6-di-tert-buty-p-cresol (128-37-0)	220.36	70	265	0.0225 at 25 ^{0}C	0.4 at 20 ^{0}C 1.1 at 20 ^{0}C	5.1
phenol, isobutylenated methylstyrenated (68457-74-9)	386 (average)		350	0.0018 at 25 ^{0}C	0.0287 – 0.375 at 30 ^{0}C pH 7.9 - 8	>6.2
phenol, styrenated (61788-44-1)	330 (average)	<0	200 - 250	0.102 at 25 ^{0}C (calculated)	59 at 20 ^{0}C pH 5.6 – 5.9	>4
(octadecanoxycarbonylether)phenol (2082-79-3)	530.9	49 -54	561 (calculated)	4.2×10^{-11} (calculated)	ND	13.4 (calculated)
4,4'-thiobis-6-(t-butyl-m-cresol) (96-69-5)	358.58	156 - 158		6.3×10^{-7} at 70 ^{0}C	<0.1 at 25 ^{0}C	8.24 (calculated)
4,4'-butylidenebis(6-t-butyl-m-cresol) (85-60-9)	382.64	210		5.26×10^{-11} at 25 ^{0}C (calculated)	<0.1 at 18 ^{0}C	9.09 (calculated)
phenol, 4,4'-(1-methylethylidene)bis[2-(1,1-dimethylethyl)]-, (79-96-9)	340.51	181 (calculated)	433 (calculated)	1.18×10^{-9} at 25 ^{0}C (calculated)	ND	7.46 (calculated)
phenol, 2,2'-methylenebis(4-methyl-6-nonyl) (7786-17-6)	480.78	252 (calculated)	584 (calculated)	6.25×10^{-15} at 25 ^{0}C (calculated)	ND	13.10 (calculated)
phenol, 4-methyl-, reaction products with dicyclopentadiene and isobutylene (68610-51-5)	750 - 850	118.3		$< 2.4 \times 10^{-7}$ at 25 ^{0}C	0.2 at 20 ^{0}C	7.17 - 8.17
tetrakis-(methylene-(3,5-di-tertbutyl-4-hydrocinnamate)methane (6683-19-8)	1178	115 - 118	1130 (calculated)	7.1×10^{-31} at 25 ^{0}C (calculated)	< 0.1	23
1,3,5-tris(3,5-di-tert-butyl-4-hydroxybenzyl)-1,3,5-triazine-2,4,6(1H,3H,5H)-trione (27676-62-6)	784.1	219.5 – 225.5	961 ^{0}C (calculated)	5×10^{-15} at 25 ^{0}C (calculated)	<1 at 25 ^{0}C	>6

ND - No data found

= Non-sponsored chemicals; used for data purposes only

Table 2
Matrix of Available and Adequate Data for the Hindered Phenols Category
Environmental Fate

Name (CAS No.)	Hydrolysis	Photo-degradation (t1/2)	Bio-degradation	Environmental Transport
2,6-di-tert-buty-p-cresol (128-37-0)	ND	25.2% remained after 8 days 17 hr (EPIWIN)	Aerobic approximately 10% after 56 days; 4.5% after 28 days.	Primarily in air (Mackay, Level I model) Adsorbs to river sediments from water.
phenol, isobutylenated methylstyrenated (68457-74-9)	cbd	cbd (EPIWIN)	Aerobic degradation <1% after 29 days	cbd (EPIWIN)
phenol, styrenated (61788-44-1)	ND	2.2 hr (EPIWIN)	Aerobic degradation 7% after 28 days	Primarily water and soil. (Level III Fugacity Model)
(octadecanoxycarbonylether)phenol (2082-79-3)	ND	3 hr (model calculated)	Partially biodegradable Inherently biodegradable	Primarily soil (Level III Fugacity Model)
4,4'-thiobis-6-(t-butyl-m-cresol) (96-69-5)	>168 hrs at pH 7 at 23 ^{0}C	1 hr (EPIWIN)	Aerobic 11% after 90 days	Primarily soil and sediments. (Level III Fugacity Model)
4,4'-butylidenebis(6-t-butyl-m-cresol) (85-60-9)	ND	0.6 hr (EPIWIN)	Aerobic 0-5% after 35 days	Primarily soil and sediments. (Level III Fugacity Model)
phenol, 4,4'-(1-methylethylidene)bis[2-(1,1-dimethylethyl)]-, (79-96-9)	ND	1.3 hr (EPIWIN)	ND	Primarily soil and sediments. (Level III Fugacity Model)
phenol, 2,2'-methylenebis(4-methyl-6-nonyl) (7786-17-6)	ND	1.9 hr (EPIWIN)	ND	Primarily soil and sediments. (Level III Fugacity Model)
phenol, 4-methyl-, reaction products with dicyclopentadiene and isobutylene (68610-51-5)	cbd	cbd (EPIWIN)	Not biodegradable	cbd (EPIWIN)
tetrakis-(methylene-(3,5-di-tertbutyl-4-hydrocinnamate)methane (6683-19-8)	ND	1.2 hr (model calculated)	Not biodegradable	Primarily soil (Level III Fugacity Model)
1,3,5-tris(3,5-di-tert-butyl-4-hydroxybenzyl)-1,3,5-triazine-2,4,6(1H,3H,5H)-trione (27676-62-6)	ND	1.9 hr (EPIWIN)	Not biodegradable	Primarily soil and sediments. (Level III Fugacity Model)

ND - No data found cbd - cannot be determined due to low solubility cbd (EPIWIN) - cannot be determined by modeling

= Non-sponsored chemicals; used for data purposes only

Table 3.
Matrix of Available and Adequate Data for the Hindered Phenols Category

Ecotoxicity

Name (CAS No.)	Acute Fish 96-hr LC50 (mg/L)	Acute Invertebrate 48-hr EC50 (mg/L)	Algal Growth Inhibition EC50 (mg/L)
2,6-di-tert-buty-p-cresol (128-37-0)	> 0.57	>.31	0.42
phenol, isobutylenated methylstyrenated (68457-74-9)	ND	ND	ND
phenol, styrenated (61788-44-1)	> 3.2	ND	ND
(octadecanoxycarbonylether)phenol (2082-79-3)	> 100	> 100 (24-hr)	> 30
4,4'-thiobis-6-(t-butyl-m-cresol) (96-69-5)	0.13 - 0.16 trout 0.24 - 0.51 bluegill 0.14 - 0.36 minnow	0.70	126
4,4'-butylidenebis(6-t-butyl-m-cresol) (85-60-9)	> 1000 in trout, blue gill and minnow	16	> 1000
phenol, 4,4'-(1-methylethylidene)bis[2-(1,1-dimethylethyl)]-, (79-96-9)	ND	ND	ND
phenol, 2,2'-methylenebis(4-methyl-6-nonyl) (7786-17-6)	ND	ND	ND
phenol, 4-methyl-, reaction products with dicyclopentadiene and isobutylene (68610-51-5)	>0.2 (limit of solubility)	>0.2 (limit of solubility)	>0.2 (limit of solubility)
tetrakis-(methylene-(3,5-di-tertbutyl-4-hydrocinnamate)methane (6683-19-8)	> 100	> 86 (24-hr)	> 100
1,3,5-tris(3,5-di-tert-butyl-4-hydroxybenzyl)-1,3,5-triazine-2,4,6(1H,3H,5H)-trione (27676-62-6)	> 100	> 32	> 100

ND - No data found

= Non-sponsored chemicals; used for data purposes only

Table 4.
Matrix of Available and Adequate Data for the Hindered Phenols Category

Acute Toxicity

Name (CAS No.)	Acute Oral (mg/kg)	Acute Dermal (mg/kg)
2,6-di-tert-buty-p-cresol (128-37-0)	> 2930	> 2000
phenol, isobutylenated methylstyrenated (68457-74-9)	> 2000	> 2000
phenol, styrenated (61788-44-1)	3550	> 5010
(octadecanoxycarbonylether)phenol (2082-79-3)	> 5000	> 2000
4,4'-thiobis-6-(t-butyl-m-cresol) (96-69-5)	4150	>5010
4,4'-butylidenebis(6-t-butyl-m-cresol) (85-60-9)	> 7940	> 7940
phenol, 4,4'-(1-methylethylidene)bis[2-(1,1-dimethylethyl)]-, (79-96-9)	ND	ND
phenol, 2,2'-methylenebis(4-methyl-6-nonyl) (7786-17-6)	ND	ND
phenol, 4-methyl-, reaction products with dicyclopentadiene and isobutylene (68610-51-5)	> 5010	> 5010
tetrakis-(methylene-(3,5-di-tertbutyl-4-hydrocinnamate)methane (6683-19-8)	> 10,250	> 3160
1,3,5-tris(3,5-di-tert-butyl-4-hydroxybenzyl)-1,3,5-triazine-2,4,6(1H,3H,5H)-trione (27676-62-6)	> 5000	> 2000

ND - No data found

= Non-sponsored chemicals; used for data purposes only

Table 5.
Matrix of Available and Adequate Data for the Hindered Phenols Category

Genotoxicity

Name (CAS No.)	Bacterial Gene Mutation	Chromosomal Aberrations	
		In vitro	In vivo
2,6-di-tert-buty-p-cresol (128-37-0)	negative	positive	negative
phenol, isobutylenated methylstyrenated (68457-74-9)	negative	ND	negative
phenol, styrenated (61788-44-1)	negative	ND	ND
(octadecanoxycarbonylether)phenol (2082-79-3)	negative	ND	negative
4,4'-thiobis-6-(t-butyl-m-cresol) (96-69-5)	negative	ND	negative
4,4'-butylidenebis(6-t-butyl-m-cresol) (85-60-9)	negative	negative	ND
phenol, 4,4'-(1-methylethylidene)bis[2-(1,1-dimethylethyl)]-, (79-96-9)	ND	ND	ND
phenol, 2,2'-methylenebis(4-methyl-6-nonyl) (7786-17-6)	ND	ND	ND
phenol, 4-methyl-, reaction products with dicyclopentadiene and isobutylene (68610-51-5)	negative	negative	ND
tetrakis-(methylene-(3,5-di-tertbutyl-4-hydrocinnamate)methane (6683-19-8)	negative	ND	negative
1,3,5-tris(3,5-di-tert-butyl-4-hydroxybenzyl)-1,3,5-triazine-2,4,6(1H,3H,5H)-trione (27676-62-6)	negative	negative	negative

ND - No data found

= Non-sponsored chemicals; used for data purposes only

Table 6.
Matrix of Available and Adequate Data for the Hindered Phenols Category

Repeated dose Toxicity

Name (CAS No.)	Subchronic Toxicity	Chronic Toxicity
2,6-di-tert-buty-p-cresol (128-37-0)	Oral toxicity in rats from 2-gen repro study. F1 gen evaluated at 4 wks and at 6, 11, 16, and 22 mo. NOAEL 25 mg/kg/day	Chronic oral toxicity in rats - 144 wk study. Liver adenomas. NOAEL 25 mg/kg/day
phenol, isobutylenated methylstyrenated (68457-74-9)	ND	ND
phenol, styrenated (61788-44-1)	12-Week feeding study in rats - Growth was retarded and liver wts relative to bw. were higher than controls; minimal focal thyroid hyperplasia. NOAEL = 50 mg/kg/day LOAEL = 158 mg/kg/day	ND
(octadecanoxycarbonylether)phenol (2082-79-3)	28-Day gavage in rats - Target organ liver. NOAEL = 30 mg/kg/day	ND
4,4'-thiobis-6-(t-butyl-m-cresol) (96-69-5)	13-Week feeding study in rats - Higher ALP and ALT; lower hematocrit and HB conc and RBC; histopath findings in liver (hypertorphy and hyperplasia), kidney (renal cortical tubule effects), and mesenteric lymph nodes (increased size and number of macrophages). NOEL = 500 ppm LOEL = 1000 ppm 13-Week feeding study in mice - Higher ALP and ALT; effects on hematocrit, HB conc and RBC; histopath findings in liver (hypertorphy and hyperplasia) and mesenteric lymph nodes (increased size and number of macrophages). NOEL = 250 ppm LOEL = 500 ppm	Two-year feeding study in rats - Higher AP, ALT and sorbitol dehydrogenase; lower hematocrit, HB conc, and RBC counts; histopath findings in liver; increased severity of nephropathy in females. Not carcinogenic. NOEL = 500 ppm LOEL = 1000 ppm Two-year feeding study in mice - Higher AP and bilirubin ; lower hematocrit, HB conc, and RBC counts Not carcinogenic. LOEL = 250 ppm

ND - no data found

= Non-sponsored chemicals; used for data purposes only

Table 6. (continued)
Matrix of Available and Adequate Data for the Hindered Phenols Category

Repeated dose Toxicity

Name (CAS No.)	Subchronic Toxicity	Chronic Toxicity
4,4'-butylidenebis(6-t-butyl-m-cresol) (85-60-9)	90-Day feeding study in rats - Increased liver weights, effects on SGOT and SGPT. Microscopic changes in liver and lymph nodes. NOAEL = 100 ppm LOAEL = 500 ppm	ND
phenol, 4,4'-(1-methylethylidene)bis[2-(1,1-dimethylethyl)]-, (79-96-9)	ND	ND
phenol, 2,2'-methylenebis(4-methyl-6-nonyl) (7786-17-6)	ND	ND
phenol, 4-methyl-, reaction products with dicyclopentadiene and isobutylene (68610-51-5)	90-Day feeding study in rats - Increased liver wts and increased adrenal wts (females only) at 1500 ppm and higher. NOAEL = 500 ppm (25 mg/kg/day)	ND
tetrakis-(methylene-(3,5-di-tertbutyl-4-hydrocinnamate)methane (6683-19-8)	13-Week feeding study in dogs - No adverse effects, NOEL = 10,000 ppm (highest dose tested)	ND
1,3,5-tris(3,5-di-tert-butyl-4-hydroxybenzyl)-1,3,5-triazine-2,4,6(1H,3H,5H)-trione (27676-62-6)	3-Month feeding study in rats - Increased food consumption in males and elevated platelet count in females. For males NOEL = 3,000 ppm (201mg/kg/day) For females NOEL = 800 ppm (50.1 mg/kg/day) 90-Day feeding study in rats - No adverse effects, NOEL = 10,000 ppm (highest dose tested) 90-Day oral feeding study in dogs - No adverse effects, NOEL = 10,000 ppm (highest dose tested)	ND

ND - No data found

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Table 7.
Matrix of Available and Adequate Data for the Hindered Phenols Category

Reproductive and Developmental Toxicity

Name (CAS No.)	Reproductive	Developmental
2,6-di-tert-buty-p-cresol (128-37-0)	2-Generation in rats at 25 to 500 mg/kg/day (F0) and 25 and 250 mg/kg/day (F1) 2-Generation in mice - Increased wt of pups at birth and during lactation. NOEL not established. LOEL=22.5 mg/kg/day	Mice by gavage - NOAEL for maternal tox = 240 mg/kg/day and NOAEL for terata >= 800 mg/kg/day. Rat teratology, not teratogenic from two publications from Japan
phenol, isobutylenated methylstyrenated (68457-74-9)	ND	ND
phenol, styrenated (61788-44-1)	ND	ND
(octadecanoxycarbonylether)phenol (2082-79-3)	2-Generation in rats - NOAEL (F0) = 1500 ppm; LOAEL (F1 and F2) = 500 ppm	In rats - Not teratogenic. NOAEL for material tox = 150 mg/kg/day. In mice - Not teratogenic. NOAEL for maternal tox > 1000 mg/kg/day.
4,4'-thiobis-6-(t-butyl-m-cresol) (96-69-5)	Histopathology of sex organs from chronic toxicity study in rats. No adverse effects. NTP postnatal mouse screening test. One dose = 485 mg/kg/day. Increased maternal mortality, decreased pup survival	Developmental in rabbits - Maternal NOEL = 0.2 mg/kg/day. Effects on fetuses only at maternally toxic doses.

ND - No data found

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Table 7 (continued).
Matrix of Available and Adequate Data for the Hindered Phenols Category

Reproductive and Developmental Toxicity

Name (CAS No.)	Reproductive	Developmental
4,4'-butylidenebis(6-t-butyl-m-cresol) (85-60-9)	Histopathology of sex organs from 90-day repeated dose study in rats. No adverse effects.	ND
phenol, 4,4'-(1-methylethylidene)bis[2-(1,1-dimethylethyl)]-, (79-96-9)	ND	ND
phenol, 2,2'-methylenebis(4-methyl-6-nonyl) (7786-17-6)	ND	ND
phenol, 4-methyl-, reaction products with dicyclopentadiene and isobutylene (68610-51-5)	Histopathology of sex organs from 90-day repeated dose study in rats. No adverse effects.	In rats - Not teratogenic; increased incidence of common fetal skeletal variations. NOAEL for maternal tox = 1000 mg/kg/day. BMD at ED_{05} for fetal variations = 740 mg/kg/day
tetrakis-(methylene-(3,5-di-tertbutyl-4-hydrocinnamate)methane (6683-19-8)	2-Generation in rats at 1000 to 10,000 ppm. NOAEL (F0, F1, F2) = 10,000 ppm	In rats - Not teratogenic. NOAEL for maternal tox > 1,000 mg/kg/day. In mice - Not teratogenic. NOAEL for maternal tox > 1000 mg/kg/day.
1,3,5-tris(3,5-di-tert-butyl-4-hydroxybenzyl)-1,3,5-triazine-2,4,6(1H,3H,5H)-trione (27676-62-6)	Histopathology of sex organs from 3-month repeated dose study in rats. No adverse effects.	ND

ND - No data found

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Legend for Table 8

Symbol	Description
A	Endpoint requirement fulfilled with adequate existing data
NA	Not applicable due to physical/chemical properties
C	Endpoint requirement fulfilled based on calculated data
R	Endpoint requirement fulfilled using category approach, SAR

Table 8.
Hindered Phenols Category Test Plan

Physicochemical Properties

Name (CAS No.)	Melting Point	Boiling Point	Vapor Pressure	Water Solubility	Partition Coefficient
2,6-di-tert-buty-p-cresol (128-37-0)	A	A	A	A	A
phenol, isobutylenated methylstyrenated (68457-74-9)	NA	A	A	A	A
phenol, styrenated (61788-44-1)	A	A	C	A	A
(octadecanoxycarbonylether)phenol (2082-79-3)	A	C	C	R	C
4,4'-thiobis-6-(t-butyl-m-cresol) (96-69-5)	A	NA	A	A	C
4,4'-butylidenebis(6-t-butyl-m-cresol) (85-60-9)	A	NA	C	A	C
phenol, 4,4'-(1-methylethylidene)bis[2-(1,1-dimethylethyl)]-, (79-96-9)	C	C	C	R	C
phenol, 2,2'-methylenebis(4-methyl-6-nonyl) (7786-17-6)	C	C	C	R	C
phenol, 4-methyl-, reaction products with dicyclopentadiene and isobutylene (68610-51-5)	A	NA	A	A	A
tetrakis-(methylene-(3,5-di-tertbutyl-4-hydrocinnamate)methane (6683-19-8)	A	C	C	A	A
1,3,5-tris(3,5-di-tert-butyl-4-hydroxybenzyl)-1,3,5-triazine-2,4,6(1H,3H,5H)-trione (27676-62-6)	A	C	C	A	A

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Table 8 (continued).
Hindered Phenols Category Test Plan

Environmental Fate

Name (CAS No.)	Hydrolysis	Photo-degradation	Bio-degradation	Environmental Transport
2,6-di-tert-buty-p-cresol (128-37-0)	NA	A	A	A
phenol, isobutylenated methylstyrenated (68457-74-9)	NA	R	A	R
phenol, styrenated (61788-44-1)	NA	C	A	C
(octadecanoxycarbonylether)phenol (2082-79-3)	NA	C	A	C
4,4'-thiobis-6-(t-butyl-m-cresol) (96-69-5)	A	C	A	C
4,4'-butylidenebis(6-t-butyl-m-cresol) (85-60-9)	NA	C	A	C
phenol, 4,4'-(1-methylethylidene)bis[2-(1,1-dimethylethyl)]-, (79-96-9)	NA	C	R	C
phenol, 2,2'-methylenebis(4-methyl-6-nonyl) (7786-17-6)	NA	C	R	C
phenol, 4-methyl-, reaction products with dicyclopentadiene and isobutylene (68610-51-5)	NA	R	A	R
tetrakis-(methylene-(3,5-di-tertbutyl-4-hydrocinnamate)methane (6683-19-8)	NA	C	A	C
1,3,5-tris(3,5-di-tert-butyl-4-hydroxybenzyl)-1,3,5-triazine-2,4,6(1H,3H,5H)-trione (27676-62-6)	NA	C	A	C

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Table 8 (continued).
Hindered Phenols Category Test Plan

Ecotoxicity

Name (CAS No.)	Acute Fish	Acute Invertebrate	Algal Growth Inhibition
2,6-di-tert-buty-p-cresol (128-37-0)	A	A	A
phenol, isobutylenated methylstyrenated (68457-74-9)	R	R	R
phenol, styrenated (61788-44-1)	A	R	R
(octadecanoxycarbonylether)phenol (2082-79-3)	A	A	A
4,4'-thiobis-6-(t-butyl-m-cresol) (96-69-5)	A	A	A
4,4'-butylidenebis(6-t-butyl-m-cresol) (85-60-9)	A	A	A
phenol, 4,4'-(1-methylethylidene)bis[2-(1,1-dimethylethyl)]-, (79-96-9)	R	R	R
phenol, 2,2'-methylenebis(4-methyl-6-nonyl) (7786-17-6)	R	R	R
phenol, 4-methyl-, reaction products with dicyclopentadiene and isobutylene (68610-51-5)	A	A	A
tetrakis-(methylene-(3,5-di-tertbutyl-4-hydrocinnamate)methane (6683-19-8)	A	A	A
1,3,5-tris(3,5-di-tert-butyl-4-hydroxybenzyl)-1,3,5-triazine-2,4,6(1H,3H,5H)-trione (27676-62-6)	A	A	A

Acute Toxicity

Name (CAS No.)	Acute Oral	Acute Dermal
2,6-di-tert-buty-p-cresol (128-37-0)	A	A
phenol, isobutylenated methylstyrenated (68457-74-9)	A	A
phenol, styrenated (61788-44-1)	A	A
(octadecanoxycarbonylether)phenol (2082-79-3)	A	A
4,4'-thiobis-6-(t-butyl-m-cresol) (96-69-5)	A	A
4,4'-butylidenebis(6-t-butyl-m-cresol) (85-60-9)	A	A
phenol, 4,4'-(1-methylethylidene)bis[2-(1,1-dimethylethyl)]-, (79-96-9)	R	R
phenol, 2,2'-methylenebis(4-methyl-6-nonyl) (7786-17-6)	R	R
phenol, 4-methyl-, reaction products with dicyclopentadiene and isobutylene (68610-51-5)	A	A
tetrakis-(methylene-(3,5-di-tertbutyl-4-hydrocinnamate)methane (6683-19-8)	A	A
1,3,5-tris(3,5-di-tert-butyl-4-hydroxybenzyl)-1,3,5-triazine-2,4,6(1H,3H,5H)-trione (27676-62-6)	A	A

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Table 8 (continued).
Hindered Phenols Category Test Plan

Genotoxicity

Name (CAS No.)	Bacterial Gene Mutation	Chromosomal Aberrations	
		In vitro	In vivo
2,6-di-tert-buty-p-cresol (128-37-0)	A	A	A
phenol, isobutylenated methylstyrenated (68457-74-9)	A	R	A
phenol, styrenated (61788-44-1)	A	R	R
(octadecanoxycarbonylether)phenol (2082-79-3)	A	R	A
4,4'-thiobis-6-(t-butyl-m-cresol) (96-69-5)	A	R	A
4,4'-butylidenebis(6-t-butyl-m-cresol) (85-60-9)	A	A	R
phenol, 4,4'-(1-methylethylidene)bis[2-(1,1-dimethylethyl)]-, (79-96-9)	R	R	R
phenol, 2,2'-methylenebis(4-methyl-6-nonyl) (7786-17-6)	R	R	R
phenol, 4-methyl-, reaction products with dicyclopentadiene and isobutylene (68610-51-5)	A	A	R
tetrakis-(methylene-(3,5-di-tertbutyl-4-hydrocinnamate)methane (6683-19-8)	A	R	A
1,3,5-tris(3,5-di-tert-butyl-4-hydroxybenzyl)-1,3,5-triazine-2,4,6(1H,3H,5H)-trione (27676-62-6)	A	A	A

= Non-sponsored chemicals; used for data purposes only

Table 8 (continued).
Hindered Phenols Category Test Plan

Repeated dose Toxicity

Name (CAS No.)	Subchronic Toxicity	Chronic Toxicity
2,6-di-tert-buty-p-cresol (128-37-0)	A	A
phenol, isobutylenated methylstyrenated (68457-74-9)	R	
phenol, styrenated (61788-44-1)	A	
(octadecanoxycarbonylether)phenol (2082-79-3)	A	
4,4'-thiobis-6-(t-butyl-m-cresol) (96-69-5)	A	A
4,4'-butylidenebis(6-t-butyl-m-cresol) (85-60-9)	A	
phenol, 4,4'-(1-methylethylidene)bis[2-(1,1-dimethylethyl)]-, (79-96-9)	R	
phenol, 2,2'-methylenebis(4-methyl-6-nonyl) (7786-17-6)	R	
phenol, 4-methyl-, reaction products with dicyclopentadiene and isobutylene (68610-51-5)	A	
tetrakis-(methylene-(3,5-di-tertbutyl-4-hydrocinnamate)methane (6683-19-8)	A	
1,3,5-tris(3,5-di-tert-butyl-4-hydroxybenzyl)-1,3,5-triazine-2,4,6(1H,3H,5H)-trione (27676-62-6)	A	

Reproductive and Developmental Toxicity

Name (CAS No.)	Reproductive	Developmental
2,6-di-tert-buty-p-cresol (128-37-0)	A	A
phenol, isobutylenated methylstyrenated (68457-74-9)	R	R
phenol, styrenated (61788-44-1)	R	R
(octadecanoxycarbonylether)phenol (2082-79-3)	A	A
4,4'-thiobis-6-(t-butyl-m-cresol) (96-69-5)	A	A
4,4'-butylidenebis(6-t-butyl-m-cresol) (85-60-9)	A	R
phenol, 4,4'-(1-methylethylidene)bis[2-(1,1-dimethylethyl)]-, (79-96-9)	R	R
phenol, 2,2'-methylenebis(4-methyl-6-nonyl) (7786-17-6)	R	R
phenol, 4-methyl-, reaction products with dicyclopentadiene and isobutylene (68610-51-5)	A	A
tetrakis-(methylene-(3,5-di-tertbutyl-4-hydrocinnamate)methane (6683-19-8)	A	A
1,3,5-tris(3,5-di-tert-butyl-4-hydroxybenzyl)-1,3,5-triazine-2,4,6(1H,3H,5H)-trione (27676-62-6)	A	R

= Non-sponsored chemicals; used for data purposes only

AR201-13382B

I U C L I D

D a t a S e t

New Chemical	ID: 68457-74-9
CAS No.	68457-74-9
EINECS No.	270-604-9
EINECS Name	Phenol, isobutylenated methylstyrenated
CAS Name	Phenol, isobutylenated methylstyrenated

Producer Related Part
- Company: Goodyear Chemicals Europe
- Creation date: 13-JUL-1998

Substance Related Part
- Company: Goodyear Chemicals Europe
- Creation date: 13-JUL-1998

Printing date:	07-MAY-2001
Revision date:	
Date of last Update:	08-FEB-2001
Number of Pages:	11
Chapter (profile):	Chapter: 2.1, 2.2, 2.4, 2.5, 2.6.1, 3.1.1, 3.1.2, 3.3.1, 3.5, 4.1, 4.2, 4.3, 5.1.1, 5.1.2, 5.1.3, 5.1.4, 5.4, 5.5, 5.6, 5.8, 5.9
Reliability (profile):	Reliability: without reliability, 1, 2, 3, 4
Flags (profile):	Flags: without flag, confidential, non confidential, WGK (DE), TA-Luft (DE), Material Safety Dataset, Risk Assessment, Directive 67/548/EEC, SIDS

2.1 Melting Point

Value:
Method: other: not relevant
24-JUL-2000

2.2 Boiling Point

Value: = 350 degree C
Method: OECD Guide-line 103 "Boiling Point/boiling Range"
Year: 1998
GLP: yes
Remark: Barometric Pressure: 1011 mbar
Reliability: (1) valid without restriction
24-JUL-2000 (1)

2.4 Vapour Pressure

Value: at 25 degree C
Method: OECD Guide-line 104 "Vapour Pressure Curve"
Year: 1998
GLP: yes
Result: .0024 Pa
Reliability: (1) valid without restriction
24-JUL-2000

2.5 Partition Coefficient

log Pow: > 6.2
Method: OECD Guide-line 117 "Partition Coefficient (n-octanol/water), HPLC Method"
Year: 1998
GLP: yes
Result: The majority of the components were found to have partition coefficient values greater than 1600000 (log10Pow >6.2), with minor components found to have partition coefficients ranging from 3200 to 560000 (log10Pow = 3.50-5.75)
Reliability: (1) valid without restriction
24-JUL-2000 (2)

2.6.1 Water Solubility

Value: 28.7 - 375 other: ug/l at 30 degree C
pH: 7.9 - 8
Method: OECD Guide-line 105 "Water Solubility"
Year: 1998
GLP: yes
Reliability: (1) valid without restriction
24-JUL-2000 (3)

3.1.1 Photodegradation
-

3.1.2 Stability in Water
-

3.3.1 Transport between Environmental Compartments
-

3.5 Biodegradation

Type:	aerobic
Inoculum:	other: mineral salts medium inoculated with activated sludge
Contact time:	29 day
Degradation:	< 1 % after 29 day
Result:	under test conditions no biodegradation observed
Method:	OECD Guide-line 301 B "Ready Biodegradability: Modified Sturm Test (CO_2 evolution)"
Year:	2000 GLP: yes
Test substance:	as prescribed by 1.1 - 1.4
Method:	The study was conducted in compliance with Good Laboratory Practice standards and regulations. A preliminary investigation to determine the carbon content of WINGSTAY C using elemental analysis was carried out by MEDAC Ltd. WINGSTAY C was added to two vessels containing mineral salts medium inoculated activated sludge to give a nominal test concentration of 10 mg Carbon/L. Control vessels were comprised of medium plus the reference substance (Sodium benzoate) and medium alone. Test control and reference mixtures were aerated for 29 days with air that had been treated to remove carbon dioxide.
Remark:	Substances are considered to be readily biodegradable in this test if CO_2 production is equal to or greater than 60% of the theoretical value within 10 days of the level achieving 10%.
Result:	Sodium benzoate was biodegraded by 66% after 8 days and 82% after 29 days in the absence of WINGSTAY C and by 64% after 8 days in the presence of WINGSTAY C. This confirmed that WINGSTAY C was not inhibitory to activity of the microbial inoculum. Mean cumulative CO_2 productions by mixtures containing WINGSTAY C were negligible and were equivalent to no more than 1% of the theoretical value by the end of the test on Day 29.
Reliability:	(1) valid without restriction

08-FEB-2001 (4)

AQUATIC ORGANISMS

4.1 Acute/Prolonged Toxicity to Fish
-

4.2 Acute Toxicity to Aquatic Invertebrates
-

4.3 Toxicity to Aquatic Plants e.g. Algae
-

5.1 Acute Toxicity

5.1.1 Acute Oral Toxicity

Type:	LD50
Species:	rat
Strain:	
Sex:	male/female
Number of Animals:	10
Vehicle:	other: Corn Oil
Value:	> 500 mg/kg bw
Method:	other: U S Department of Transportation Regulations, 49 CFR 173.132 (1992)
Year:	1993 GLP: yes
Test substance:	as prescribed by 1.1 - 1.4
Reliability:	(1) valid without restriction

24-JUL-2000 (5)

Type:	LD50
Species:	rat
Strain:	
Sex:	male/female
Number of Animals:	
Vehicle:	
Value:	1541 mg/kg bw
Method:	other: Acute Oral in Rats
Year:	1977 GLP: no
Test substance:	no data
Result:	Male Rats: LD50 1771 mg/kg bw; Female rats: LD50 1342 mg/kg bw; combined LD50 1541 mg/kg bw
Reliability:	(2) valid with restrictions Although this study is old and probably not conducted to GLP, the test parameters were based on an established procedure for the time period and was conducted by a well known laboratory.

24-JUL-2000 (6)

Type:	LD50
Species:	rat
Strain:	
Sex:	male/female
Number of Animals:	30
Vehicle:	
Value:	> 2000 mg/kg bw
Method:	OECD Guide-line 401 "Acute Oral Toxicity"
Year:	1998 GLP: yes
Test substance:	as prescribed by 1.1 - 1.4
Method:	Five (5) females and five (5) male rats (Cri:CD(SD)BR) per group received a single dose of 1538, 1754, or 2000 mg/kg of the test substance via gavage. Test animals were observed for clinical signs of toxicity and mortality at approximately one (1), three (3), and four (4) hours after

dosing. Test animals were subsequently observed daily for clinical signs of toxicity and twice daily for mortality for a 14-day period. Body weights were recorded before fasting (Study Day-minus 1), at initiation (Study Day-0), one (1) week (Study Day-7) and at termination (Study Day-14) of the study. Gross necropsy was conducted on all test animals.

Remark: Administered orally, by gavage,

Result: One female in the 2000 mg/kg group died on Study Day-7. Mortality was 0/10, 0/10 and 1/10 for the 1538, 1754, or 2000 mg.kg test groups, respectively.

Clinical findings were present in all dose groups. Test article related observations included various discolored areas described as wet and/or dried red and/or yellow around the eyes, nose, forelimbs, hindlimbs, anogenital, and/or urogenital areas. Mucoid feces also were noted. No test article related clinical observations were noted by Study Day-12 with one (1) exception. One (1) female in the high dose group had soft stool on Study Days-13 nad -14. The female in the 2000 mg/kg group that died on Study Day-7 was noted to have decreased defecation/urination and hypothermia.

There were no test article related effects on body weight or observations at necropsy.

Reliability: (1) valid without restriction

24-JUL-2000 (7)

5.1.2 Acute Inhalation Toxicity

-

5.1.3 Acute Dermal Toxicity

Type: LD50
Species: rat
Strain:
Sex: male/female
Number of Animals: 10
Vehicle:
Value: > 2000 mg/kg bw
Method: OECD Guide-line 402 "Acute dermal Toxicity"
Year: 1998 GLP: yes
Test substance: as prescribed by 1.1 - 1.4
Method: Five (5) male and five (5) female (Crl:CD(SD)IGS BR) rats had the test substance applied in a single dose of 2,000 mg/kg to clipped areas of intact skin. The exposure was semi-occluded and lasted for 24-hours. The rats were observed at one (1), three (3), and four (4) hours after treatment, and daily thereafter for 14-days for signs of mortality and clinical signs of toxicity. The exposure sites were examined for erythema, edema, and other dermal signs

30-60 minutes after bandage removal and daily for 13-days. Body weights were recorded at initation (Study Day-0) of the study, Study Day-7, and at termination (Study Day-14). Gross necropsies were performed on all rats at the termination of the study.

Result: No deaths occurred during the study. There were no clinical observations associated with the test substance. There were no erythema or edema noted diring the study. Desquamation and/or focal eschar were observed in one (1) female on Study Day-2 through -4; in one (1) female on Study Day-4 through -8; and in one (1) male on Study Day-11. There were no effects on body weight and there were no test article related gross necropsy findings.

Reliability: (1) valid without restriction

24-JUL-2000 (8)

Type: LD50
Species: rabbit
Strain:
Sex:
Number of Animals:
Vehicle:
Value: > 20000 mg/kg bw
Method: other: Acute Dermal Toxicity
Year: 1977 GLP: no
Test substance: no data
Reliability: (4) not assignable
Data from original report not available. However, information may be useful for information purposes.

24-JUL-2000 (6)

5.1.4 Acute Toxicity, other Routes

-

5.4 Repeated Dose Toxicity

-

5.5 Genetic Toxicity 'in Vitro'

Type:	Ames test
System of testing:	Salmonella typhimurium-strains TA1535, TA1537, TA98, TA100 and TA102/Escherichia coli-strain WP2 uvrA.
Concentration:	0.005, 0.0167, 0.050, 0.167, 0.500 and 1.00 ul/plate. DMSO solvent control
Cytotoxic Conc.:	
Metabolic activation:	with and without
Result:	negative
Method:	other: Ames/Salmonella-E.coli Reverse Mutation Assay
Year:	1998 GLP: yes
Test substance:	as prescribed by 1.1 - 1.4
Method:	Based on the results of a range-finding study with Salmonella typhimurium (tester strain TA100 and TA1537) and Escherichia coli (tester strain WP2 uvrA), the doses used for the test were 0.0050, 0.0167, 0.0500, and 1.00 ug per plate of the test substance in both the presence and absence of S9 metabolic activation. S. typhimurium strains TA98, TA100, TA102, TA1535, and TA1537, and the E. coli strain WP2 uvrA were evalutaed with and without metabolic activation (S9) using both plate incorporation methodology and liquid preincubation methology. In addition, reevaluation was done on tester strain TA1535 with and without metabolic activation by the liquid preincubation method and with tester strain WP2 uvrA with metabolic activation by the plate incorporation method. The exogenous metabolic activation system (S9) was derived from livers of Aroclor-induced Spraque-Dawley rats. DMSO was used as the vehicle for the test substance. Vehicle and positive controls were included in the assay. All doses of the test substance, the vehicle control, and positive controls were plated in triplicate.
Result:	At doses of 0.167 ug/plate and higher, the test substance was insoluble. Growth inhibition was observed at doses of 0.167 ug/plate and higher in the plate incorporation assays and at 0.0500 ug/plate and higher in the liquid preincubation tests. The revertant frequencies of cultures exposed to the test substance were comparable to the vehicle controls for all cultures, except for WP2 uvrA with metabolic activation in the plate incorporation method and for tester strain TA1535 with and without metabolic activation in the liquid preincubation test. In the plate incorporation assay with metabolic activation, the revertant frequency was approximately two (2) times the control in the WP2 uvrA cells. In the liquid preincubation assay with and without metabolic activation, the revertant frequency was approximately two (2) times the control in the TA1535 cells and a dose dependent effect was suggested without metabolic activation. The increased mutation frequencies observed in the initial

assays were not confirmed in the repeat assays. The mutation frequency of WP2 uvrA cells with metabolic activation in the plate incorporation assay was comparable with the controls. With the TA1535 cells in the liquid preincubation test, no increase in the mutation frequency was observed with metabolic activation, but statistically significant increase in revertant frequency (approximately 1.6 times higher than controls) was noted in the TA1535 strain, the increase was not dose related and was within historic negative control ranges.

Reliability: (1) valid without restriction
24-JUL-2000 (9)

Type: Mouse lymphoma assay
System of testing: L5178Y mouse lymphoma cells, clone -3.7.2C, designated L5178Y TK +/-
Concentration: 1.00, 5.00, 10.0, 20.0, 30.0, 40.0 and 50.0 ug/ml
Cytotoxic Conc.:
Metabolic activation: with and without
Result: negative
Method: OECD Guide-line 476 "Genetic Toxicology: In vitro Mammalian Cell Gene Mutation Tests"
Year: 1998 GLP: yes
Test substance: as prescribed by 1.1 - 1.4
Method: Based on the results of a range-finding study, doses of 1.00, 5.00, 10.0, 20.0, 30.0, 40.0, and 50.0 ug/mL of the test substance were evaluated with and without metabolic activation. The assays were conducted using microtiter plate methodology. Duplicate samples of the test article, vehicle control, and positive controls were used. Cells were exposed to the test substance for four (4) hours, followed by a two-day expression period. At the end of the expression period, cells were suspended in selection medium and plated in duplicate in 96-well microtiter plates. Cultures were incubated in the presence of triflurothymidine (TFT) for fourteen days. After the incubation period, the plates were scored to determine the number of negative wells. Percent relative growth was determined. The size of each mutant colony (large, small, or pindot) was recorded.

DMSO was used as the vehicle for the test substance. The positive controls were Methyl methane sulfonate (MMS), without metabolic activation, and Cyclophosphamide (CP), with metabolic activation. The exogenus metabolic activation system (S9) was derived from livers of Aroclor-induced Sprague-Dawley rats.

The results of the initial assay were confirmed in an independent test. Due to toxicity at the highest doses in the initial assay, the doses selected for the confirmatory assay were 1.00, 5.00, 10.0, 20.0, 25.0, 30.0, 35.0, and 40.0 ug/mL.
Result: In the initial assay, the test substance was extremely toxic

at the highest concentrations. Cultures exposed to 40 ug/mL and higher were not evaluated. At 30 ug/mL, average relative survival was 8.82% without metabolic activation and 22.61% with meatbolic activation. Without metabolic activation, the mutation frequency in cultures treated with the test substance was comparable to the control cultures. With metabolic activation, mutation frequencies were statistically higher at 5.00, 10.0. and 30.0 ug/mL and statistical analysis indicated a dose-dependent trend. THe increases were approximately 1.7- to 1.9-fold higher than control values and were within acceptable values for the vehicle control. THe results of the assay were considered equivocal.

In the confirmatory assay, without metabolic activation, the highest dose evaluated was 35.0 ug/mL. With metabolic activation, all doses were evaluated. At the highest dose, 40.0 ug/mL, average relative survival was 9.19%. In the second assay, there were no increases in mutation frequency in the cultures exposed the the test substance with or without metabolic activation, thus, indicating that the slight increases in mutation frequencies in the initial assay were due to normal variation and not treatment with the test substance,

The positive controls caused the expected increases in mutation freqiency.

Colony sizing showed that the size distributions in the cultures treated with the test substance were similar to the vehicle control cultures.

Reliability: (1) valid without restriction
24-JUL-2000 (10)

5.6 Genetic Toxicity 'in Vivo'

Type: Micronucleus assay
Species: mouse Sex: male/female
Strain: CD-1
Route of admin.: oral unspecified
Exposure period: Single oral dose
Doses: 175, 875, 1500 and 1750 mg/kg
Result: negative
Method: OECD Guide-line 474 "Genetic Toxicology: Micronucleus Test"
Year: 1998 GLP:
Test substance:
Method: In a preliminary toxicity screen, two mice/sex/group were dosed with 1000, 1500, 2000, 2500, or 5000 mg/kg. Animals were observed for mortality and clinical signs for 72-hours after dosing.

Based on the results of the preliminary toxicity test, single oral doses of 0, 175, 875, or 1750 mg/kg of the test substance were administerd to male and female

Crl:CD-1(ICR)BR mice. Corn oil was used as the vehicle for the test substance. Sufficient numbers of mice/sex/group were dosed so that five (5)/sex/group were available for evaluation. Bone marrow cells were evaluated 24-, 48-, and 72-hours after dosing with the test substance. All dose levels and the vehicle control were evaluated at the three (3) sampling times. The positive control, Cyclophosphamide, was included at the 24-hour sacrifice time.

Bone marrow was taken from the hind limbs. Slides were prepared from the bone marrow extracts, fixed with methanol and stained with Modified Wright's Stain Pak (4481). Two thousand PCE per mouse were evaluated for micronuclei. The ratio of polychromatic erythrocytes to nonchromatic erythrocytes was determined for 1000 erythrocytes per mouse. To control bias, all slides were coded prior to analysis.

Result: In the preliminary toxicity screen, deaths occurred at 2000, 2500, and 5000 mg/kg. At 2000 and 2500 mg/kg, three (3) of the four (4) animals died. At 5000 mg/kg, all mice had died by the 72-hour observation period.

In the micronucleous test, deaths were observed at the highest dose tested and additional mice were dosed in order that five (5) mice per sex were available for evaluation. The test substance did not produce any statistically significant increases in micronucleated PCEs relative to the vehicle controls at any of the harvest times evaluated. The positive control, Cyclophosphamide, induced a statistically significant increas in monnucleated PCEs when compared to the vehicle control.

Reliability: (1) valid without restriction
24-JUL-2000 (11)

5.8 Toxicity to Reproduction
-

5.9 Developmental Toxicity/Teratogenicity
-

(1) Boiling Temperature, Huntingdon Life Science Ltd., Test Sponsor: The Goodyear Tire & Rubber Company, December 9, 1998.

(2) Partition Coefficient, Huntingdon Life Sciences Ltd, Test Sponsor: The Goodyear Tire & Rubber Company, December 9, 1999.

(3) Water Solubility, Huntingdon Life Sciences Ltd, Test Sponsor: The Goodyear Tire & Rubber Company, December 9, 1998.

(4) WINGSTAY C: Assessment of Ready Biodegradability-Modified Sturm Test, Report # GDR010/002361, Huntingdon Life Sciences, 11/6/00

(5) Acute Oral Toxicity Study in Rats with WINGSTAY C, Study # 93-0199, Ricerca, Inc., October 15, 1993

(6) Acute Toxicity Studies of WINGSTAY C in Rabbits and Rats, Study # 255-099, International Research and Development Corporation, 9/28/1977.

(7) Acute Oral Toxicity of WINGSTAY C in Albino Rats, WIL Research Laboratories, Inc., Laboratory Study #:WIL-140017, Test Sponsor:The Goodyear Tire & Rubber Company,September 30, 1998

(8) Acute Dermal Toxocity of Wingstay C in Albino Rats, WIL Research Laboratories, Inc., Laboratory Study #: WIL-140018, Test Sponsor: The Goodyear Tire & Rubber Company, September 30, 1998.

(9) Ames/salmonella-E. coli Reverse Mutation Assay on Wingstay C, Chrysalis, Study #: 0301FG05.001, Test Sponsor: The Goodyear Tire & Rubber Company, September, 8, 1998.

(10) L5178Y Mouse Lymphoma Cell TK+/- Forward Gene Mutation Assay on Wingstay C, Chrysalis, Study #: 0313FG05.001, Study Sponsor: The Goodyear Tire & Rubber Company, September 9, 1998.

(11) In Vivo Micronucleus Test in Mouse Bone Marrow Erythropoietic Cells with Wingstay C, Chrysalis, Study #: 0309FG05.001, Study Sponsor: The Goodyear Tire & Rubber Company, September 9, 1998.

I U C L I D

D a t a S e t

New Chemical	ID: 61788-44-1
CAS No.	61788-44-1
EINECS No.	262-975-0
EINECS Name	Phenol, styrenated
CAS Name	Phenol, styrenated

Producer Related Part	
Company:	
Creation date:	08-NOV-2001
Substance Related Part	
Company:	
Creation date:	08-NOV-2001

Memo:	RAPA Hindered Phenols

Printing date:	14-NOV-2001
Revision date:	
Date of last Update:	14-NOV-2001

Number of Pages:	25

Chapter (profile):	Chapter: 1, 2, 3, 4, 5, 7
Reliability (profile):	Reliability: without reliability, 1, 2, 3, 4
Flags (profile):	Flags: without flag, confidential, non confidential, WGK (DE), TA-Luft (DE), Material Safety Dataset, Risk Assessment, Directive 67/548/EEC, SIDS

1.0.1 OECD and Company Information

Type: lead organisation
Name: American Chemistry Council (formerly Chemical Manufacturers Association) Rubber and Plastics Additives (RAPA) HPV Panel
Street: 1300 Wilson Boulevard
Town: 22209 Arlington, VA
Country: United States
Phone: 703-741-5600
Telefax: 703-741-6091

13-NOV-2001

Type: cooperating company
Name: Bayer Corporation
Country: United States

13-NOV-2001

Type: cooperating company
Name: Ciba Specialty Chemicals Corporation
Country: United States

13-NOV-2001

Type: cooperating company
Name: Crompton Corporation
Country: United States

13-NOV-2001

Type: cooperating company
Name: Flexsys America L.P.
Country: United States

13-NOV-2001

Type: cooperating company
Name: Noveon, Inc (formerly BF Goodrich)
Country: United States

13-NOV-2001

Type: cooperating company
Name: R.T. Vanderbilt Company, Inc.
Country: United States

13-NOV-2001

Type: cooperating company
Name: The Goodyear Tire & Rubber Company
Country: United States

13-NOV-2001

Type: cooperating company
Name: The Lubrizol Corporation
Country: United States

13-NOV-2001

Type: cooperating company
Name: UOP, LLC.
Country: United States

13-NOV-2001

1.0.2 Location of Production Site
-

1.0.3 Identity of Recipients
-

1.1 General Substance Information

Substance type: organic
Physical status: liquid
13-NOV-2001

1.1.0 Details on Template
-

1.1.1 Spectra
-

1.2 Synonyms

Anox G2
Source: Lowi Polymer Stabilizers GmbH Waldkraiburg
EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)
26-NOV-1997

Lowinox P24S
Source: Lowi Polymer Stabilizers GmbH Waldkraiburg
EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)
26-NOV-1997

Mixed styrenated phenols
Source: Goodyear Chemicals Europe, ECTC Les Ulis Cedex
EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)
31-MAR-1993

Montaclere
Source: Goodyear Chemicals Europe, ECTC Les Ulis Cedex
EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)
10-MAY-1995

Naugard SP
Source: Goodyear Chemicals Europe, ECTC Les Ulis Cedex
EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)
10-MAY-1995

Phenol, styrenated
Source: Sidobre Sinnova Meaux
Goodyear Chemicals Europe, ECTC Les Ulis Cedex
Lowi Polymer Stabilizers GmbH Waldkraiburg
EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)
11-MAY-1998

Phenol, styrolisiert
Source: Sidobre Sinnova Meaux
Bayer AG Leverkusen
EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)
11-MAY-1998

SPH
Source: Goodyear Chemicals Europe, ECTC Les Ulis Cedex
EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)
31-MAR-1993

Styrenated phenol
Source: Sidobre Sinnova Meaux
EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)
11-MAY-1998

Styrenated phenols
Source: Goodyear Chemicals Europe, ECTC Les Ulis Cedex
EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)
31-MAR-1993

Vulkanox SP
Source: Goodyear Chemicals Europe, ECTC Les Ulis Cedex
Bayer AG Leverkusen
EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)
10-MAY-1995

WINGSTAY S
Source: Goodyear Chemicals Europe, ECTC Les Ulis Cedex
EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)
10-MAY-1995

Source: Bayer AG Leverkusen
EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)
05-FEB-1998

1.3 Impurities
-

1.4 Additives
-

1.5 Quantity
-

1.6.1 Labelling
-

1.6.2 Classification
-

1.7 Use Pattern

Type: type
Category: Use resulting in inclusion into or onto matrix
Source: EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA) 11-FEB-2000

Type: industrial
Category: Polymers industry
Source: EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA) 11-FEB-2000

Type: industrial
Category: Textile processing industry
Source: EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA) 11-FEB-2000

Type: use
Category: Intermediates
Source: EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA) 11-FEB-2000

Type: use
Category: Stabilizers
Source: EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA) 11-FEB-2000

1.7.1 Technology Production/Use
-

1.8 Occupational Exposure Limit Values
-

1.9 Source of Exposure
-

1.10.1 Recommendations/Precautionary Measures
-

1.10.2 Emergency Measures
-

1.11 Packaging
-

1.12 Possib. of Rendering Subst. Harmless
-

1.13 Statements Concerning Waste
-

1.14.1 Water Pollution
-

1.14.2 Major Accident Hazards
-

1.14.3 Air Pollution
-

1.15 Additional Remarks
-

1.16 Last Literature Search
-

1.17 Reviews
-

1.18 Listings e.g. Chemical Inventories
-

2.1 Melting Point

Value: 25.82 degree C
Decomposition: no
Sublimation: no
Reliability: (2) valid with restrictions
Accepted calculation method
Remark: Liquid at 0°C
13-NOV-2001

Value: < 0 degree C
Decomposition: no
Sublimation: no
Remark: Liquid at 0°C
13-NOV-2001

2.2 Boiling Point

Value: 209.22 degree C
Decomposition: no
GLP: no data
13-NOV-2001
Reliability: (2) valid with restrictions
Accepted calculation method

Value: 230 degree C
Decomposition: no
GLP: no data
13-NOV-2001 (1)

Value: 200 - 250 degree C
Method: other
GLP: no data
Reliability: (2) valid with restrictions
Remark: Method: Actual method is unknown
Pressure:Atmospheric
Source: Goodyear Chemicals Europe, ECTC Les Ulis Cedex
EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)
13-NOV-2001

2.3 Density

Type: relative density
Value: 1.08 at 20 degree C
Method: other: Flexsys Standard Method of Analysis FF97.4-1
GLP: yes
Remark: Hydrometer method. Hydrometer must meet standards set in ASTM-E-100
Reliability: (1) valid without restriction
GLP study
Flag: Critical study for SIDS endpoint
13-NOV-2001 (2)

Type:
Value:
Method: other: ASTM-891
Year: 1988
GLP: no
Reliability: (2) valid with restrictions
Remark: Specific Gravity: 1.08
Source: Goodyear Chemicals Europe, ECTC Les Ulis Cedex
EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)
13-NOV-2001 (3)

2.3.1 Granulometry
-

2.4 Vapour Pressure

Value: 0.102 mm Hg
Reliability: (2) valid with restrictions
Accepted calculation method
13-NOV-2001

2.5 Partition Coefficient

log Pow: 2.415 at 25 degree C
Method: other (calculated): KOWWIN Program (v1.65)
Year: 1999
GLP: no
Testsubstance: other TS: molecular structure
Reliability: (2) valid with restrictions
Accepted calculation method
Flag: Critical study for SIDS endpoint
13-NOV-2001 (4)

log Pow: > 4 at 22 degree C
Method: other (measured)
Year:
GLP: no
Reliability: (2) valid with restrictions
Source: Goodyear Chemicals Europe, ECTC Les Ulis Cedex
EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)
Flag: Critical study for SIDS endpoint
13-NOV-2001 (5)

2.6.1 Water Solubility

pH: 6.9 - 7.2 at 1 vol% and 25 degree C
Method: other: Flexsys Standard Method of Analysis FF83.11-1
GLP: yes
Remark: Potentiometric measurement
Reliability: (1) valid without restriction
GLP study
Flag: Critical study for SIDS endpoint
13-NOV-2001 (6)

Value: 59 mg/l at 20 degree C
pH: 5.6 - 5.9
Method: other
GLP: yes
Source: Goodyear Chemicals Europe, ECTC Les Ulis Cedex
EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)
Reliability: (1) valid without restriction
GLP study
Flag: Critical study for SIDS endpoint
13-NOV-2001 (7)

2.6.2 Surface Tension
-

2.7 Flash Point

Value: > 180 degree C
Type: opened cup
Method: other: ASTM D92-98a
Year: 2000
GLP: no data
Reliability: (2) valid with restrictions
Source: Flexsys America

Value: > 160 degree C
Type: closed cup
Method: other: Pensky Martin Closed Cup
Year: 1975
GLP: no data
Reliability: (2) valid with restrictions
Remark: Pensky Martin Closed Cup
Source: Goodyear Chemicals Europe, ECTC Les Ulis Cedex
EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)
24-APR-1995

2.8 Auto Flammability
-

2.9 Flammability
-

2.10 Explosive Properties
-

2.11 Oxidizing Properties
-

2.12 Additional Remarks
-

3.1.1 Photodegradation

Type: air
INDIRECT PHOTOLYSIS
Sensitizer: OH
Conc. of sens.: 1560000 molecule/cm3
Rate constant: .0000000000577729 cm3/(molecule * sec)
Degradation: 50 % after 2.2 hour(s)
Method: other (calculated): AOP Program (v1.89)
Year: 1999 GLP: no
Test substance: other TS: molecular structure
Reliability: (2) valid with restrictions
Accepted calculation method
Flag: Critical study for SIDS endpoint
13-NOV-2001 (4)

3.1.2 Stability in Water
-

3.1.3 Stability in Soil
-

3.2 Monitoring Data (Environment)

3.3.1 Transport between Environmental Compartments

Type: fugacity model level III
Media: other: air, water, soil, sediment
Air (Level I):
Water (Level I):
Soil (Level I):
Biota (L.II/III):
Soil (L.II/III):
Method: other: EPIWIN Level III Fugacity Model
Year: 1999
Result:

Media	Concentration (percent)	Half-Life (hr)	Emissions (kg/hr)	Fugacity (atm)
Air	0.429	3.32	1000	9.06e-012
Water	39.8	444	1000	5.94e-012
Soil	59.7	444	1000	3.5e-011
Sediment	0.1	444	0	2.12e-012

Media	Reaction (kg/hr)	Advection (kg/hr)	Reaction (percent)	Advection (percent)
Air	931	44.5	31	1.48
Water	644	413	21.5	13.8
Soil	966	0	32.2	0
Sediment	1.62	0.0207	0.054	0.000692

Persistence Time: 346 hr
Reaction Time: 408 hr
Advection Time: 2.27e+003 hr
Percent Reacted: 84.8
Percent Advected: 15.2

Reliability: (2) valid with restrictions
Accepted calculation method
Flag: Critical study for SIDS endpoint
13-NOV-2001 (4)

3.3.2 Distribution
-

3.4 Mode of Degradation in Actual Use
-

3.5 Biodegradation

Type: aerobic
Inoculum: activated sludge
Degradation: 7 % after 28 day
Method: other: OECD 301 Manometric Respirometry modified according to EEC Round Robin Test "Assessment of Biodegradability of Chemicals in Water by Manometric Respirometry" DGX 1/283/82 Rev 5, EEC 79/831, Annex 5, Part C
Year: 1990 GLP: yes
Test substance: other TS: 99.97%
Source: Goodyear Chemicals Europe, ECTC Les Ulis Cedex
EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)
Reliability: (1) valid without restriction
GLP Guideline study
13-NOV-2001 (8)

3.6 BOD5, COD or BOD5/COD Ratio
-

3.7 Bioaccumulation

Type: BCF estimate from Log Kow (BCFWIN v2.12)
Method: other: BCFWIN v2.12 Model
Year: 1999
Result: Log BCF = 1.159
BCF = 14.43
Reliability: (2) valid with restrictions
Accepted calculation method

3.8 Additional Remarks
-

AQUATIC ORGANISMS

4.1 Acute/Prolonged Toxicity to Fish

Type:	static
Species:	Brachydanio rerio (Fish, fresh water)
Exposure period:	96 hour(s)
Unit:	mg/l Analytical monitoring: yes
LC0:	1
LC100:	10
Geom. mean: :	3.2
Method:	other: UBA-Verfahrensvorschlag "Letale Wirkung beim Zebrabaerbling Brachydanio rerio" (LC0, LC 50, LC100: 48-96 Studen) (May, 1984)
Year:	1991 GLP: yes
Test substance:	other TS: 99.97%
Remark:	Nominal concentrations; to produce the test solutions, the substance was weighed into water and homogenized in an Ultra-Turrax unit for 60 seconds at 8000 r.p.m. Undissolved particles (oily droplets) of the substance remained on the surface of the test medium at all test concentrations (10 mg/l turbid emulsion).
Source:	Goodyear Chemicals Europe, ECTC Les Ulis Cedex EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)
Reliability:	(1) valid without restriction GLP study, meets generally accepted scientific standards, well documented and acceptable for assessment
Flag:	Critical study for SIDS endpoint

13-NOV-2001 (9)

4.2 Acute Toxicity to Aquatic Invertebrates

-

4.3 Toxicity to Aquatic Plants e.g. Algae

-

4.4 Toxicity to Microorganisms e.g. Bacteria

Type: aquatic
Species: activated sludge
Exposure period: 3 hour(s)
Unit: mg/l Analytical monitoring: no
EC50: 362
Method: ISO 8192 "Test for inhibition of oxygen consumption by activated sludge"
Year: 1990 GLP: yes
Test substance: other TS: 99.97%
Source: Goodyear Chemicals Europe, ECTC Les Ulis Cedex
EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)
Reliability: (1) valid without restriction
GLP Guideline study
13-NOV-2001 (9)

4.5 Chronic Toxicity to Aquatic Organisms

4.5.1 Chronic Toxicity to Fish
-

4.5.2 Chronic Toxicity to Aquatic Invertebrates
-

TERRESTRIAL ORGANISMS

4.6.1 Toxicity to Soil Dwelling Organisms
-

4.6.2 Toxicity to Terrestrial Plants
-

4.6.3 Toxicity to other Non-Mamm. Terrestrial Species
-

4.7 Biological Effects Monitoring
-

4.8 Biotransformation and Kinetics
-

4.9 Additional Remarks
-

5.1 Acute Toxicity

5.1.1 Acute Oral Toxicity

Type:	LD50
Species:	rat
Strain:	Sprague-Dawley
Sex:	male/female
Number of Animals:	
Vehicle:	
Value:	3550 mg/kg bw
Method:	other: Defined Lethal Dose
Year:	GLP: no data
Test substance:	other TS: Clear amber liquid, purity: 98%
Result:	Groups of male and female rats were dosed with 2510, 3160, 3980 and 5010 mg/kg/body weight. Signs of toxicity included reduced appetite and activity (two to five days for survivors), increasing weakness, diarrhea, collapse and death. Gross autopsy results on survivors (14 days) showed that viscera appeared normal. Results on decedents included lung hyperemia, slight liver discoloration and gastrointestinal inflammation.
Reliability:	(2) valid with restrictions Meets generally accepted scientific standards, well documented and acceptable for assessment.
Flag:	Critical study for SIDS endpoint

14-NOV-2001 (10)

Type:	LD50
Species:	rat
Strain:	
Sex:	
Number of Animals:	
Vehicle:	
Value:	2500 mg/kg bw
Method:	other: Unknown
Year:	1956 GLP: no
Test substance:	as prescribed by 1.1 - 1.4
Remark:	The material was administered as a 50% solution in corn oil and the animals were observed for 7 days.
Source:	Goodyear Chemicals Europe, ECTC Les Ulis Cedex EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)

10-MAY-1995 (11)

Type: LD50
Species: rat
Strain:
Sex:
Number of Animals:
Vehicle:
Value: 3550 mg/kg bw
Method: other: no data
Year: 1974 GLP: no
Test substance: as prescribed by 1.1 - 1.4
Remark: Method: 2-3 males and 2-3 females/dose level. Tested as 50% in corn oil.
Source: Goodyear Chemicals Europe, ECTC Les Ulis Cedex
EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)

Reliability: (2) valid with restrictions
Meets generally accepted scientific standards, well documented and acceptable for assessment.

17-MAY-1995 (12)

Type: LDLo
Species: rat
Strain:
Sex:
Number of Animals:
Vehicle:
Value: > 500 mg/kg bw
Method: other: United States Department Of Transportation Regulations, 49CFR173.132(1992)
Year: 1993 GLP: yes
Test substance: as prescribed by 1.1 - 1.4
Remark: No body weight deficits, clinical or gross anatomical changes were observed.
The material was suspended in corn oil and administered at a dosage of 500 mg/kg to rats. The animals were observed for 14 days and there was no lethality in the 10 rats.
Source: Goodyear Chemicals Europe, ECTC Les Ulis Cedex
EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)

Reliability: (1) valid without restriction
GLP Guideline study

24-APR-1995 (13)

5.1.2 Acute Inhalation Toxicity

Type:	LC50
Species:	rat
Strain:	Sprague-Dawley
Sex:	male
Number of Animals:	
Vehicle:	
Exposure time:	6 hour(s)
Value:	> 2.5 mg/l
Method:	other: Limit Test
Year:	GLP: no data
Test substance:	other TS: Clear amber liquid, purity: 98%
Result:	No mortalities and no toxic effects observed at 2.5 mg/L at 4L/min over 6 hours. Autopsy showed all viscera appeared normal
Reliability:	(2) valid with restrictions Meets generally accepted scientific standards, well documented and acceptable for assessment.
Flag:	Critical study for SIDS endpoint

14-NOV-2001 (14)

5.1.3 Acute Dermal Toxicity

Type:	LD50
Species:	rabbit
Strain:	New Zealand white
Sex:	male/female
Number of Animals:	
Vehicle:	
Value:	> 5010 mg/kg bw
Method:	other: Defined Lethal Dose
Year:	GLP: no data
Test substance:	other TS: Clear amber liquid, purity:98%
Result:	The undiluted test article was applied to the shaved skin of male and female rabbits. Signs of toxicity were reduced appetite and activity (three to seven days in survivors), increasing weakness, collapse and death. Gross autopsy results on survivors were that all viscera appeared normal. Results on decedents showed slight lung congestion, slight liver and kidney discoloration, enlarged gall bladder and gastrointestinal inflammation.
Reliability:	(2) valid with restrictions Meets generally accepted scientific standards, well documented and acceptable for assessment.
Flag:	Critical study for SIDS endpoint

14-NOV-2001 (10)

Type: LD50
Species: rabbit
Strain:
Sex:
Number of Animals:
Vehicle:
Value: > 7940 mg/kg bw
Method: other: No data
Year: 1974 GLP: no
Test substance: as prescribed by 1.1 - 1.4
Remark: Method: 1 male and 1 female/dose level.
Source: Goodyear Chemicals Europe, ECTC Les Ulis Cedex
EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)

Reliability: (2) valid with restrictions
Meets generally accepted scientific standards, well documented and acceptable for assessment.

17-MAY-1995 (15)

5.1.4 Acute Toxicity, other Routes

Type: LC50
Species: rat
Strain:
Sex:
Number of Animals:
Vehicle:
Route of admin.: other: inhalation
Exposure time: 6 hour(s)
Value: > .21 mg/l
Method: other: No data
Year: 1974 GLP: no
Test substance: as prescribed by 1.1 - 1.4
Remark: Method: 6 rats exposed to air passed through test material for 6 hours at ambient temperature.
Source: Goodyear Chemicals Europe, ECTC Les Ulis Cedex
EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)

Reliability: (2) valid with restrictions
Meets generally accepted scientific standards, well documented and acceptable for assessment.

17-MAY-1995 (16)

5.2 Corrosiveness and Irritation

5.2.1 Skin Irritation

Species: rabbit
Concentration:

Exposure:
Exposure Time:
Number of
Animals:
PDII:
Result: slightly irritating
EC classificat.: not irritating
Method: OECD Guide-line 404 "Acute Dermal Irritation/Corrosion"
Year: 1991 GLP: yes
Test substance:
Source: Goodyear Chemicals Europe, ECTC Les Ulis Cedex
EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)
Reliability: (1) valid without restriction
GLP Guideline study
14-NOV-2001 (17)

Species: rabbit
Concentration:

Exposure:
Exposure Time:
Number of
Animals:
PDII:
Result: slightly irritating
EC classification.: not irritating
Method: other: United States Federal Hazardous Substance Act
Year: 1974 GLP: no
Test substance: as prescribed by 1.1 - 1.4
Remark: Method: (US) Federal Hazardous Substance Act- 0.5 ml (vol) applied to intact and abraded skin for 24 hours to 6 albino rabbits. Score: 0.7/8.0
Source: Goodyear Chemicals Europe, ECTC Les Ulis Cedex
EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)
Reliability: (2) valid with restrictions
Meets generally accepted scientific standards, well documented and acceptable for assessment.
14-NOV-2001 (18)

Species: rabbit
Concentration: undiluted

Exposure:
Exposure Time: 24 hour(s)
Number of
Animals:
PDII:
Result:
EC classification.: Primary Skin Irritant
Method:
Year: GLP:No data
Test substance:

Result: 6.1/8.0
Classified as a Primary Skin Irritant when applied undiluted under the test conditions. A defatting effect was noted, and skin sloughed off in 10 to 14 days. There was no injury in depth.
14-NOV-2001 (10)

5.2.2 Eye Irritation

Species: rabbit
Concentration:
Dose:
Exposure Time:
Comment:
Number of Animals:
Result: not irritating
EC classification.: not irritating
Method: OECD Guide-line 405 "Acute Eye Irritation/Corrosion"
Year: 1991 GLP: yes
Test substance:
Source: Goodyear Chemicals Europe, ECTC Les Ulis Cedex
EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)
Reliability: (1) valid without restriction
GLP Guideline study
14-NOV-2001 (17)

Species: rabbit
Concentration:
Dose:
Exposure Time:
Comment:
Number of Animals:
Result: slightly irritating
EC classification.: not irritating
Method: other: United States Federal Hazardous Substance Act
Year: 1974 GLP: no
Test substance: as prescribed by 1.1 - 1.4
Remark: Method: (US) Federal Hazardous Substance Act - 0.1 ml (vol) applied for 24 hours to 6 albino rabbits. Score: 4/110
Source: Goodyear Chemicals Europe, ECTC Les Ulis Cedex
EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)

Reliability: (2) valid with restrictions
Meets generally accepted scientific standards, well documented and acceptable for assessment.
14-NOV-2001 (19)

5.3 Sensitization

-

5.4 Repeated Dose Toxicity

Species:	rat	Sex: male/female
Strain:	no data	
Route of admin.:	oral feed	
Exposure period:	90 days (12 weeks)	
Frequency of treatment:	Daily	
Post. obs. period:		
Doses:	Five levels ranging from 5 to 500 mg/kg.	
Control Group:	Yes	
NOAEL:	50 mg/kg	
LOAEL:	158 mg/kg	
Method:	other: Protocol complied with "Appraisal of Food and Drug Chemicals in Foods, Drugs, and Cosmetics", Association of Food and Drug Officials of the United States, 1959.	
Year:	1961	GLP: no
Test substance:	as prescribed by 1.1 - 1.4	

Result: 12–week feeding study in rats was done at doses from 5 to 500 mg/kg/day. At 158 and 500 mg/kg/day, body weights gain were significantly lower than controls. Liver weights relative to body weights were higher than controls. (No absolute organ weight reported).) Minimal focal thyroid hyperplasia was observed at 500 mg/kg/day. No adverse effects were noted in the clinical pathology evaluations (including coagulation and prothrombin time.)

Source: Goodyear Chemicals Europe, ECTC Les Ulis Cedex
EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)

Reliability: (2) valid with restrictions
Meets generally accepted scientific standards, well documented and acceptable for assessment.

24-APR-1995 (21)

Species: rat Sex: male/female
Strain: no data
Route of admin.: oral feed
Exposure period: 36 Weeks
Frequency of treatment: Daily
Post. obs. period:
Doses: Five levels ranging from 5 to 500 mg/kg.
Control Group:
NOAEL: 150 mg/kg
LOAEL: 500 mg/kg
Method: other: Protocol complied with "Appraisal of Food and Drug Chemicals in Foods, Drugs, and Cosmetics", Association of Food and Drug Officals ot the United States, 1959.
Year: 1962 GLP: no
Test substance: as prescribed by 1.1 - 1.4

Result: 36-week feeding study in rats was done at doses from 5 to 500 mg/kg/day. Statistically lower body weights at 158 and 500 mg/kg/day (body weight gain not reported). Report states that growth was depressed only at 500 mg/kg/day. Increased liver and kidney weights relative to body weight (no absolute organ weights reported). No histopathology and clinical pathology examinations were conducted.
Source: Goodyear Chemicals Europe, ECTC Les Ulis Cedex
EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)

Reliability: (4) not assignable
24-APR-1995 (22)

5.5 Genetic Toxicity 'in Vitro'

Type: Ames test
System of testing: Salmonella typhimurium TA-98, 100, 1535, 1537, 1538. Saccaharomyces cerevisiae D4.
Concentration: 0.001, 0.01, 0.1, 1.0, 5.0 ul/plate
Cytotoxic Conc.: With metabolic activation: Toxic to all strains at the 1 and 5 microliter levels
Metabolic activation: with and without
Result: negative
Method: other: Ames Mutagenicity Plate Assay
Year: 1975 GLP: yes
Test substance: other TS: Viscous amber liquid, purity: 98%
Result: No mutagenic activity in any of the assays conducted in this evaluation and therefore considered not mutagenic under test conditions.
Reliability: (1) valid without restriction
GLP study, meets generally accepted scientific standards, well documented and acceptable for assessment
Flag: Critical study for SIDS endpoint
14-NOV-2001 (23)

Type: Gene mutation in Saccharomyces cerevisiae
System of testing: Saccharomyces cerevisiae. D4
Concentration: 0.001, 0.01, 0.1, 1.0 and 5.0 microliters/plate
Cytotoxic Conc.: With metabolic activation:.Toxic at the 1 and 5 microliter levels
Metabolic activation: with and without
Result: negative
Method: other: Ames Mutagenicity Plate Assay
Year: 1975 GLP: yes
Test substance: other TS: Viscous amber liquid, purity: 98%
Result: No mutagenic activity in any of the assays conducted in this evaluation and therefore considered not mutagenic under test conditions.
Reliability: (1) valid without restriction
GLP study, meets generally accepted scientific standards, well documented and acceptable for assessment
Flag: Critical study for SIDS endpoint
14-NOV-2001 (23)

Type: DNA damage and repair assay
System of testing: E. coli Pol A+ and Pol A1- Liquid Suspension Assay
Concentration: 10, 25, 50, 75, and 100 micrograms/l
Cytotoxic Conc.:
Metabolic activation: without
Result: positive
Method: other
Year: 1981 GLP: no
Test substance: as prescribed by 1.1 - 1.4
Remark: A test for the ability of the chemical to damage cellular DNA in the E. coli Pol A1- Liquid Suspension Assay.
Source: Goodyear Chemicals Europe, ECTC Les Ulis Cedex
EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)

Reliability: (2) valid with restrictions
Meets generally accepted scientific standards, well documented and acceptable for assessment.
Flag: Critical study for SIDS endpoint
14-NOV-2001 (24)

Type: Ames test
System of testing: Salmonella typhimurium TA-98, 100, 1535, and 1537
Concentration: 0.1, 1, 10, 100, 1000 micrograms/l
Cytotoxic Conc.:
Metabolic activation: with and without
Result: negative
Method: other
Year: 1980 GLP: no

Test substance: as prescribed by 1.1 - 1.4
Source: Goodyear Chemicals Europe, ECTC Les Ulis Cedex
EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)

Reliability: (2) valid with restrictions
Meets generally accepted scientific standards, well documented and acceptable for assessment.

06-MAR-1995 (25)

5.6 Genetic Toxicity 'in Vivo'
-

5.7 Carcinogenicity
-

5.8 Toxicity to Reproduction
-

5.9 Developmental Toxicity/Teratogenicity
-

5.10 Other Relevant Information
-

5.11 Experience with Human Exposure
-

(1) Monsanto Toxicology Profile - Montaclere, November 15, 1988

(2) Flexsys Standard Method of Analysis FF97.4-1, ASTM D891-94 method equivalent

(3) The Goodyear Tire & Rubber Company, WINGSTAY S, Material Safety Data Sheet, 1988.

(4) Meylan W. and Howard P. (1999) EPIWin Modeling Program. Syracuse Research Corporation. Environmental Science Center, 6225 Running Ridge Road, North Syracuse, NY 13212-2510.

(5) Bayer AG, Unpublished Data

(6) Flexsys Standard Method of Analysis FF83.11-1, JIS K6220 Product Specification Test Method.

(7) Bayer AG, Unpublished Data.

(8) Bayer AG Data.

(9) Bayer AG Data

(10) Monsanto Y-75-78 Younger Laboratories May 7, 1975. Toxicological Examination of Montaclere and Montaclere SE - Acute Oral LD50, Acute Dermal LD50, Acute Eye Irritation, Primary Skin Irritation.

(11) Wisconsin Alumni Research Foundation, Acute Oral Determinations to The Goodyear Tire & Rubber Company, 1956.

(12) Monsanto (1974), Acute Oral Toxicity Study, No. Y-73-192. Younger Laboratories, July 1, 1974.

(13) Ricerca, Inc., Report # 5797-93-0201-TX-001 to The Goodyear Tire & Rubber Company, 1993.

(14) Monsanto Y-75-78 Younger Laboratories May 7, 1975 Toxicological Examination of Montaclere - Acute Inhalation LC50.

(15) Monsanto (1974), Acute Dermal Toxicity Study, No. Y-73-192. Younger Laboratories, July 1, 1974.

(16) Monsanto (1974), Inhalation Toxicity Study, No. Y-73-192. Younger Laboratories, July 1, 1974.

(17) Bayer AG, Report Number 19858, January 11, 1991.

(18) Monsanto (1974), Primary Skin Irritation. No. Y-73-192. Younger Laboratories, July 1, 1974.

(19) Monsanto (1974), Primary Eye Irritation, No. Y-73-192. Younger Laboratories, July 1, 1974.

(20) 15.4/110.0.
Classified as an Eye Irritant when applied undiluted under the test conditions. Only slight discomfort immediately. All signs of irritation gone after 10 days.

(21) Food and Drug Research Laboratories, Inc., Report Number 81351, 90 Day Oral Feeding Studies in Rats to The Goodyear Tire & Rubber Company, 1961.

(22) Food and Drug Research Laboratories, Inc., Report Number 81351. Continuation of 90 Day Oral Feeding in Rats to The Goodyear Tire & Rubber Company, 1962.

(23) Monsanto (1976)- BIO-76-318 Litton Bionetics January 31, 1977. Mutagenicity Evaluation of Montaclere (CP 33121)

(24) The Goodyear Tire & Rubber Company,Styrenated Phenol Lot 6-1005 in the E.coli Pol A1- Assay, 1981.

(25) The Goodyear Tire & Rubber Company, Mutagenicity Evaluation of Wingstay S, 1980.

7.1 End Point Summary

-

7.2 Hazard Summary

-

7.3 Risk Assessment

-

I U C L I D

D a t a S e t

Existing Chemical	ID: 96-69-5
CAS No.	96-69-5
TSCA Name	61788-44-1
Producer Related Part	
Company:	
Creation date:	08-NOV-2001
Substance Related Part	
Company:	
Creation date:	08-NOV-2001
Memo:	RAPA Hindered Phenols
Printing date:	15-NOV-2001
Revision date:	
Date of last Update:	15-NOV-2001
Number of Pages:	30
Chapter (profile):	Chapter: 1, 2, 3, 4, 5, 7
Reliability (profile):	Reliability: without reliability, 1, 2, 3, 4
Flags (profile):	Flags: without flag, confidential, non confidential, WGK (DE), TA-Luft (DE), Material Safety Dataset, Risk Assessment, Directive 67/548/EEC, SIDS

1.0.1 OECD and Company Information

Type: lead organisation
Name: American Chemistry Council (formerly Chemical Manufacturers Association) Rubber and Plastics Additives (RAPA) HPV Panel
Street: 1300 Wilson Boulevard
Town: 22209 Arlington, VA
Country: United States
Phone: 703-741-5600
Telefax: 703-741-6091

14-NOV-2001

Type: cooperating company
Name: Bayer Corporation
Country: United States

14-NOV-2001

Type: cooperating company
Name: Ciba Specialty Chemicals Corporation
Country: United States

14-NOV-2001

Type: cooperating company
Name: Crompton Corporation
Country: United States

14-NOV-2001

Type: cooperating company
Name: Flexsys America L.P.
Country: United States

14-NOV-2001

Type: cooperating company
Name: Noveon, Inc (formerly BF Goodrich)
Country: United States

14-NOV-2001

Type: cooperating company
Name: R.T. Vanderbilt Company, Inc.
Country: United States

14-NOV-2001

Type: cooperating company
Name: The Goodyear Tire & Rubber Company
Country: United States

14-NOV-2001

Type: cooperating company
Name: The Lubrizol Corporation
Country: United States

14-NOV-2001

Type: cooperating company
Name: UOP, LLC.
Country: United States

14-NOV-2001

1.0.2 Location of Production Site
-

1.0.3 Identity of Recipients
-

1.1 General Substance Information
-

1.1.0 Details on Template
-

1.1.1 Spectra
-

1.2 Synonyms
-

1.3 Impurities
-

1.4 Additives
-

1.5 Quantity
-

1.6.1 Labelling
-

1.6.2 Classification
-

1.7 Use Pattern
-

1.7.1 Technology Production/Use
-

1.8 Occupational Exposure Limit Values
-

1.9 Source of Exposure
-

1.10.1 Recommendations/Precautionary Measures
-

1.10.2 Emergency Measures
-

1.11 Packaging
-

1.12 Possib. of Rendering Subst. Harmless
-

1.13 Statements Concerning Waste
-

1.14.1 Water Pollution
-

1.14.2 Major Accident Hazards
-

1.14.3 Air Pollution
-

1.15 Additional Remarks
-

1.16 Last Literature Search
-

1.17 Reviews
-

1.18 Listings e.g. Chemical Inventories
-

2.1 Melting Point

Value:	156 - 158 degree C
Decomposition:	no
Sublimation:	no
Method:	other: FF83.9-1 Initial and Final Melting Point of Organic Compounds.
Year:	1996
GLP:	yes
Remark:	Capillary Tube Method. Thermal decomposition noted above 250°C
Reliability:	(1) valid without restriction GLP study, meets generally accepted scientific standards, well documented and acceptable for assessment
Flag:	Critical study for SIDS endpoint

14-NOV-2001 (1)

2.2 Boiling Point

-

2.3 Density

Type:	relative density
Value:	1.09
Method:	other: FF97.8-1 Flexsys Standard Method
Year:	1997
GLP:	yes
Remark:	Density of solids by displacement
Reliability:	(1) valid without restriction GLP study, meets generally accepted scientific standards, well documented and acceptable for assessment
Flag:	Critical study for SIDS endpoint

14-NOV-2001 (2)

2.3.1 Granulometry

-

2.4 Vapour Pressure

Value:	.0000008399 hPa at 70 degree C
Method:	other (measured): Perkin Elmer TGS, Weight Loss vs. Temperature plot.
GLP:	no
Remark:	Weight loss was linear with respect to time
Flag:	Critical study for SIDS endpoint

14-NOV-2001 (3)

2.5 Partition Coefficient

log Pow: 8.24
Method: other (calculated): SRC LogKow (KowWin) Program
Year: 1995
GLP: no
Testsubstance: other TS: molecular structure
Reliability: (2) valid with restrictions
Accepted calculation method
Flag: Critical study for SIDS endpoint
14-NOV-2001 (4)

2.6.1 Water Solubility

Value: < .1 mg/l at 25 degree C
Qualitative: of very low solubility
Method: other: no data
Reliability: (2) valid with restrictions
Data from Handbook or collection of data
Flag: Critical study for SIDS endpoint
14-NOV-2001 (5)

2.6.2 Surface Tension
-

2.7 Flash Point
-

2.8 Auto Flammability
-

2.9 Flammability
-

2.10 Explosive Properties
-

2.11 Oxidizing Properties
-

2.12 Additional Remarks
-

3.1.1 Photodegradation

Type: air
INDIRECT PHOTOLYSIS
Sensitizer: OH
Conc. of sens.: 1560000 molecule/cm3
Rate constant: .0000000001297621 cm3/(molecule * sec)
Degradation: 50 % after 1 hour(s)
Method: other (calculated): AOP Program (v1.89)
Year: 1999 GLP: no
Test substance: other TS: molecular structure
Reliability: (2) valid with restrictions
Accepted calculation method
Flag: Critical study for SIDS endpoint
15-NOV-2001 (6)

3.1.2 Stability in Water

Type: abiotic
t1/2 pH7: > 168 hour(s) at 23 degree C
Method: other: Oxidative/Hydrolytic Stability
Year: GLP: no data
Test substance: other TS: Santowhite Crystals Lot# NI109-006, purity: 95%
Remark: Sample was extracted with methylene chloride and analyzed by gas chromatography. 63% of the test article remained after 168 hours.
Flag: Critical study for SIDS endpoint
14-NOV-2001 (7)

3.1.3 Stability in Soil
-

3.2 Monitoring Data (Environment)
-

3.3.1 Transport between Environmental Compartments

Type: fugacity model level III
Media: other: air, water, soil, sediment
Air (Level I):
Water (Level I):
Soil (Level I):
Biota (L.II/III):
Soil (L.II/III):
Method: other: EPIWIN Level III Fugacity Model
Year: 1999
Result:

Media	Concentration (percent)	Half-Life (hr)	Emissions (kg/hr)	Fugacity (atm)
Air	0.00224	1.98	1000	7.05e-016
Water	2.05	1.44e+003	1000	6.57e-020
Soil	39.2	1.44e+003	1000	9.51e-022

Sediment 58.7 5.76e+003 0 6.4e-020

Media	Reaction (kg/hr)	Advection (kg/hr)	Reaction (percent)	Advection (percent)
Air	76	2.17	2.53	0.0724
Water	95.7	199	3.19	6.63
Soil	1.83e+003	0	61	0
Sediment	684	114	22.8	3.79

Persistence Time: 3.23e+003 hr
Reaction Time: 3.61e+003 hr
Advection Time: 3.08e+004 hr
Percent Reacted: 89.5
Percent Advected: 10.5

Reliability: (2) valid with restrictions
Accepted calculation method
Flag: Critical study for SIDS endpoint
15-NOV-2001 (6)

3.3.2 Distribution
-

3.4 Mode of Degradation in Actual Use
-

3.5 Biodegradation

Type: aerobic
Inoculum:
Concentration: 3 mg/l related to Test substance
Degradation: 11 % 7 after 90 day
Result: under test conditions no biodegradation observed
Method: other: Semi-Continuous Activated Sludge (Primary Degradation) Shake Flask Test (Ultimate Biodegradation) Gedhill, 1975; Thompson-Duthie-Sturm (Ultimate Biodegradation) 1973
Year: GLP: no data
Test substance: other TS: Santowhite Crystals Lot# NI09-006, purity:95%
Remark: Analytical monitoring involved extraction with methylene chloride, sample concentration, and analysis via a gas chromatograph equipped with dual FID. The test compound showed significant resistance to primary degradation by either chemical or biological processes. Slight inhibition of the normal sludge growth was observed during the SCAS test
Shake Flask : 18.7% and 20.4% theoretical CO2.in 35 days
T-D-S: 0.0% in 49 days
Reliability: (2) valid with restrictions
Meets generally accepted scientific standards, well documented and acceptable for assessment
Flag: Critical study for SIDS endpoint
14-NOV-2001 (7)

3.6 BOD5, COD or BOD5/COD Ratio
-

3.7 Bioaccumulation
-

3.8 Additional Remarks
-

AQUATIC ORGANISMS

4.1 Acute/Prolonged Toxicity to Fish

Type:	static
Species:	Pimephales promelas (Fish, fresh water)
Exposure period:	96 hour(s)
Unit:	mg/l Analytical monitoring: no
NOEC:	.1
LC50:	.36
Method:	other: EPA Methods for Acute Toxicity Tests with Fish, Macroinvertebrates and Amphibians
Year:	1972 GLP: yes
Test substance:	other TS: White crystalline solid , purity: 99%
Remark:	Test solutions in nanograde acetone; No food; Water quality parameters of temperature, dissolved oxygen and pH measured.
Result:	LC50 (24h) = 0.70 mg/l LC50 (48h) = 0.54 mg/l LC50 (96h) = 0.36 mg/l NOEC = 0.10 mg/l LOEC = Not Determined
Reliability:	(1) valid without restriction GLP study, meets generally accepted scientific standards, well documented and acceptable for assessment
Flag:	Critical study for SIDS endpoint

14-NOV-2001 (8)

Type:	static
Species:	Salmo gairdneri (Fish, estuary, fresh water)
Exposure period:	96 hour(s)
Unit:	mg/l Analytical monitoring: no
NOEC:	.1
LC50:	.13 - .16
LOEC :	.14
Method:	other: EPA Methods for Acute Toxicity Tests with Fish, Macroinvertebrates and Amphibians
Year:	1972 GLP: yes
Test substance:	other TS: White colored powder Lots NE04-022, NB09-002 purity: 99%
Remark:	Test solutions in nanograde acetone; No food; Water quality parameters of temperature, dissolved oxygen and pH measured.
Result:	LC50 (24h) = 0.27 - 0.44 mg/l LC50 (48h) = 0.16 - 0.21 mg/l LC50 (96h) = 0.13 - 0.16 mg/l NOEC = 0.10 mg/l LOEC = 0.14 mg/l
Reliability:	(1) valid without restriction GLP study, meets generally accepted scientific standards, well documented and acceptable for assessment
Flag:	Critical study for SIDS endpoint

14-NOV-2001 (9) (10)

Type:	static
Species:	Lepomis macrochirus (Fish, fresh water)
Exposure period:	96 hour(s)
Unit:	mg/l Analytical monitoring: no
LC50:	.24 - .51
Method:	other: EPA Methods for Acute Toxicity Tests with Fish, Macroinvertebrates and Amphibians
Year:	1972 GLP: yes
Test substance:	other TS: White colored powder Lots NE04-022, NB09-002 purity: 99%.
Remark:	Test solutions in nanograde acetone; No food; Water quality parameters of temperature, dissolved oxygen and pH measured.
Result:	LC50 (24h) = 0.73 - 1.20 mg/l LC50 (48h) = 0.29 - 0.61 mg/l LC50 (96h) = 0.24 - 0.51 mg/l NOEC = 0.14 mg/l LOEC = 0.18 mg/l
Reliability:	(1) valid without restriction GLP study, meets generally accepted scientific standards, well documented and acceptable for assessment
Flag:	Critical study for SIDS endpoint

14-NOV-2001 (9) (10)

Type:	flow through
Species:	Pimephales promelas (Fish, fresh water)
Exposure period:	14 day
Unit:	mg/l Analytical monitoring: yes
NOEC:	< .031
LC50:	.054
LOEC :	.031
Method:	other: EPA Methods for Acute Toxicity Tests with Fish, Macroinvertebrates and Amphibians Time Independent Study
Year:	GLP: yes
Test substance:	other TS: White crystalline solid Lot#N109-006, purity: 99%
Remark:	The toxicity of Santowhite Crystals to fathead minnows was assessed in a 14-day flow-through study. The 6 test tanks were 17 liter aquaria holding a volume of 15 liters. Flow rate of 6L/hr provided 6 volume replacements/day. Stock solution prepared with DMF. 30 fathead minnows were placed in each tank. Feeding was 1x/day.
Result:	Under test conditions, Santowhite Crystals was found to be both highly toxic and an accumulative toxin to the test species. LC50 on Day 14 = 0.054 mg/L LC50 (24h) = 0.21 mg/l LC50 (48h) = 0.17 mg/l LC50 (72h) = 0.15 mg/l LC50 (96h) = 0.14 mg/l NOEC = <0.031 mg/l LOEC = 0.031 mg/l
Reliability:	(1) valid without restriction Meets generally accepted scientific standards, well documented and acceptable for assessment

14-NOV-2001 (11)

4.2 Acute Toxicity to Aquatic Invertebrates

Type:	static
Species:	Daphnia magna (Crustacea)
Exposure period:	48 hour(s)
Unit:	mg/l Analytical monitoring: no
NOEC:	.18
EC50:	.7
Method:	other: Standard Methods for Examination of Water and Wastewater; Methods of Acute Toxicity Test with Fish, Macroinvertebrates and Amphibians
Year:	1975 GLP: yes
Test substance:	other TS: White powder, purity: 99%
Remark:	Test solutions in nanograde acetone; No food; Water quality parameters of temperature, dissolved oxygen and pH measured.
Result:	EC50 (24h) = 1.10 mg/l EC50 (48h) = 0.70 mg/l NOEC = 0.18 mg/l
Reliability:	(1) valid without restriction GLP study, meets generally accepted scientific standards, well documented and acceptable for assessment
Flag:	Critical study for SIDS endpoint

15-NOV-2001 (12)

Type:	static
Species:	other: Paratanytarsus parthenogenetica (Midge)
Exposure period:	48 hour(s)
Unit:	mg/l Analytical monitoring:
NOEC:	100
EC50:	> 1000
Method:	other: Static Acute Bioassay
Year:	GLP:
Test substance:	

15-NOV-2001 (13)

4.3 Toxicity to Aquatic Plants e.g. Algae

Species:	Selenastrum capricornutum (Algae)
Endpoint:	biomass
Exposure period:	96 hour(s)
Unit:	mg/l Analytical monitoring: no
NOEC:	60
EC50:	126
Method:	other: US EPA Phytotoxicity
Year:	1971 GLP: no data
Test substance:	other TS: Off-white powder, purity: 95%
Remark:	Closed system; Test run in triplicate; In vivo chlorophyll measurements via Turner Model 111 fluorometer; Cell counts using a hemacytometer and Zeiss Standard 14 Compound microscope.
Result:	Chlorophyll a. EC50 (96.h) = 90 mg/l Cell Count EC50 (96.h) = 126 mg/l NOEC = 60 mg/l LOEC = Not Determined
Reliability:	(2) valid with restrictions Meets generally accepted scientific standards, well documented and acceptable for assessment
Flag:	Critical study for SIDS endpoint

15-NOV-2001 (14)

4.4 Toxicity to Microorganisms e.g. Bacteria

-

4.5 Chronic Toxicity to Aquatic Organisms

4.5.1 Chronic Toxicity to Fish

-

4.5.2 Chronic Toxicity to Aquatic Invertebrates

-

TERRESTRIAL ORGANISMS

4.6.1 Toxicity to Soil Dwelling Organisms
-

4.6.2 Toxicity to Terrestrial Plants
-

4.6.3 Toxicity to other Non-Mamm. Terrestrial Species
-

4.7 Biological Effects Monitoring
-

4.8 Biotransformation and Kinetics
-

4.9 Additional Remarks
-

5.1 Acute Toxicity

5.1.1 Acute Oral Toxicity

Type:	LD50
Species:	rat
Strain:	Sprague-Dawley
Sex:	male/female
Number of Animals:	
Vehicle:	other: corn oil
Value:	4150 mg/kg bw
Method:	other: Defined Lethal Dose
Year:	GLP: no data
Test substance:	other TS: Santowhite Crystals Lot# NB-09-002, purity:95%
Remark:	Santowhite Crystals were fed to 4 groups of male and female rats as a 25.0% suspension in corn oil at dose levels of 2510, 3160, 3980 and 5010 mg/kg/body weight. Clinical signs of toxicity included reduced appetite and activity (three to five days in survivors), followed by increasing weakness, collapse and death. Gross autopsy findings were slight lung congestion in some survivors; lung and liver hyperemia and gastrointestinal inflammation was noted in decedents.
Reliability:	(2) valid with restrictions Meets generally accepted scientific standards, well documented and acceptable for assessment
Flag:	Critical study for SIDS endpoint

15-NOV-2001 (15)

5.1.2 Acute Inhalation Toxicity

-

5.1.3 Acute Dermal Toxicity

Type:	LD50
Species:	rabbit
Strain:	New Zealand white
Sex:	male/female
Number of Animals:	
Vehicle:	other: corn oil
Value:	> 5010 mg/kg bw
Method:	other: Defined Lethal Dose
Year:	GLP: no data
Test substance:	other TS: Santowhite Crystals Lot# NB-09-002 purity: 95%
Remark:	Santowhite Crystals as a 40.0% suspension in corn oil was applied to the shaved skin of three groups of male and female rabbits at dose levels of 3160, 5010 and 7940 mg/kg/body weight. Clinical signs of toxicity included reduced appetite and activity (three to seven days in survivors), increasing weakness, collapse and death. Gross autopsy findings on the survivors included slight lung congestion and slight liver and kidney discoloration. Findings on the decedents included lung

hyperemia, liver discoloration, enlarged gall bladders, discoloration of spleen and kidneys, and gastrointestinal inflammation.
Reliability: (2) valid with restrictions
Meets generally accepted scientific standards, well documented and acceptable for assessment
Flag: Critical study for SIDS endpoint
15-NOV-2001 (15)

5.1.4 Acute Toxicity, other Routes
-

5.2 Corrosiveness and Irritation

5.2.1 Skin Irritation

Species: rabbit
Concentration:

Exposure:
Exposure Time: 24 hour(s)
Number of Animals:
PDII: .9
Result:
EC classificat.: not irritating
Method:
Year: GLP:
Test substance:
Remark: Not a primary skin irritant under test conditions. Very mild erythema, no edema.
15-NOV-2001 (15)

5.2.2 Eye Irritation

Species: rabbit
Concentration:
Dose:
Exposure Time: 24 hour(s)
Comment:
Number of Animals:
Result:
EC classificat.:
Method:
Year: GLP:
Test substance:
Result: 5.0/110.0
Slight eye irritant under test conditions. Only slight discomfort immediately. All signs of irritation gone at 72 hours.
15-NOV-2001 (15)

5.3 Sensitization

Type:	Patch-Test
Species:	human
Number of Animals:	50
Vehicle:	
Result:	not sensitizing
Classification:	
Method:	other: Shelanski and Shelanski Method
Year:	GLP:
Test substance:	
Result:	Patch tests were conducted on 50 human volunteers. The test material was applied to linteen discs and taped to the subjects' upper arms with Blenderm tape. After 24 hours, the patches were removed and the reactions graded and recorded. After a 24-hour rest period, the process was repeated until 15 sucessive patches had been applied. A two-week rest period followed, and then a challenge application was made to the same site. There were no reactions produced by any of the primary applications or by the challenge application. The test article was judged as neither a primary irritant nor a skin fatiguing agent. There was no evidence of skin sensitization.

15-NOV-2001 (16)

Type:	Patch-Test
Species:	human
Number of Animals:	
Vehicle:	
Result:	
Classification:	
Method:	
Year:	GLP:
Test substance:	
Result:	TBMC was one of 13 common commercial antioxidants tested on patients who exhibited symptoms of rubber allergy and/or contact dermatitis. No positive responses to the test article were noted at concentrations of 0.1%, 1% and 10%.

15-NOV-2001 (17)

5.4 Repeated Dose Toxicity

Species:	rat	Sex: male/female
Strain:	Fischer 344	
Route of admin.:	oral feed	
Exposure period:	13 weeks	
Frequency of treatment:	daily	
Post. obs. period:		
Doses:	0, 250, 500, 1000, 2500 or 5000 ppm	
Control Group:	yes, concurrent no treatment	
NOAEL:	500 ppm	
LOAEL:	1000 ppm	
Method:	other: NTP Toxicology and Carcinogenesis Study	
Year:	GLP: yes	
Test substance:	other TS: TBBC, purity: 99%	
Result:	Groups of 10 male and 10 female rats were fed TBBC in a controlled study. Higher ALP and ALT values were seen at 2500ppm and above. Lower hematocrit and hemoglobin concentrations and MCV values were significantly lower at 1000, 2500 and 5000 ppm males than in controls. MCV values also lower for 5000 ppm females. Histopathology findings in liver (hypertrophy and hyperplasis) and kidney (renal cortical tubule effects at 2500 and 500 ppm, and in mesenteric lymph nodes (increased size, number of macrophages) at 5000 ppm.	
Reliability:	(1) valid without restriction GLP study, meets generally accepted scientific standards, well documented and acceptable for assessment	
Flag:	Critical study for SIDS endpoint	

15-NOV-2001 (18)

Species:	mouse	Sex: male/female
Strain:	B6C3F1	
Route of admin.:	oral feed	
Exposure period:	13 weeks	
Frequency of treatment:	daily	
Post. obs. period:		
Doses:	0. 100. 250, 500, 1000 or 2500 ppm	
Control Group:	yes, concurrent no treatment	
NOAEL:	250 ppm	
LOAEL:	500 ppm	
Method:	other: NTP Toxicology and Carcinogenesis Study	
Year:	GLP: yes	
Test substance:	other TS: TBBC, purity: 99%	
Result:	Groups of 10 male and 10 female mice were fed TBBC in a controlled study. Higher ALP and ALT values were seen at 2500 ppm and above. Effects on hematocrit HB concentration and RBC count were seen at 1000 ppm and higher. Histopathology findings in liver (hypertrophy and hyperplasia) and in mesenteric lymph nodes (increased size and number of macrophages) at 2500 ppm.	
Reliability:	(1) valid without restriction	

GLP study, meets generally accepted scientific standards, well documented and acceptable for assessment
Flag: Critical study for SIDS endpoint
15-NOV-2001 (18)

Species: rat Sex: male/female
Strain: Fischer 344
Route of admin.: oral feed
Exposure period: 2 year
Frequency of treatment: daily
Post. obs. period:
Doses: 0, 500, 1000 or 2500 ppm
Control Group: yes, concurrent no treatment
NOAEL: 500 ppm
LOAEL: 1000 ppm
Method: other: NTP Toxicology and Carcinogenesis Study
Year: GLP: yes
Test substance: other TS: TBBC, purity: 99%
Remark: Dose: Males: 20, 40 or 100 mg/kg/day
Females: 20, 45 or 120 mg/kg/day
Result: 115 male and 75 female rats were fed TBBC over 2 years in a controlled study. Feed consumption, behavior and general health and appearance of exposed males and females were similar to controls. Higher ALT, AP and sorbitol dehydrogenase levels at 1000 and 2500 ppm. Lower hematocrit, HB concentration and RBC counts at 1000 and 2500 ppm. Histopathology findings in liver (Kupffer cell hypertrophy, cytoplasmic vacuolization and others) in males and females at 1000 and 2500 ppm. Increased severity of nephropathy in females at 2500 ppm. Significant negative trend in the incidence of mammary gland fibroadenoma, adenoma or carcinoma in female rats when compared with control animals. Not carcenogenic under test conditions.
Reliability: (1) valid without restriction
GLP study, meets generally accepted scientific standards, well documented and acceptable for assessment
Flag: Critical study for SIDS endpoint
15-NOV-2001 (18)

Species: mouse Sex: male/female
Strain: B6C3F1
Route of admin.: oral feed
Exposure period: 2 year
Frequency of treatment: daily
Post. obs. period:
Doses: 250, 500 and 1000 ppm
Control Group: yes, concurrent no treatment
LOAEL: 250 ppm
Method: other: NTP Toxicology and Carcinogenesis Study
Year: GLP: yes
Test substance: other TS: TBBC, purity: 99%
Remark: Dose: Males: 30, 60 or 145 mg/kg/day
Females: 45, 110 or 255 mg/kg/day
Result: Groups of 80 male and 80 female mice were fed TBBC over a 2-year period. Higher AP activities in both males and females was noted at 1000 ppm, and higher bilirubin levels in all treated male groups. Lower hematocrit, HB concentration and RBC counts noted at 1000 ppm. Not carcinogenic.
Reliability: (1) valid without restriction
GLP study, meets generally accepted scientific standards, well documented and acceptable for assessment
Flag: Critical study for SIDS endpoint
15-NOV-2001 (18)

Species: rat Sex: male/female
Strain: Fischer 344
Route of admin.: oral feed
Exposure period: 15 days
Frequency of treatment: daily
Post. obs. period:
Doses: 0, 1000, 2500, 5000, 10000 or 25000 ppm
Control Group: yes, concurrent no treatment
NOAEL: 2500 ppm
LOAEL: 5000 ppm
Method: other: NTP Toxicology and Carcinogenesis Study
Year: GLP: yes
Test substance: other TS: TBBC, purity: 99%
Remark: Doses = Males: 95, 235, 335 or 365 mg/kg/day
Females: 85, 220, 325, or 270 mg/kg/day
Result: Groups of 10 male and 10 female rats were fed diets containing TBBC in a controlled study. Deaths occurred at the 10,000 and 25,000 ppm levels. Lowered body weights at 5000 ppm and above. Diarrhea at 5000 ppm and above. Renal papillary and tubal necrosis at 10,000 ppm. Focal necrosis or erosions of the glandular stomach in some animals at 10,000ppm.
Reliability: (1) valid without restriction
GLP study, meets generally accepted scientific standards, well documented and acceptable for assessment
Flag: Critical study for SIDS endpoint
15-NOV-2001 (19)

Species: mouse Sex: male/female
Strain: B6C3F1
Route of admin.: oral feed
Exposure period: 15 days
Frequency of treatment: daily
Post. obs. period:
Doses: 0, 1000, 2500, 5000, 10000 or 25000 ppm
Control Group: yes, concurrent no treatment
NOAEL: 1000 ppm
LOAEL: 2500 ppm
Method: other: NTP Toxicology and Carcinogenesis Study
Year: GLP: yes
Test substance: other TS: TBBC, purity: 99%
Remark: Dose = Males: 285, 585, 475 mg/kg/day
Females: 360, 950 or 1030 mg/kg/day
Result: Groups of 10 male and 10 female mice were fed diets containing TBBC in a controlled study. Deaths occurred at the 5000, 10,000 and 25,000 ppm levels. Lowered body weights at 2500 ppm and above. Feed consumption markedly reduced at 5000ppm. Diarrhea at 5000 ppm and above. Renal tube necrosis in 8 males and 3 females at 5000 ppm.
Reliability: (1) valid without restriction
GLP study, meets generally accepted scientific standards, well documented and acceptable for assessment
Flag: Critical study for SIDS endpoint
15-NOV-2001 (18)

5.5 Genetic Toxicity 'in Vitro'

Type: Mitotic recombination in Saccharomyces cerevisiae
System of testing: Saccharomyces cerevisiae Strain D4
Concentration: 0.1 to 500 micrograms/plate
Cytotoxic Conc.:
Metabolic activation: with and without
Result: negative
Method: OECD Guide-line 481 "Genetic Toxicology: Saccharomyces cerevisiae Mitotic Recombination Assay"
Year: GLP: no data
Test substance: other TS: Off-White powder, purity: 95%
Remark: Not mutagenic in any assay with and without metabolic activation.
Reliability: (1) valid without restriction
Guideline study
Flag: Critical study for SIDS endpoint
15-NOV-2001 (20)

Type: Ames test
System of testing: Salmonella typhimurium TA-1535, TA-1537, TA-1538, TA-98, TA-100
Concentration: 0.1 to 500 micrograms/plate
Cytotoxic Conc.: With metabolic activation: Strain TA-98 at 500 micrograms/plate
Metabolic activation: with and without
Result: negative
Method: other: Ames Mutagenicity Plate Assay 1975 OECD 471 Equivalent
Year: GLP: yes
Test substance: other TS: White solid, purity: 99%
Remark: Not mutagenic in any assay with and without metabolic activation.
Reliability: (1) valid without restriction
GLP study, meets generally accepted scientific standards, well documented and acceptable for assessment
Flag: Critical study for SIDS endpoint
15-NOV-2001 (21)

5.6 Genetic Toxicity 'in Vivo'

Type: other: Mammalian Bone Marrow Chromosomal Aberration Test
Species: rat Sex: male/female
Strain: Fischer 344
Route of admin.: gavage
Exposure period: 6, 18 and 30 Hours
Doses: 700 mg/kg and 1400 mg/kg
Result: negative
Method: other: In vivo Bone Marrow Cytogenetics Rat Metaphase Analysis 1981 OECD 475 Equivalent
Year: GLP: yes
Test substance: other TS: White powder Lot# N004-005, purity: 99%
Remark: Oral gavage in corn oil vehicle.
Result: Groups of 65 male and 65 female rats were dosed with the test article in a controlled study. All animals exhibited decreased body tone, diarrhea, abnormal gait, piloerection and brown discoloration around the oral-nasal region and forepaws. The pharmacotoxic signs indicated that the test article was at or near the maximum tolerated dose. Animals from each group and dose level were sacrificed at 6, 18 and 30 hours after dosing. Examination of bone marrow cells from the distal end of both femurs indicated no statistically significant increases in the number of aberrations or in the number of aberrant metaphases at any of the three sacrifice times evaluated. Therefore, under assay conditions, the test article was not clastogenic to the hemopoietic cells of rat bone marrow.
Reliability: (1) valid without restriction
GLP study, meets generally accepted scientific standards, well documented and acceptable for assessment
Flag: Critical study for SIDS endpoint
15-NOV-2001 (22)

5.7 Carcinogenicity

Species:	rat	Sex: male/female
Strain:	Fischer 344	
Route of admin.:	oral feed	
Exposure period:	2 year	
Frequency of treatment:	daily	
Post. obs. period:		
Doses:	0, 500, 1000 or 2500 ppm	
Result:	negative	
Control Group:	yes, concurrent no treatment	
Method:	other: NTP Toxicology and Carcinogenesis Study	
Year:		GLP: yes
Test substance:	other TS: TBBC, purity 99%	
Remark:	Dose: Males: 20, 40 or 100 mg/kg/day Females: 20, 45 or 120 mg/kg/day	
Result:	115 male and 75 female rats were fed TBBC over 2 years in a controlled study. Feed consumption, behavior and general health and appearance of exposed males and females were similar to controls. Higher ALT, AP and sorbitol dehydrogenase levels at 1000 and 2500 ppm. Lower hematocrit, HB concentration and RBC counts at 1000 and 2500 ppm. Histopathology findings in liver (Kupffer cell hypertrophy, cytoplasmic vacuolization and others) in males and females at 1000 and 2500 ppm. Increased severity of nephropathy in females at 2500 ppm. Significant negative trend in the incidence of mammary gland fibroadenoma, adenoma or carcinoma in female rats when compared with control animals. Not carcenogenic under test conditions.	
Reliability:	(1) valid without restriction GLP study, meets generally accepted scientific standards, well documented and acceptable for assessment	

15-NOV-2001 (19)

Species:	mouse	Sex: male/female
Strain:	B6C3F1	
Route of admin.:	oral feed	
Exposure period:	2 year	
Frequency of treatment:	daily	
Post. obs. period:		
Doses:	250, 500 and 1000 ppm	
Result:	negative	
Control Group:	yes, concurrent no treatment	
Method:	other: NTP Toxicology and Carcinogenesis Study	
Year:		GLP: yes
Test substance:	other TS: TBBC, purity 99%	
Remark:	Dose: Males: 30, 60 or 145 mg/kg/day Females: 45, 110 or 255 mg/kg/day	
Result:	Groups of 80 male and 80 female mice were fed TBBC over a 2-year period. Higher AP activities in both males and females was noted at 1000 ppm, and higher bilirubin levels in all	

treated male groups. Lower hematocrit, HB concentration and RBC counts noted at 1000 ppm. Not carcinogenic.
Reliability: (1) valid without restriction
GLP study, meets generally accepted scientific standards, well documented and acceptable for assessment
15-NOV-2001 (19)

5.8 Toxicity to Reproduction

Type: other
Species: rat Sex: male/female
Strain: Fischer 344
Route of admin.: oral feed
Exposure Period: 2 year
Frequency of treatment: daily
Duration of test: 2 year
Doses:
Control Group:
Method: other: NTP Toxicology and Carcinogenesis Study
Year: GLP: yes
Test substance: other TS: TBBC, purity: 99%
Remark: Adequate repeat dose studies that demonstrate no effects on reproductive organs, in particular the testes, can be considered as an adequate test for reproductive/developmental effect. Target Organs and Levels of Evidence for NTP Technical Report Number 435 data indicates examination of the reproductive organs of the female rats (Clitoral Gland, Ovary, Uterus, Vagina) and male rats (Epididymus, Preputial Gland, Prostate, Seminal Vesicle, Testes) showed no statistical effects from the test article.
Reliability: (2) valid with restrictions
Meets generally accepted scientific standards, well documented and acceptable for assessment
Flag: Critical study for SIDS endpoint
15-NOV-2001 (19)

5.9 Developmental Toxicity/Teratogenicity

Species:	rabbit Sex: female
Strain:	New Zealand white
Route of admin.:	gavage
Exposure period:	Days 6-18 of gestation
Frequency of treatment:	1 time/day
Duration of test:	13 days
Doses:	0. 0.2, 2.0 or 20.0 mg/kg/day
Control Group:	yes, concurrent vehicle
NOAEL Maternalt.:	.2 ml/kg bw
Method:	other: Mammalian Teratogenicity
Year:	GLP: yes
Test substance:	other TS: P&G ETC 63 CAS# 96-69-5, purity: Not specified
Remark:	TOXLINE citation
Result:	Groups of 13 female rabbits were dosed with the test article and observed for general appearance, behavior, weight gain and food intake during the life phase of the study. Fetuses were delivered via cesarean section following sacrifice and observed for visceral abnormalities and skeletal anomalies. Maternal general toxicity: Clinical signs of toxicity were anorexia, marked weight loss and abortion in one animal at 2.0 mg/kg/day and in four animals at 20.0 mg/kg/day. Rabbits at the two lowest dose levels exhibited mild decreased weight gains. Rabbits at the highest dose level exhibited weight loss. Pregnancy/litter data: Five animals (1/13 at 2 mg, 4/13 at 20 mg) experienced total litter loss. Litter size was reduced in the high dose animals. If animals with total litter loss are included, the incidence of embryonic death was markedly increased at the high dose level. Foetal data: The incidence of visceral abnormalities was higher at 20.0 mg/kg than in controls, and the pups at this dose level had a slightly higher incidence of skeletal anomalies, but these differences were judged to be not statistically significant (p>0.05).
Reliability:	(2) valid with restrictions Meets generally accepted scientific standards, well documented and acceptable for assessment
Flag:	Critical study for SIDS endpoint

15-NOV-2001 (23)

5.10 Other Relevant Information

Type:	Neurotoxicity
Result:	From the NTP 2-year feeding study on 115 male and 75 female F334/N.rats, there were no significant inhibitory effects of TBBC on motor nerve excitability or conduction, neuromuscular transmission or muscle contractility. There were no microscopic lesions in the sciatic nerve, quadriceps muscle or teased nerve preparations of sciatic nerve that could be attributed to the test article.

15-NOV-2001 (19)

Type: Toxicokinetics
Method: Absorption, distribution, metabolism and excretion in rats
Result: Metabolic fate of C14-labeled TBBC was studied in male rats. Oral treatment showed a dose-related decrease in the rate of absorption due to a dose-related increase in stomach retention time. The test article was completely absorbed after oral treatment and rapidly distributed throughout the body, with the liver being the major tissue depot. Significant accumulations of the test article were also present in blood, muscle, skin and adipose tissue. The test article was rapidly cleared from all tissue except adipose, although a small percentage of the total dose tended to persist in liver and skin.
>50% was excreted on Day 1, primarily via bile into feces. Little of the C14 labeled compound was detected in the urine. Metabolites of the test article were detected in tissues shortly after administration, but all were rapidly excreted. The major metabolites were identified as glucuronide conjugates of the test article.

15-NOV-2001 (24)

Type: other: Extractability/Migration from plastics
Remark: TBMC is approved for use in several food-contact applications.
Result: The migration of antioxidants in packaging materials or utensils made from polystyrene and polypropylene was studied using the following pilot foods: Water, 3% Acetic Acid, 15% Ethanol, 50% Ethanol, Heptane and Sunflower Seed Oil. The conditions of exposure were 200 cm2/250 ml test solution for 10 days at 45°C. For the polystrene compounds containing a maximum of 0.5% 4,4'-Thiobis(6-tert-butyl-m-cresol), there was little tendency to migrate to the water, acid, 15% alcohol or vegetable oil. For polypropylene, major amounts of the test article was extracted by the vegetable oil. Migration amounts were also high with heptane.

15-NOV-2001 (25) (26)

Type: other: Reproductive Hazards Screening
Remark: NIOSH-sponsored test
Result: 4,4'-Thiobis(6-tert-butyl-m-cresol) was screened for the potential to cause reproductive effects using a postnatal mouse screening test. Experiments were designed to determine the appropriate dose level, and the reproductive effects were studies. The predicted median lethal dose level for the test article was determined to be 485 mg/kg/day. All animals received a constant volume of 10 ml/kg/day. The test article caused an increase in maternal mortality and a decreased percentage of surviving pups. There was no effect on the number of viable litters, litter size, birth weight, or the weight gain of pups.

15-NOV-2001 (27)

5.11 Experience with Human Exposure
-

(1) ASTM D-1519 / Flexsys Physical Methods of Analysis

(2) Flexsys Physical Methods of Analysis

(3) Monsanto memo, May 20, 1976

(4) Meylan, W.M. and. P.H. Howard, 1995 J. Pharm. Sci. 84: 83-92

(5) NTP Chemical Repository 4,4'-Thiobis(6-tert-butyl-m-cresol)

(6) Meylan W. and Howard P. (1999) EPIWin Modeling Program. Syracuse Research Corporation. Environmental Science Center, 6225 Running Ridge Road, North Syracuse, NY 13212-2510.

(7) Monsanto ES-78-SS-28. Environmental Persistence Screening of Selected Rubber Chemicals, Monsanto Industrial Chemicals Environmental Sciences Report (1978)

(8) Monsanto AB-79-1384322-3b Acute Toxicity of Santowhite Crystals to Fathead Minnows (Pimephales promelas) Analytical Bio Chemistry Laboratories August 15, 1979

(9) Monsanto BN-76-264 Acute (96-hour) Toxicity of Santowhite Crystals to Rainbow Trout and Bluegill, EG&G Bionomics Aquatic Toxicity Laboratory, January 1977

(10) Monsanto BN-76-265 Acute (96-hour) Toxicity of Santonox R Crystals to Rainbow Trout and Bluegill, EG&G Nionomics Aquatic Toxicity Laboratory, January 1977.

(11) Monsanto ES-79-SS-17 / MO-80-495 Acute Toxicity of Santowhite Crystals to Fathead Minnows: A Time Independent Study, W.J. Adams, W.J. Renaudette and W.E. Gledhill, Monsanto Industrial Chemicals Environmental Sciences Report, December 27, 1979

(12) Monsanto AB-78-1384322-3a Acute Toxicity of Santowhite Crystals to Daphnia Magna, Analytical Bio Chemistry Laboratories, September 30, 1978

(13) Monsanto 9AB981012, Acute Toxicity of Santowhite Crystals to Midge (Paratanysarsus parthenogenetica) Analytical Bio-Chemistry Laboratories, October 23, 1981

(14) Monsanto BN-78-138432 Acute Toxicity of Santowhite Crystals to the Freshwater Alga Selenastrum capricornutum, EG&G Bionomics, September 1978

(15) Monsanto Y-73-191 Toxicological Investigation of CP 1815, Younger Laboratories Incorporated, November 16, 1973

(16) Monsanto SH-66-7 Repeated Insult Patch Test - Santonox R, Industrial Biology Laboratories, August 02, 1966

(17) Kanto, Hiromi Allergens in Rubber Products Toho University, Tokyo Japan, Toho Igakkai Zasshi 1999

(18) TR-435 NTIS# PB95-225751 Toxicology and Carcinogenesis Studies of 4,4'-Thiobis(6-t-butyl-m-cresol) (CAS No. 96-96-5) n F344/N Rats and B6C3F1 Mice (Feed Studies) Battelle Labs, December 1994.

(19) TR-435 NTIS# PB95-225751 Toxicology and Carcinogenesis Studies of 4,4'-Thiobis(6-t-butyl-m-cresol) (CAS No. 96-96-5) n F344/N Rats and B6C3F1 Mice (Feed Studies) Battelle Labs, December 1994

(20) Monsanto BIO-76-235 Mutagenic Evaluation of Santowhite Crystals, Litton Bionetics December 30, 1976

(21) Monsanto BIO-76-236 Mutagenic Evaluation of Santonox R Crystals, Litton Bionetics December 30, 1976

(22) Monsanto PK-87-344 In Vivo Bone marrow Cytogenetics Rat metaphase Analysis - Santowhite Crystals, Pharmakon Research International, June 10, 1988

(23) Proctor & Gamble Co. Effects of ECT 63 on Pregnancy of the New Zealand White Rabbit, Huntingdon Research Center Ltd. 1992 EPA/OTS; Doc #88-920004937

(24) Birnbaum, L.S., Eastin Jr, W.C., Matthews, H.B., Disposition of 4,4'-Thiobis(6-tert-butyl-m-cresol) in Rats, National Institute of Environmental Health Sciences, Drug. Metab. Dispos. (1983), 11(6), 537-43

(25) Uhde, W.J., Woggon, H. Testing of Plastic Utensils. Migration behavior of Antioxidants from Food Packaging Materials. Deut. Lebensm.-Rundsch. (1971), 67(8), 257-62

(26) Zentralinst. Ernaehr., Dtsch. Akad. Wiss. Berlin, Germany 1971

(27) Screening of Priority Chemicals for Reproductive Hazards. 4,4'-Thiobis(6-t-butyl-m-cresol) Cas. No. 96-69-5 Environmental Health Research and Testing, Inc. 1989

7.1 End Point Summary

-

7.2 Hazard Summary

-

7.3 Risk Assessment

-

I U C L I D

D a t a S e t

Existing Chemical	ID: 85-60-9
CAS No.	85-60-9
TSCA Name	4,4'-Butylidenebis(6-tert-butyl-m-cresol)

Producer Related Part	
Company:	
Creation date:	08-NOV-2001

Substance Related Part	
Company:	
Creation date:	08-NOV-2001

Memo:	RAPA Hindered Phenols

Printing date:	13-NOV-2001
Revision date:	
Date of last Update:	13-NOV-2001

Number of Pages:	22

Chapter (profile):	Chapter: 1, 2, 3, 4, 5, 7
Reliability (profile):	Reliability: without reliability, 1, 2, 3, 4
Flags (profile):	Flags: without flag, confidential, non confidential, WGK (DE), TA-Luft (DE), Material Safety Dataset, Risk Assessment, Directive 67/548/EEC, SIDS

1.0.1 OECD and Company Information

Type: lead organisation
Name: American Chemistry Council (formerly Chemical Manufacturers Association) Rubber and Plastics Additives (RAPA) HPV Panel
Street: 1300 Wilson Boulevard
Town: 22209 Arlington, VA
Country: United States
Phone: 703-741-5600
Telefax: 703-741-6091

09-NOV-2001

Type: cooperating company
Name: Bayer Corporation
Country: United States

09-NOV-2001

Type: cooperating company
Name: Ciba Specialty Chemicals Corporation
Country: United States

09-NOV-2001

Type: cooperating company
Name: Crompton Corporation
Country: United States

09-NOV-2001

Type: cooperating company
Name: Flexsys America L.P.
Country: United States

09-NOV-2001

Type: cooperating company
Name: Noveon, Inc. (formerly BF Goodrich)
Country: United States

09-NOV-2001

Type: cooperating company
Name: R.T. Vanderbilt Company, Inc.
Country: United States

09-NOV-2001

Type: cooperating company
Name: The Goodyear Tire & Rubber Company
Country: United States

09-NOV-2001

Type: cooperating company
Name: The Lubrizol Corporation
Country: United States

09-NOV-2001

Type: cooperating company
Name: UOP, LLC.
Country: United States

09-NOV-2001

1.0.2 Location of Production Site
-

1.0.3 Identity of Recipients
-

1.1 General Substance Information
-

1.1.0 Details on Template
-

1.1.1 Spectra
-

1.2 Synonyms
-

1.3 Impurities
-

1.4 Additives
-

1.5 Quantity
-

1.6.1 Labelling
-

1.6.2 Classification
-

1.7 Use Pattern
-

1.7.1 Technology Production/Use
-

1.8 Occupational Exposure Limit Values
-

1.9 Source of Exposure
-

1.10.1 Recommendations/Precautionary Measures
-

1.10.2 Emergency Measures
-

1.11 Packaging
-

1.12 Possib. of Rendering Subst. Harmless
-

1.13 Statements Concerning Waste
-

1.14.1 Water Pollution
-

1.14.2 Major Accident Hazards
-

1.14.3 Air Pollution
-

1.15 Additional Remarks
-

1.16 Last Literature Search
-

1.17 Reviews
-

1.18 Listings e.g. Chemical Inventories
-

2.1 Melting Point

Value:	210 degree C
Decomposition:	no
Sublimation:	no
Method:	other: FF83.9-1 Initial and Final Melting Point of Organic Compounds.
Year:	1996
GLP:	yes
Testsubstance:	other TS: 4,4'-Butylidenebis(6-tert-butyl-m-cresol); purity not noted
Remark:	Capillary method.
Reliability:	(1) valid without restriction GLP Guideline study
Flag:	Critical study for SIDS endpoint

13-NOV-2001 (1)

2.2 Boiling Point

-

2.3 Density

Type:	relative density
Value:	1.03
Method:	other: FF97.8-1 Flexsys Standard Method
Year:	1997
GLP:	yes
Testsubstance:	other TS: 4,4'-Butylidenebis(6-tert-butyl-m-cresol); purity not noted
Remark:	Density of solids by displacement
Reliability:	(1) valid without restriction GLP Guideline study
Flag:	Critical study for SIDS endpoint

13-NOV-2001 (2)

2.3.1 Granulometry

-

2.4 Vapour Pressure

-

2.5 Partition Coefficient

log Pow:	9.09
Method:	other (calculated): SRC LogKow (KowWin) Program
Year:	1995
GLP:	no
Testsubstance:	other TS: molecular structure
Reliability:	(2) valid with restrictions Accepted calculation method
Flag:	Critical study for SIDS endpoint

13-NOV-2001 (3)

2.6.1 Water Solubility

Value:	< .1 other: mg/ml at 18 degree C
Qualitative:	of very low solubility
Method:	other
GLP:	no data
Testsubstance:	other TS: 4,4'-Butylidenebis(6-tert-butyl-m-cresol); purity not noted
Flag:	Critical study for SIDS endpoint

09-NOV-2001 (4)

2.6.2 Surface Tension
-

2.7 Flash Point
-

2.8 Auto Flammability
-

2.9 Flammability
-

2.10 Explosive Properties
-

2.11 Oxidizing Properties
-

2.12 Additional Remarks
-

3.1.1 Photodegradation

Type: air
INDIRECT PHOTOLYSIS
Sensitizer: OH
Conc. of sens.: 1560000 molecule/cm3
Rate constant: .000000000206671 cm3/(molecule * sec)
Degradation: 50 % after .6 hour(s)
Method: other (calculated): AOP Program (v1.89)
Year: 1999 GLP: no
Test substance: other TS: molecular structure
Reliability: (2) valid with restrictions
Accepted calculation method
Flag: Critical study for SIDS endpoint
09-NOV-2001 (5)

3.1.2 Stability in Water
-

3.1.3 Stability in Soil
-

3.2 Monitoring Data (Environment)
-

3.3.1 Transport between Environmental Compartments

Type: fugacity model level III
Media: other: air - water - soil - sediment
Air (Level I):
Water (Level I):
Soil (Level I):
Biota (L.II/III):
Soil (L.II/III):
Method: other: EPIWIN Level III Fugacity Model
Year: 1999
Result:

Media	Concentration (percent)	Half-Life (hr)	Emissions (kg/hr)	Fugacity (atm)
Air	0.0188	1.24	1000	2.95e-015
Water	2.34	1.44e+003	1000	2.9e-019
Soil	30.2	1.44e+003	1000	2.81e-021
Sediment	67.4	5.76e+003	0	2.82e-019

Media	Reaction (kg/hr)	Advection (kg/hr)	Reaction (percent)	Advection (percent)
Air	826	14.8	27.5	0.494
Water	88.5	184	2.95	6.13
Soil	1.14e+003	0	38.1	0
Sediment	638	106	21.3	3.53

Persistence Time: 2.62e+003 hr

Reaction Time: 2.92e+003 hr
Advection Time: 2.58e+004 hr
Percent Reacted: 89.8
Percent Advected: 10.2

Reliability: (2) valid with restrictions
Accepted calculation method
Flag: Critical study for SIDS endpoint
09-NOV-2001 (5)

3.3.2 Distribution
-

3.4 Mode of Degradation in Actual Use
-

3.5 Biodegradation

Type: aerobic
Inoculum: predominantly domestic sewage, adapted
Concentration: 20.7 mg/l related to Test substance
Degradation: 0 - 5 % after 35 day
Result: under test conditions no biodegradation observed
Method: other: Ultimate Biodegradation by Shake Flask CO2 Evolution; ASTM E35.24 Draft 3, 1980
Year: GLP: yes
Test substance: other TS: Santowhite Powder Lot#NM03-039, purity: >96%.
Remark: Test run in triplicate. Biodegradation either unlikely or rate of mineralization is very slow.
Reliability: (1) valid without restriction
GLP Guideline study
Flag: Critical study for SIDS endpoint
13-NOV-2001 (6) (7)

3.6 BOD5, COD or BOD5/COD Ratio
-

3.7 Bioaccumulation
-

3.8 Additional Remarks
-

AQUATIC ORGANISMS

4.1 Acute/Prolonged Toxicity to Fish

Type:	static
Species:	Salmo gairdneri (Fish, estuary, fresh water)
Exposure period:	96 hour(s)
Unit:	mg/l Analytical monitoring: no
NOEC:	1000
LC50:	> 1000
Method:	other: EPA Methods for Toxicity Tests with Fish, Macroinvertebrates And Amphibians EPA-660/3-75-009 April 1979
Year:	1979 GLP: yes
Test substance:	other TS: White powder., purity: 96.2%
Remark:	Working standard prepared in acetone. Water quality parameters monitored throughout test. No mortalities.
Result:	LC50 (24h) = >1000 mg/l LC50 (48h) = >1000 mg/l LC50 (72h) = >1000 mg/l LC50 (96h) = >1000 mg/l NOEC = 1000 mg/l LOEC = Not Determined
Reliability:	(1) valid without restriction GLP Guideline study
Flag:	Critical study for SIDS endpoint

13-NOV-2001 (8)

Type:	static
Species:	Lepomis macrochirus (Fish, fresh water)
Exposure period:	96 hour(s)
Unit:	mg/l Analytical monitoring: no
NOEC:	1000
LC50:	> 1000
Method:	other: EPA Methods for Toxicity Tests with Fish, Macroinvertebrates And Amphibians EPA-660/3-75-009 April 1979
Year:	1979 GLP: yes
Test substance:	other TS: White powder, purity: 96.2%
Remark:	Working standard prepared in acetone. Water quality parameters monitored throughout test. No mortalities.
Result:	LC50 (24h) = >1000 mg/l LC50 (48h) = >1000 mg/l LC50 (72h) = >1000 mg/l LC50 (96h) = >1000 mg/l NOEC = 1000 mg/l LOEC = Not Determined
Reliability:	(1) valid without restriction GLP Guideline study
Flag:	Critical study for SIDS endpoint

13-NOV-2001 (9)

Type: static
Species: Pimephales promelas (Fish, fresh water)
Exposure period: 96 hour(s)
Unit: mg/l Analytical monitoring: no
NOEC: 1000
LC50: > 1000
Method: other: EPA Methods for Toxicity Tests with Fish, Macroinvertebrates And Amphibians EPA-660/3-75-009 April 1979
Year: 1979 GLP: yes
Test substance: other TS: White powder, purity: 96.2
Remark: Working standard prepared in acetone. Water quality parameters monitored throughout test. No mortalities.
Result: LC50 (24h) = >1000 mg/l
LC50 (48h) = >1000 mg/l
LC50 (72h) = >1000 mg/l
LC50 (96h) = >1000 mg/l
NOEC = 1000 mg/l
LOEC = Not Determined
Reliability: (1) valid without restriction
GLP Guideline study
Flag: Critical study for SIDS endpoint
13-NOV-2001 (10)

4.2 Acute Toxicity to Aquatic Invertebrates

Type: static
Species: Daphnia magna (Crustacea)
Exposure period: 48 hour(s)
Unit: mg/l Analytical monitoring: no
EC50: 16
Method: other: EPA Methods for Toxicity Tests with Fish, Macroinvertebrates And Amphibians EPA-660/3-75-009 April 1979
Year: 1979 GLP: yes
Test substance: other TS: White powder purity: 96.2%
Remark: Working standard prepared in DMF. Water quality parameters monitored throughout test. A NOEL was not observed for the test article after 48 hours.
Result: EC50 (24h) = 24 mg/l
EC50 (48h) = 16 mg/l
NOEC = Not Observed
Reliability: (1) valid without restriction
GLP Guideline study
Flag: Critical study for SIDS endpoint
13-NOV-2001 (11)

4.3 Toxicity to Aquatic Plants e.g. Algae

Species:	Selenastrum capricornutum (Algae)
Endpoint:	biomass
Exposure period:	96 hour(s)
Unit:	Analytical monitoring: no
EC50:	> 1000
Method:	other: EPA Selenastrum capricornutum Printz Algal Assay Test 1978
Year:	1978 GLP: yes
Test substance:	other TS: White powder, purity: 96.2%
Remark:	Working standard prepared in DMF. Water quality parameters monitored throughout test; pH was 7.5; closed system
Result:	EC50 (24 h) = >500<1000 ppm EC50 (96 h) = >1000 ppm LOEC = 125 ppm
Reliability:	(1) valid without restriction GLP Guideline study
Flag:	Critical study for SIDS endpoint

13-NOV-2001 (12)

4.4 Toxicity to Microorganisms e.g. Bacteria

-

4.5 Chronic Toxicity to Aquatic Organisms

4.5.1 Chronic Toxicity to Fish

-

4.5.2 Chronic Toxicity to Aquatic Invertebrates

-

TERRESTRIAL ORGANISMS

4.6.1 Toxicity to Soil Dwelling Organisms
-

4.6.2 Toxicity to Terrestrial Plants
-

4.6.3 Toxicity to other Non-Mamm. Terrestrial Species
-

4.7 Biological Effects Monitoring
-

4.8 Biotransformation and Kinetics
-

4.9 Additional Remarks
-

5.1 Acute Toxicity

5.1.1 Acute Oral Toxicity

Type:	LD50
Species:	rat
Strain:	Sprague-Dawley
Sex:	male/female
Number of Animals:	
Vehicle:	other: corn oil
Value:	> 7940 mg/kg bw
Method:	other: Defined Lethal Dose
Year:	GLP: no data
Test substance:	other TS: Santowhite Powder Lot# NB10-010, purity: >96%.
Remark:	Santowhite Powder was fed to 2 groups of male and female rats as a 20.0% suspension in corn oil at dose levels of 6310 and 7940 mg/kg/body weight in a single oral dose study. Clinical signs of toxicity included reduced appetite and activity (one to three days in survivors), followed by increasing weakness, collapse and death. Gross autopsy findings were that all viscera appeared normal in all survivors; lung and liver hyperemia and gastrointestinal inflammation was noted in decedents.
Reliability:	(2) valid with restrictions Meets generally accepted scientific standards, well documented and acceptable for assessment
Flag:	Critical study for SIDS endpoint

13-NOV-2001 (13)

5.1.2 Acute Inhalation Toxicity

-

5.1.3 Acute Dermal Toxicity

Type:	LD50
Species:	rabbit
Strain:	New Zealand white
Sex:	male/female
Number of Animals:	
Vehicle:	other: corn oil
Value:	> 7940
Method:	other: Defined Lethal Dose
Year:	GLP: no data
Test substance:	other TS: Santowhite Powder Lot# NB10-101, purity: >96%
Remark:	Santowhite Powder as a 40.0% suspension in corn oil was applied to the shaved skin of two groups of male and female rabbits in a single dermal application study at dose levels of 5010 and 7940 mg/kg/body weight. Clinical signs of toxicity included reduced appetite and activity for two or three days. There were no mortalities. All viscera appeared normalin the animals sacrificed after 14 days.

Reliability: (2) valid with restrictions
Meets generally accepted scientific standards, well documented and acceptable for assessment
Flag: Critical study for SIDS endpoint
13-NOV-2001 (13)

5.1.4 Acute Toxicity, other Routes
-

5.2 Corrosiveness and Irritation

5.2.1 Skin Irritation
-

5.2.2 Eye Irritation
-

5.3 Sensitization

Type: Patch-Test
Species: human
Number of Animals:
Vehicle:
Result: not sensitizing
Classification:
Method:
Year: GLP:
Test substance:
Remark: 50 human volunteers. No positive reactions following initial application. No positive reactions following 15 serial applications. No positive reactions on subsequent challenge after 2 weeks.
Result: Not considered to be a primary irritatant, a cumulative irritant, or a sensitizing agent under test conditions.
13-NOV-2001 (14)

5.4 Repeated Dose Toxicity

Species:	rat	Sex: male/female
Strain:	Sprague-Dawley	
Route of admin.:	oral feed	
Exposure period:	4 weeks	
Frequency of treatment:	daily	
Post. obs. period:		
Doses:	0, 1000, 2500, 5000 and 10,000 ppm	
Control Group:	yes, concurrent no treatment	
NOAEL:	< 1000 ppm	
LOAEL:	1000 ppm	
Method:	other: 28-Day Repeat Dose/OECD 407 equivalent	
Year:	GLP: yes	
Test substance:	other TS: Santowhite Powder Lot#N7E-009, purity: >95%	
Result:	Santowhite Powder was fed to groups of ten male and female rats. There were no significant clinical signs, and all animals survived to terminal sacrifice. Reduced food intake and body weights in both sexes were noted at the three highest dose levels. Gross examination results were liver discoloration and increased absolute and relative hepatic weights for all animals at all dose levels. Microscopic findings were hepatocellular vacuolation at all dose levels. The three highest dose levels also showed hepatocellular degeneration/necrosis.	
Reliability:	(1) valid without restriction GLP Guideline study	
Flag:	Critical study for SIDS endpoint	

13-NOV-2001 (15)

Species:	rat	Sex: male/female
Strain:	Sprague-Dawley	
Route of admin.:	oral feed	
Exposure period:	90 Days	
Frequency of treatment:	Daily	
Post. obs. period:		
Doses:	0, 100, 500 and 1000 ppm.	
Control Group:	yes, concurrent no treatment	
NOAEL:	100 ppm	
LOAEL:	500 ppm	
Method:	other: 90-Day Repeat Dose / OECD 408 equivalent	
Year:	GLP: yes	
Test substance:	other TS: Santowhite Powder Lot#N7E-009, purity: >95%.	
Result:	Groups of 15 male and female rats were fed Santowhite Powder for 90 days. All animals survived to terminal sacrifice. There were no clinical signs considered related to treatment. Highest-dose animals exhibited slightly reduced body weights and food consumption, altered serum enzymes (SGOT, SGPT), increased liver weights, and microscopic liver and lymph node changes. Mid-dose animals showed similar changes in SGOT and SGPT, in liver weights and in liver and lymph node tissue.	

Reliability: (1) valid without restriction
GLP Guideline study
Flag: Critical study for SIDS endpoint
13-NOV-2001 (16)

5.5 Genetic Toxicity 'in Vitro'

Type: Ames test
System of testing: Salmonella typhimurium TA-1535, TA-1537, TA-1538, TA-98, TA-100
Concentration: 0.1, 1.0, 10, 100 and 500 micrograms/plate
Cytotoxic Conc.:
Metabolic activation: with and without
Result: negative
Method: other: Ames Mutagenicity Plate Assay
Year: 1975 GLP: no data
Test substance: other TS: White powder, purity: 95+%
Reliability: (2) valid with restrictions
Meets generally accepted scientific standards, well documented and acceptable for assessment
Flag: Critical study for SIDS endpoint
13-NOV-2001 (17)

Type: Yeast gene mutation assay
System of testing: Saccharomyces cerevisiae, D4
Concentration: 0.1, 1.0, 10, 100 and 500 micrograms/plate
Cytotoxic Conc.:
Metabolic activation: with and without
Result: negative
Method: other: Ames Mutagenicity Plate Assay
Year: 1975 GLP: no data
Test substance: other TS: White powder, purity: 95+%
Reliability: (2) valid with restrictions
Meets generally accepted scientific standards, well documented and acceptable for assessment
Flag: Critical study for SIDS endpoint
13-NOV-2001 (17)

Type: Unscheduled DNA synthesis
System of testing: Primary rat liver cells
Concentration: 1,5,10, 50, 100 and 250 micrograms/L
Cytotoxic Conc.:
Metabolic activation: without
Result: negative
Method: other: according to Williams, G.M. 1977; Detection of Chemical Carcinogens by Unscheduled DNA Synthesis in Rat Liver Primary Cell Cultures.
Year: GLP: yes
Test substance: other TS: Santowhite Powder Lot# N6E-021, purity: >96%.
Remark: Negative - not a genotoxic agent under test conditions
Reliability: (1) valid without restriction
GLP study, meets generally accepted scientific standards, well documented and acceptable for assessment
Flag: Critical study for SIDS endpoint
13-NOV-2001 (18)

Type: Cytogenetic assay
System of testing: CHO Cells.
Concentration: 2, 4 and 8 micrograms/ml.in the absence of metabolic activation; 12.5, 25 and 50 micrograms/ml in the presence of metabolic activation
Cytotoxic Conc.: Precipitation conc:200 micrograms/ml.
Metabolic activation: with and without
Result: negative
Method: other: according to Preston et. al. 1981; Mammalian in vivo and in vitro.Cytogenetic Assays
Year: GLP: yes
Test substance: other TS: Santowhite Powder Lot# N6E-021, purity: >96%.
Remark: Negative - did not induce chromosomal aberrations in Chinese Hamster ovary cells (CHO) both in the presence or absence of rat S-9 metabolic activation.
The cells were evaluated via microscope for mitotic indices and for chromosomal aberrations.
Solvent and positive controls were included in the study.
Reliability: (1) valid without restriction
GLP study, meets generally accepted scientific standards, well documented and acceptable for assessment
Flag: Critical study for SIDS endpoint
13-NOV-2001 (19)

5.6 Genetic Toxicity 'in Vivo'

-

5.7 Carcinogenicity

-

5.8 Toxicity to Reproduction

Type:	other
Species:	rat Sex: male/female
Strain:	Sprague-Dawley
Route of admin.:	oral feed
Exposure Period:	90 days
Frequency of treatment:	
Duration of test:	90 days
Doses:	0, 100, 500 and 1000 ppm
Control Group:	yes, concurrent no treatment
NOAEL Parental:	100 ppm
Method:	other: 90-Day Repeat Dose / OECD 408 equivalent
Year:	GLP: yes
Test substance:	other TS: Santowhite Powder Lot# N7E-009, purity: >95%.
Remark:	OECD/SIDS program accepts adequate repeat dose 90-day studies that demonstrate no effect on reproductive organs. General parental toxicity: All animals survived. No clinical signs of treatment-related toxicity. Gross and microscopic examination of both male and female reproductive organs at sacrifice noted no significant differences in the organs of the control group vs. the treated groups. Reproductive system organs examined included testes with epididymides, ovaries and uterus. Testes with epididymides were weighed as well as examined.
Reliability:	(2) valid with restrictions GLP study, meets generally accepted scientific standards, well documented and acceptable for assessment
Flag:	Critical study for SIDS endpoint

13-NOV-2001 (16)

5.9 Developmental Toxicity/Teratogenicity

-

5.10 Other Relevant Information

Type:	Toxicokinetics
Method:	A group of 5 male Sprague-Dawley rats were fed BBMC in the diet for one week at an exposure level of 1.135 mmol/100g of feed, with the average mean intake reported as 0.466 mmol/rat/day.
Remark:	Authors noted that BBMC seemed to have "anticholinesteremic and antidibetic effects" and to produce hepatic fatty infiltration in rats fed 0.005% of the test substance in their diet for 90 days.
Result:	A slight increase in the prothrombin index, increased relative liver weights, and changes in liver and plasma lipid concentrations were reported. Alterations in lipid levels included increases in triglycerides, diglycerides, non-esterified fatty acids, cholesterol and cholesterol esters in the liver and decreases in trigylcerides, cholesterol and non-esterified fatty acids in plasma. The findings may

suggest a decrease in fat excretion in the liver.
13-NOV-2001 (20) (21)

5.11 Experience with Human Exposure
-

(1) ASTM D-1519./ Flexsys Physical Methods of Analysis FF83.9-1 Initial and Final Melting Point of Organic Compounds. 1996.

(2) FF97.8-1 Flexsys Standard Method 1997 - Density by Displacement

(3) Meylan, W.M. and. P.H. Howard, 1995 J. Pharm. Sci. 84: 83-92

KowWin Log P Calculations/Database

(4) NTP Chemical Repository

(5) Meylan W. and Howard P. (1999) EPIWin Modeling Program. Syracuse Research Corporation. Environmental Science Center, 6225 Running Ridge Road, North Syracuse, NY 13212-2510.

(6) Monsanto ES-80-SS-42 Environmental Sciences Labs 1980

(7) Monsanto ES-80-SS-42 Environmental Sciences Labs 1980. Biodegradation Screening of Selected Rubber Chemicals - Ultimate Biodegradation by Shake Flask CO2 Evolution / ASTM E35.24 Draft 3 - 1980.

(8) Monsanto AB-80-536 Analytical BioChemistry Labs, July 1980. Acute Toxicity of Santowhite Powder to Rainbow Trout (Salmo gairdneri).

(9) Monsanto AB-80-538 Analytical BioChemistry Labs, July 1980. Acute Toxicity of Santowhite Powder to Bluegill Sunfish (Lepomis macrochirus).

(10) Monsanto AB-80-537 Analytical BioChemistry Labs, July 1980. Acute Toxicity of Santowhite Powder to Fathead Minnows (Pimephales promelas).

(11) Monsanto AB-80-543 Analytical BioChemistry Labs, November 1980. Acute Toxicity of Santowhite Powder to Daphnia magna.

(12) Monsanto BN-80-535 EG&G Bionomics August 1980. Toxicity of Santowhite Powder to the freshwater algae Selenastrum capricurnutum

(13) Monsanto Y-73-289 Younger Laboratories Feb. 15, 1974. Toxicological Investigation of Santowhite Powder - Acute Oral LD50, Acute Dermal LD50, Acute Eye Irritation, Primary Skin Irritation

(14) Monsanto SH-66-6 Industrial Biology Laboratories May 1966. Repeat Insult Patch Test - Santowhite Powder Antioxidant

(15) Monsanto ML-87-150 Monsanto Environmental Health Laboratory February 17, 1988 Four Week Feeding Study of Santowhite Powder in Sprague-Dawley Rats

(16) Monsanto ML-87-311 Monsanto Environmental Health Laboratory November 8, 1988. Three Month Study of Santowhite Powder Antioxidant Administered to Feed in Sprague-Dawley Rats

(17) Monsanto BIO-76-233 Litton Bionetics December 30, 1976. Mutagenicity Evaluation of CP 3388 (Santowhite Powder) Final Report

(18) Monsanto SR-86-391 SRI International February 2, 1987. Evaluation of the Potential of Santowhite Powder to Induce Unscheduled DNA Synthesis in Primary Rat Hepatocyte Cultures

(19) Monsanto SR-86-392 SRI International January 1987. An Assessment of the Clastogenic Potential of Santowhite Powder Utilizing the Mammalian Cell Cytogenics Assay with CHO Cells

(20) Takahashi, O. and Hirage, K. (1981) Effects of Four Bis-Phenolic Antioxidants on Prothrombin levels of Rat Plasma. Toxicol. Lett. 7, 405-408

(21) Takahashi, O. and Hirage, K. (1981) Effects of Four Bis-Phenolic Antioxidants on Prothrombin levels of Rat Plasma. Toxicol. Lett. 8, 77-86

7.1 End Point Summary

-

7.2 Hazard Summary

-

7.3 Risk Assessment

-

I U C L I D

D a t a S e t

Existing Chemical	ID: 79-96-9
CAS No.	79-96-9
EINECS Name	Phenol, 4,4'-(1-methylethylidene)bis 2-(1,1-dimethylethyl)-
Molecular Weight	340.51
TSCA Name	Phenol, 4,4'-(1-methylethylidene)bis 2-(1,1-dimethylethyl)-
Molecular Formula	C23H32O2

Producer Related Part

Company:	Bayer Corporation
Creation date:	15-NOV-2001

Substance Related Part

Company:	Bayer Corporation
Creation date:	15-NOV-2001

Printing date:	16-NOV-2001
Revision date:	
Date of last Update:	16-NOV-2001

Number of Pages:	15

Chapter (profile):	Chapter: 1, 2, 3, 4, 5, 7
Reliability (profile):	Reliability: without reliability, 1, 2, 3, 4
Flags (profile):	Flags: without flag, confidential, non confidential, WGK (DE), TA-Luft (DE), Material Safety Dataset, Risk Assessment, Directive 67/548/EEC, SIDS

1.0.1 OECD and Company Information

Type: lead organisation
Name: American Chemistry Council (formerly Chemical Manufacturers Association) Rubber and Plastics Additives (RAPA) HPV Panel
Street: 1300 Wilson Boulevard
Town: 22209 Arlington, VA
Country: United States
Phone: 703-741-5600
Telefax: 703-741-6091

15-NOV-2001

Type: cooperating company
Name: Bayer Corporation
Country: United States

15-NOV-2001

Type: cooperating company
Name: Ciba Specialty Chemicals Corporation
Country: United States

15-NOV-2001

Type: cooperating company
Name: Crompton Corporation
Country: United States

15-NOV-2001

Type: cooperating company
Name: Flexsys America L.P.
Country: United States

15-NOV-2001

Type: cooperating company
Name: Noveon, Inc. (formerly BF Goodrich)
Country: United States

15-NOV-2001

Type: cooperating company
Name: R.T. Vanderbilt Company, Inc.
Country: United States

15-NOV-2001

Type: cooperating company
Name: The Goodyear Tire & Rubber Company
Country: United States

15-NOV-2001

Type: cooperating company
Name: The Lubrizol Corporation
Country: United States

15-NOV-2001

Type: cooperating company
Name: UOP, LLC.
Country: United States

15-NOV-2001

1.0.2 Location of Production Site
-

1.0.3 Identity of Recipients
-

1.1 General Substance Information

Substance type: organic
Physical status:
15-NOV-2001

1.1.0 Details on Template
-

1.1.1 Spectra
-

1.2 Synonyms

Goodrite 3171
15-NOV-2001

Stabilox Intermediate
15-NOV-2001

1.3 Impurities
-

1.4 Additives
-

1.5 Quantity
-

1.6.1 Labelling
-

1.6.2 Classification
-

1.7 Use Pattern
-

1.7.1 Technology Production/Use
-

1.8 Occupational Exposure Limit Values
-

1.9 Source of Exposure
-

1.10.1 Recommendations/Precautionary Measures
-

1.10.2 Emergency Measures
-

1.11 Packaging
-

1.12 Possib. of Rendering Subst. Harmless
-

1.13 Statements Concerning Waste
-

1.14.1 Water Pollution
-

1.14.2 Major Accident Hazards
-

1.14.3 Air Pollution
-

1.15 Additional Remarks
-

1.16 Last Literature Search
-

1.17 Reviews
-

1.18 Listings e.g. Chemical Inventories
-

2.1 Melting Point

Value:	181.4 degree C
Method:	other: MPBPWIN (v1.31)
Year:	1999
GLP:	no
Remark:	Melting Point: 349.84 deg C (Adapted Joback Method) Melting Point: 139.27 deg C (Gold and Ogle Method) Mean Melt Pt : 244.55 deg C (Joback; Gold,Ogle Methods) Selected MP: 181.38 deg C (Weighted Value) Accepted calculation method
Flag:	Critical study for SIDS endpoint

15-NOV-2001 (1)

2.2 Boiling Point

Value:	433.2 degree C at 1013 hPa
Method:	other: MPBPWIN (v1.31) ; Adapted Stein & Brown Method
Year:	1999
GLP:	no
Testsubstance:	other TS: molecular structure
Reliability:	(2) valid with restrictions Accepted calculation method
Flag:	Critical study for SIDS endpoint

15-NOV-2001 (1)

2.3 Density

-

2.3.1 Granulometry

-

2.4 Vapour Pressure

Value:	.00000000157 hPa at 25 degree C
Method:	other (calculated): MPBPWIN (v1.31) Modified Grain Method
Year:	1999
GLP:	no
Testsubstance:	other TS: molecular structure
Result:	Vapor Pressure Estimations (25 deg C): (Using BP: 433.17 deg C (estimated)) (Using MP: 181.38 deg C (estimated)) VP: 8.63E-011 mm Hg (Antoine Method) VP: 1.18E-009 mm Hg (Modified Grain Method) VP: 7.58E-008 mm Hg (Mackay Method) Selected VP: 1.18E-009 mm Hg (Modified Grain Method)
Reliability:	(2) valid with restrictions Accepted calculation method
Flag:	Critical study for SIDS endpoint

15-NOV-2001 (1)

2.5 Partition Coefficient

log Pow: 7.46 at 25 degree C
Method: other (calculated): KOWWIN Program (v1.65)
Year: 1999
GLP: no
Testsubstance: other TS: molecular structure
Reliability: (2) valid with restrictions
Accepted calculation method
Flag: Critical study for SIDS endpoint
15-NOV-2001 (1)

2.6.1 Water Solubility

Value: .01139 mg/l at 25 degree C
Method: other: WSKOW (v1.36)
Year: 1999
GLP: no
Testsubstance: other TS: molecular structure
Remark: Log Kow used by Water solubility estimates: 7.46
Equation Used to Make Water Sol estimate:
Log S (mol/L) = 0.796 - 0.854 log Kow - 0.00728 MW +
Correction (used when Melting Point NOT available)

Correction(s):	Value
Phenol	0.580

Log Water Solubility (in moles/L) : -7.475
Water Solubility at 25 deg C (mg/L): 0.01139
Reliability: (2) valid with restrictions
Accepted calculation method
Flag: Critical study for SIDS endpoint
15-NOV-2001 (1)

2.6.2 Surface Tension
-

2.7 Flash Point
-

2.8 Auto Flammability
-

2.9 Flammability
-

2.10 Explosive Properties
-

2.11 Oxidizing Properties
-

2.12 Additional Remarks
-

3.1.1 Photodegradation

Type: air
INDIRECT PHOTOLYSIS
Sensitizer: OH
Conc. of sens.: 1560000 molecule/cm3
Rate constant: .0000000000975473 cm3/(molecule * sec)
Degradation: 50 % after 1.3 hour(s)
Method: other (calculated):AOPWin (v1.88) Estimations Program
Year: 1999 GLP: no
Test substance: other TS: chemical structure
Reliability: (2) valid with restrictions
Accepted calculation method
Flag: Critical study for SIDS endpoint
15-NOV-2001 (1)

3.1.2 Stability in Water
-

3.1.3 Stability in Soil
-

3.2 Monitoring Data (Environment)
-

3.3.1 Transport between Environmental Compartments

Type: fugacity model level III
Media: other: air - water - soil - sediment
Air (Level I):
Water (Level I):
Soil (Level I):
Biota (L.II/III):
Soil (L.II/III):
Method: other: EPIWIN Level III Fugacity Model
Year: 1999
Result:

Media	Concentration (percent)	Half-Life (hr)	Emissions (kg/hr)	Fugacity (atm)
Air	0.00509	2.63	1000	1.53e-014
Water	2.15	1.44e+003	1000	9.07e-018
Soil	39	1.44e+003	1000	1.3e-019
Sediment	58.9	5.76e+003	0	8.84e-018

Media	Reaction (kg/hr)	Advection (kg/hr)	Reaction (percent)	Advection (percent)
Air	127	4.84	4.25	0.161
Water	98.2	204	3.27	6.8
Soil	1.78e+003	0	59.4	0
Sediment	673	112	22.4	3.73

Persistence Time: 3.17e+003 hr

Reaction Time: 3.55e+003 hr
Advection Time: 2.96e+004 hr
Percent Reacted: 89.3
Percent Advected: 10.7
Reliability: (2) valid with restrictions
Accepted calculation method
Flag: Critical study for SIDS endpoint
15-NOV-2001 (1)

3.3.2 Distribution
-

3.4 Mode of Degradation in Actual Use
-

3.5 Biodegradation
-

3.6 BOD5, COD or BOD5/COD Ratio
-

3.7 Bioaccumulation
-

3.8 Additional Remarks
-

AQUATIC ORGANISMS

4.1 Acute/Prolonged Toxicity to Fish

Type:	other		
Species:	other: fish		
Exposure period:	96 hour(s)		
Unit:	mg/l	Analytical monitoring:	no
LC50:	.022		
Method:	other: (calculated) ECOSAR v0.99e		
Year:	1999	GLP:	no
Test substance:	other TS: molecular structure		
Remark:	Chemical may not be soluble enough to measure this predicted effect.		
Reliability:	(2) valid with restrictions Accepted calculation method		

15-NOV-2001 (1)

4.2 Acute Toxicity to Aquatic Invertebrates

Type:	other: calculated		
Species:	Daphnia sp. (Crustacea)		
Exposure period:	48 hour(s)		
Unit:	mg/l	Analytical monitoring:	no
EC50:	.107		
Method:	other: (calculated) ECOSAR v0.99e		
Year:	1999	GLP:	no
Test substance:	other TS: molecular structure		
Remark:	Chemical may not be soluble enough to measure this predicted effect.		
Reliability:	(2) valid with restrictions Accepted calculation method		

15-NOV-2001 (1)

4.3 Toxicity to Aquatic Plants e.g. Algae

Species:	other algae: green algae		
Endpoint:	growth rate		
Exposure period:	96 hour(s)		
Unit:	mg/l	Analytical monitoring:	no
EC50:	.002		
Method:	other: (calculated) ECOSAR v0.99e		
Year:	1999	GLP:	no
Test substance:	other TS: molecular structure		
Reliability:	(2) valid with restrictions Accepted calculation method		

15-NOV-2001 (1)

4.4 Toxicity to Microorganisms e.g. Bacteria

-

4.5 Chronic Toxicity to Aquatic Organisms

4.5.1 Chronic Toxicity to Fish
-

4.5.2 Chronic Toxicity to Aquatic Invertebrates
-

TERRESTRIAL ORGANISMS

4.6.1 Toxicity to Soil Dwelling Organisms
-

4.6.2 Toxicity to Terrestrial Plants
-

4.6.3 Toxicity to other Non-Mamm. Terrestrial Species
-

4.7 Biological Effects Monitoring
-

4.8 Biotransformation and Kinetics
-

4.9 Additional Remarks
-

5.1 Acute Toxicity

5.1.1 Acute Oral Toxicity
-

5.1.2 Acute Inhalation Toxicity
-

5.1.3 Acute Dermal Toxicity
-

5.1.4 Acute Toxicity, other Routes

Type: LD50
Species: mouse
Strain:
Sex:
Number of Animals:
Vehicle:
Route of admin.: i.p.
Value: 40 mg/kg bw
Method:
Year: GLP:
Test substance: other TS: CAS# 79-96-9; purity not noted
16-NOV-2001 (2)

5.2 Corrosiveness and Irritation

5.2.1 Skin Irritation
-

5.2.2 Eye Irritation
-

5.3 Sensitization
-

5.4 Repeated Dose Toxicity
-

5.5 Genetic Toxicity 'in Vitro'
-

5.6 Genetic Toxicity 'in Vivo'
-

5.7 Carcinogenicity
-

5.8 Toxicity to Reproduction
-

5.9 Developmental Toxicity/Teratogenicity
-

5.10 Other Relevant Information
-

5.11 Experience with Human Exposure
-

(1) Meylan W. and Howard P. (1999) EPIWin Modeling Program. Syracuse Research Corporation. Environmental Science Center, 6225 Running Ridge Road, North Syracuse, NY 13212-2510.

(2) NTIS Issue 99-3 (August, 1999) AD691-490

7.1 End Point Summary

-

7.2 Hazard Summary

-

7.3 Risk Assessment

-

I U C L I D

D a t a S e t

Existing Chemical	ID: 7786-17-6
EINECS Name	2,2'-methylenebis(6-nonyl-p-cresol)
EINECS No.	232-092-5
Molecular Formula	C33H52O2

Producer Related Part	
Company:	Epona Associates, LLC
Creation date:	04-DEC-2001
Substance Related Part	
Company:	Epona Associates, LLC
Creation date:	04-DEC-2001

Printing date:	06-DEC-2001
Revision date:	
Date of last Update:	06-DEC-2001

Number of Pages:	6

Chapter (profile):	Chapter: 2.1, 2.2, 2.4, 2.5, 2.6.1, 3.1.1, 3.1.2, 3.3.1, 3.5, 4.1, 4.2, 4.3, 5.1.1, 5.1.2, 5.1.3, 5.1.4, 5.4, 5.5, 5.6, 5.8, 5.9
Reliability (profile):	Reliability: without reliability, 1, 2, 3, 4
Flags (profile):	Flags: without flag, confidential, non confidential, WGK (DE), TA-Luft (DE), Material Safety Dataset, Risk Assessment, Directive 67/548/EEC, SIDS

2.1 Melting Point

Value: = 251.8 degree C
Method: other
GLP: no
Testsubstance: other TS
Test substance: Phenol, 2,2'-methylenebis 4-methyl-6-nonyl-
04-DEC-2001 (1)

2.2 Boiling Point

Value: = 584 degree C
Method: other
GLP: no
Testsubstance: other TS
Test substance: Phenol, 2,2'-methylenebis 4-methyl-6-nonyl-
04-DEC-2001 (1)

2.4 Vapour Pressure

Value: = .8332648 hPa at 25 degree C
Method: other (calculated)
GLP: no
Testsubstance: other TS
Test substance: Phenol, 2,2'-methylenebis 4-methyl-6-nonyl-
04-DEC-2001 (1)

2.5 Partition Coefficient

log Pow: = 13.1
Method:
Year:
GLP: no
Testsubstance: other TS
Test substance: Phenol, 2,2'-methylenebis 4-methyl-6-nonyl-
06-DEC-2001 (1)

2.6.1 Water Solubility

Value: = 0 mg/l at 25 degree C
Method: other
GLP: no
Testsubstance: other TS

Test substance: Phenol, 2,2'-methylenebis 4-methyl-6-nonyl-
04-DEC-2001 (1)

3.1.1 Photodegradation

Type: air
DIRECT PHOTOLYSIS
Halflife t1/2: = 1.9 hour(s)
Method:
Year: GLP: no
Test substance: other TS
Test substance: Phenol, 2,2'-methylenebis 4-methyl-6-nonyl-
04-DEC-2001 (1)

3.1.2 Stability in Water
-

3.3.1 Transport between Environmental Compartments

Type: fugacity model level III
Media:
Air (Level I):
Water (Level I):
Soil (Level I):
Biota (L.II/III):
Soil (L.II/III):
Method: other
Year:
Result: Air 0.0911 %, 3.85 hr half-life, 1000 kg/hr
Sediment 67.3%, 3.6E+3 hr half-life, 1000 kg/hr
Soil 29.2%, 900 hr half-life, 1000 kg/hr
Water 3.39%, 900 hr half-life, 1000 kg/hr
04-DEC-2001 (1)

3.5 Biodegradation

Type:
Inoculum:
Degradation: =
Method:
Year: GLP: no
Test substance: other TS
Result: BIOWIN (v3.67) Program Results:
==========
SMILES : Oc(c(cc(c1)C)Cc(c(O)c(cc2C)CCCCCCCCC)c2)c1CCCCCCCCC
CHEM : Phenol, 2,2'-methylenebis 4-methyl-6-nonyl-
MOL FOR: C33 H52 O2
MOL WT : 480.78
---------- BIOWIN v3.67 Results

Linear Model Prediction : Biodegrades Fast
Non-Linear Model Prediction: Biodegrades Fast
Ultimate Biodegradation Timeframe: Weeks-Months
Primary Biodegradation Timeframe: Days-Weeks
Test substance: Phenol, 2,2'-methylenebis 4-methyl-6-nonyl-
05-DEC-2001 (1)

AQUATIC ORGANISMS

4.1 Acute/Prolonged Toxicity to Fish
-

4.2 Acute Toxicity to Aquatic Invertebrates
-

4.3 Toxicity to Aquatic Plants e.g. Algae
-

5. Toxicity

5.1 Acute Toxicity

5.1.1 Acute Oral Toxicity

-

5.1.2 Acute Inhalation Toxicity

-

5.1.3 Acute Dermal Toxicity

-

5.1.4 Acute Toxicity, other Routes

-

5.4 Repeated Dose Toxicity

-

5.5 Genetic Toxicity 'in Vitro'

-

5.6 Genetic Toxicity 'in Vivo'

-

5.8 Toxicity to Reproduction
-

5.9 Developmental Toxicity/Teratogenicity
-

6. References

(1) EPIWIN

I U C L I D

D a t a S e t

Existing Chemical	Substance ID: 68610-51-5
CAS No.	68610-51-5
EINECS Name	Phenol 4-methyl-, reaction products with dicyclopenadiene and isobutylene
EINECS No.	271-867-2
Molecular Formula	C10H12.C7H8O.C4H8

Producer Related Part

Company:	Goodyear Chemicals Europe
Creation date:	04-APR-98

Substance Related Part

Company:	Goodyear Chemicals Europe
Creation date:	04-APR-98

Printing date:	09-MAY-01
Revision date:	
Date of last Update:	**04-SEP-98**

Number of Pages: **34**

Chapter (profile):	Chapter: 1, 2, 3, 4, 5, 7
Reliability (profile):	Reliability: without reliability, 1, 2, 3, 4
Flags (profile):	Flags: without flag, confidential, non confidential, WGK (DE), TA-Luft (DE), Material Safety Dataset, Risk Assessment, Directive 67/548/EEC

1.0.1 OECD and Company Information

Type: lead organisation
Name: International Working Group on the Toxicology of Rubber Chemicals
Partner: Bayer AG **Date:** 06-APR-98
Town: D-51368 Leverkusen
Country: Germany

14-JUL-98

Partner: Goodyear Chemical Europe **Date:** 06-APR-98
Street: 14, Avenue Des Tropiques-Z.A. de courtaboeuf 2
Town: 91955 Les Ulis Cedex
Country: France

14-JUL-98

1.0.2 Location of Production Site

-

1.0.3 Identity of Recipients

-

1.1 General Substance Information

Substance type: organic
Physical status: solid
Purity: > 98 % w/w
Result: Molecular weight: 650
05-APR-98

1.1.1 Spectra

-

1.2 Synonyms

4-Methylphenol reaction products with dicyclopentadiene and isobutylene
06-APR-98

Butylated reaction product of p-cresol and dicyclopentadiene

04-APR-98

p-Cresol, dicyclopentadiene, isobutylene reaction products
06-APR-98

Polymeric hindered phenol
06-APR-98

SANTOWHITE ML
04-APR-98

VULKANOX SKF
04-APR-98

WINGSTAY L
04-APR-98

WINGSTAY L HLS
04-SEP-98

WINGSTAY LA
04-SEP-98

WTR Number 69
04-SEP-98

1.3 Impurities

-

1.4 Additives

-

1.5 Quantity

Production during the last 12 months:
Import during the last 12 months:
Quantity produced :
14-MAY-98

Production during the last 12 months:
Import during the last 12 months:

Quantity produced :
14-MAY-98

Production during the last 12 months:
Import during the last 12 months:
Quantity produced :
14-MAY-98

1.6.1 Labelling

Labelling: as in Directive 67/548/EEC
R-Phrases: (53) May cause long-term adverse effects in the aquatic environment

1.6.2 Classification

Classification: no classification required (no dangerous properties)
Class of danger:
R-Phrases:
04-APR-98

1.7 Use Pattern

Type: type
Category: Use resulting in inclusion into or onto matrix
04-APR-98

Type: industrial
Category: Polymers industry
04-APR-98

Type: use
Category: Stabilizers
04-APR-98

1.7.1 Technology Production/Use

-

1.8 Occupational Exposure Limit Values

-

1.9 Source of Exposure

-

1.10.1 Recommendations/Precautionary Measures

-

1.10.2 Emergency Measures

-

1.11 Packaging

-

1.12 Possib. of Rendering Subst. Harmless

-

1.13 Statements Concerning Waste

-

1.14.1 Water Pollution

-

1.14.2 Major Accident Hazards

-

1.14.3 Air Pollution

-

1.15 Additional Remarks

-

1.16 Last Literature Search

-

1.17 Reviews

-

1.18 Listings e.g. Chemical Inventories

Type: TSCA

20-AUG-98

Type: EINECS
Additional Info: EINECS Number 271-867-2

20-AUG-98

Type: DSL

20-AUG-98

Type: AICS

20-AUG-98

Type: ECL
Additional Info: ECL SERIAL Number 9206-699

20-AUG-98

Type: ENCS
Additional Info: ENCS Number 7-2034

20-AUG-98

2.1 Melting Point

Value: 115 degree C
Method: other: ASTM D-1519
Year: 1991
GLP: no data
Reliability: (2) valid with restrictions
Although this study was probably not conducted to GLP, the test parameters used were based on a known and well established procedure.

(21)

Value: 118.3 degree C
Method: OECD Guide-line 102 "Melting Point/Melting Range"
Year: 1997
GLP: yes
Reliability: (1) valid without restriction

(32)

2.2 Boiling Point

Value:
Method: other: Not relevant

2.3 Density

Type:
Value: 1.0736 g/cm3 at 20 degree C
Method: OECD Guide-line 109 "Density of Liquids and Solids"
Year: 1997
GLP: yes
Reliability: (1) valid without restriction

(32)

Type:
Value:
Method: other: ASTM D-891
Year: 1991
GLP: no data
Remark: Specific Gravity is 1.10
Reliability: (2) valid with restrictions
Although this study was probably not conducted to GLP, the test parameters used were based on a known and well established procedure.

(21)

2.3.1 Granulometry

Type of distribution:

Method: other: Not relevant

2.4 Vapour Pressure

Value: < .00000032 hPa at 25 degree C
Method: Directive 84/449/EEC, A.4 "Vapour pressure"
Year: 1997
GLP: yes
Result: Actual value was < 3.2x10-5 Pa
Reliability: (1) valid without restriction

(30)

2.5 Partition Coefficient

log Pow: 7.17 - 8.17 at 30 degree C
Method: OECD Guide-line 117 "Partition Coefficient (n-octanol/water), HPLC Method"
Year: 2000
GLP: yes
Method: The partition coefficient was estimated by the HPLC method using isocratic elution. The procedure conformed to those outlined in EC Directive 92/69/Annex V method A8 and OECD Guidelines 117 (1995). The HLPC system used: Detector-Jasco UV-875 set to 220 nm; Column-Spherisorb 5 um ODSB, 25x0.46 cm; Mobile phase-Acetonitrile/water, 90/10; Column temperature-30 degrees C. The dead time TO was measured using formamide as a non-retained solute (void volume marker). The HPLC column was calibrated for partition coefficient against retention time using calibration substancesa of known partition ceefficients dissolved in appropriate mobile phase. Duplicate estimations were performed for each series. The capacity factor, K, was calculated from the retention times using the following equation, where TR is retention time for the calibration substance: K= (TR-TO)/TO. The log of the capacity factor is plotted against the log of the partition coefficient to derive a calibration graph. The test substance was dissolved in mobile phase and the retention time recorded. The estimated partition coefficient was calculated from the calibration graph obtained using the calibration substances.
Result: The partition coefficient for the major components of WINGSTAY L-HLS was estimated by an HPLC procedure to be in the range from 7.17 to 8.17 with a 95% confidence limit in the range 5.86 to 13.10.
Reliability: (1) valid without restriction

(28)

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log Pow: > 10 at 25 degree C
Method: other (measured): Official Journal of the European Communities, L383 A-Part A.8

Year: 1995
GLP: no
Result: The Pow of WINGSTAY L-HLS at 25 degrees C was concluded to be greater than 10000.
Reliability: (2) valid with restrictions
Although the study was old and was not conducted to GLP, the test parameters were based on a scientifically sound procedure for that time period and the study was properly conducted.

(26)

2.6.1 Water Solubility

Value: < .2 other: ug/ml at 20 degree C
Method: Directive 84/449/EEC, A.6 "Water solubility"
Year: 1997
GLP: yes
Reliability: (1) valid without restriction

(31)

2.6.2 Surface Tension

Method: other: Not relevant

2.7 Flash Point

Value:
Type:
Method: other: Not relevant
Year:

2.8 Auto Flammability

Value:
Method: other: Not relevant

2.9 Flammability

Result: non flammable
Method: Directive 84/449/EEC, A.10 "Flammability (solids)"
Year: 1997
GLP: yes
Reliability: (1) valid without restriction

(32)

2.10 Explosive Properties

Result:
Method: other: Not relevant

2.11 Oxidizing Properties

Result:
Method: other: Not relevant

2.12 Additional Remarks

Memo: Not relevant

3.1.1 Photodegradation

Type:
Method: other (calculated): Not relevant
Year: **GLP:**
Test substance:

3.1.2 Stability in Water

Type:
Method: other: the test substance is essentially insoluble in water.
Year: **GLP:**
Test substance:

3.1.3 Stability in Soil

-

3.2 Monitoring Data (Environment)

-

3.3.1 Transport between Environmental Compartments

-

3.3.2 Distribution

-

3.4 Mode of Degradation in Actual Use

Memo: Not relevant

3.5 Biodegradation

Type:
Inoculum:
Result: other: Under conditions of study, not inherently biodegradable
Method: other: OECD Guide-line 301B and OECD Guide-line 302B
Year: 1998 **GLP:** yes
Test substance: as prescribed by 1.1 - 1.4
Reliability: (1) valid without restriction

3.6 BOD5, COD or BOD5/COD Ratio

B O D 5

Method: other
Year: **GLP:** no
BOD5: 2200 mgO2/l

C O D

Method: other
Year: **GLP:** no
COD: .92 mg/g substance

Remark: The COD was on the water soluble portion
TOC was 33.4 mg/l on the preparation and 9.5 mg/l on the same preparation after filtration on cellulose acatate (0.2 microns)
Reliability: (2) valid with restrictions
Although this study was probably not conducted to GLP, the test parameters used were based on a known and well established procedure.

(19)

3.7 Bioaccumulation

-

3.8 Additional Remarks

-

AQUATIC ORGANISMS

4.1 Acute/Prolonged Toxicity to Fish

Type: semistatic
Species: Oncorhynchus mykiss (Fish, fresh water)
Exposure period: 96 hour(s)
Unit: mg/l **Analytical monitoring:** yes
NOEC: .2
LC50: > .2
Method: OECD Guide-line 204 "Fish, Prolonged Toxicity Test: 14-day Study"
Year: 1998 **GLP:** yes
Test substance: as prescribed by 1.1 - 1.4
Method: Prior to the test initation, a 20 mg/mL stock solution was prepared by adding the test substance directly to methanol. The solution was further diluted with methanol to prepare a 2 mg/mL stock solution. The 2 mg/mL stock solution was added to dilution water to provide a nominal concentration of 0.2 mg/L. The identical procedure was used to prepare fresh test solutions at 24 hour intervals. Throughout the test, all test media were clear, colorless solutions.

The toxicity test was conducted in 15 Liter aquaria, each of which contained 14 L of test solution. One test aquarium was maintained for the treatment level (0.2 mg/L, the solubility limit of the test substance in water) and for the two controls, one containing methanol (0.01%) at the same concentration as the test medium and one containing dilution water only.

The 96-hour semistatic limit toxicity test was carried out with renewal of the test media at 24 hour intervals. The test vessels were covered with perspex lids during the study. Seven (7) Oncorhynchus mykiss (trout) (mean for fork length of 5.6 cm and mean weight of 1.894 grams) were placed

in each of the test vessels at the start of the study. The fish were not fed during the study. The vessels were aerated during the study.

Remark: The solubility limit of the test substance was 0.2 mg/L in water

Result: Samples of the freshly prepared stock solution were analysed for the test substance after preparation. No analysis of the 0.2 mg/L test medium was possible. The mean measured concentrations of the test substance in 20 and 2 mg/mL methanol stock solutions were 18.524 and 2.021 mg/mL (representing 93 and 101% of nominal cocentrations). There were no mortalities in any fish exposed to the test substance throughout the duration of the study. The 24-, 48-, 72- and 96-hours LC50 values of the test substance to Oncorhynchus mykiss (Trout) were observed to be > 0.2 mg/L (the highest nominal concentration tested). The highest concentration causing no mortality was 0.2 mg/L.

Reliability: (1) valid without restriction

(25)

4.2 Acute Toxicity to Aquatic Invertebrates

Species: Daphnia magna (Crustacea)
Exposure period: 48 hour(s)
Unit: mg/l **Analytical monitoring:** no
NOEC: .2
EC50: > .2
Method: OECD Guide-line 202, part 1 "Daphnia sp., Acute Immobilisation Test"
Year: 1998 **GLP:** yes
Test substance: as prescribed by 1.1 - 1.4
Method: The toxicity test was conducted in 150 mL glass crystallizing dishes, each of which contained 100 mL of the exposure solution. Four replicate test vessels were established for each treatment level and the dilution water and methanol controls. A stock solution was prepared by direct addition of the test substance to methanol to provide a nominal concentration of 20 mg/mL then further diluted with methanol to prepare a stock solution of 2.0 mg/mL. The 2 mg/mL stock solution was added to dilution water to provide a nominal concentration of 0.2 mg/L. Two control treatments were prepared, one containing methanol (0.01%) at the same concentration as the test medium and one containing dilution water only. An identical procedure was used to prepare fresh test media after 24 hours.

The 48-hour limit semistatic toxicity test was carried out with renewal of the test medium after 24 hours. Aliquots of 100 mL of the test medium were added to four replicate test vessels at a nominal exposure concentration of 0.2 mg/L. The 0.2 mg/L test medium was clear and colorless at the start and end of each exposure period.

Remark: The solubility limit of the test substance was 0.2 mg/L in water

Result: The combined limit and range-finding test resulted in no immobility to the Daphnia magna exposed to the 0.2 mg/L (the solubility limit of the test substance in water) treatment level for 48 hours.

Reliability: (1) valid without restriction

(24)

4.3 Toxicity to Aquatic Plants e.g. Algae

Species: Selenastrum capricornutum (Algae)
Endpoint: growth rate
Exposure period: 72 hour(s)
Unit: mg/l **Analytical monitoring:** yes
NOEC: .2
EC50: > .2
Method: OECD Guide-line 201 "Algae, Growth Inhibition Test"
Year: 1998 **GLP:** yes
Test substance: as prescribed by 1.1 - 1.4
Method: Prior to test initiation, a 20 mg/mL stock solution was prepared by adding the test substance directly to methanol, then it was further diluted with methanol to prepare a stock solution of 2 mg/mL. The 2.0 mg/mL stock solution was added to nutrient medium to provide a nominal concentration of 0.2 mg/L (the solubility limit of the test substance in water). The treatment level for this study was 0.2 mg/L. Two control treatments were prepared, one containing methanol (0.01%) at the same concentration as the test medium and one containing

growth medium only.

The test vessels were 250-mL Erlenmeyer glass flasks. Test substance treatment aliquots (100 mL), prepared as described above, were added to five (5) Erlenmeyer flasks. Eight (8) flasks were prepared containing the methanol control medium and four (4) flasks were prepared containing the growth medium only. Two (2) of the four (4) growth medium control flasks, three (3) of the five (5) test substance flasks and six (6) of the eight (8) methanol control flasks were inoculated with sufficient Selenastrum capricornutum to achive a nominal cell concentration of 10,000 cells/mL. The remaining flasks were used for determining water quality and background electronic count.

The flasks were loosely capped and incubated in a cooled orbital incubator under constant illumination.

Remark: The solubility limit of the test substance was 0.2 mg/L in water

Result: Samples of freshly prepared stock solutions were analysed after preparation, no analysis of the 0.2 mg/L test medium was possible. The mean measured concentrations of the test substance in 20 and 2 mg/L methanol stock solutions were 18.552 and 1.882 mg/L (representing 93 and 94 % of nominal concentrations).

The pH of the test media increased by more than 1.5 units in some of the control and test vessels. Growth of the control cultures was greater than a factor of 16 over the 72-hours test period, demonstrating that the environmental conditions were acceptable for the study. The growth rate of the algae exposed to the test substance was comparable to the algae exposed to the negative controls. Based on the areas under the growth curves and the average specific growth rate, the

0- to 72-hours EC50 were observed to be > 0.2 mg/L, the highest concentration tested. The highest NOEC of the test substance was establisned to be 0.2 mg/L for this study.

Reliability: (1) valid without restriction

(27)

4.4 Toxicity to Microorganisms e.g. Bacteria

-

4.5 Chronic Toxicity to Aquatic Organisms

4.5.1 Chronic Toxicity to Fish

-

4.5.2 Chronic Toxicity to Aquatic Invertebrates

-

TERRESTRIAL ORGANISMS

4.6.1 Toxicity to Soil Dwelling Organisms

-

4.6.2 Toxicity to Terrestrial Plants

-

4.6.3 Toxicity to other Non-Mamm. Terrestrial Species

-

4.7 Biological Effects Monitoring

-

4.8 Biotransformation and Kinetics

-

4.9 Additional Remarks

-

5.1 Acute Toxicity

5.1.1 Acute Oral Toxicity

Type: LD50
Species: rat
Sex:

Number of Animals:
Vehicle:
Value: > 16000 mg/kg bw
Method: other
Year: 1964 **GLP:** no
Test substance: as prescribed by 1.1 - 1.4
Remark: Animals fed single doses exhibited no clinical signs of toxicity during a two week observation period
Reliability: (4) not assignable
Data from original report not available. However, information may be useful for information purposes.
(5)

Type: LD50
Species: rat
Sex: male/female
Number of Animals: 10
Vehicle: other: corn oil
Value: > 200 mg/kg bw
Method: other: United States Department of Transportation Regulations, 49CFR173.132(1992)
Year: 1993 **GLP:** yes
Test substance: as prescribed by 1.1 - 1.4
Reliability: (1) valid without restriction
(16)

Type: LD50
Species: rat
Sex: male/female
Number of Animals:
Vehicle:
Value: > 5010 mg/kg bw
Method: other: No data
Year: 1986 **GLP:** yes
Test substance: as prescribed by 1.1 - 1.4
Remark: 5 males and 5 females/per dose level
Reliability: (1) valid without restriction
(12)

Type: LD50

Species: rat
Sex: male/female
Number of Animals: 10
Vehicle: other: corn oil
Value: > 5000 mg/kg bw
Method: OECD Guide-line 401 "Acute Oral Toxicity"
Year: 2000 **GLP:** yes
Test substance: as prescribed by 1.1 - 1.4
Method: A group of ten Spraque-Dawley rats (5 males and 5 females) were administered the test substance via gavage (corn oil) in a single oral dose at 5000 mg/kg. Clinical observations were recorded at 1 and 4 hours post dose (+ or - 15 minutes) and daily thereafter through day 15. Body weights were recorded on Day 1 (fasted), Day 8 and Day 15. At study termination, the animals were subjected to a gross necropsy.
Result: All animals survived the 15 day testing/observation period. Soft feces and/or poor grooming were observed in some animals on Day 1 through 3. No other clinical signs were observed. All animals exhibited increases in bodyweight throughout the study. Mottled kidneys were observed in one male at terminal necropsy. No other vivible lesions were observed in any other animals at necropsy.
Reliability: (1) valid without restriction

(2)

5.1.2 Acute Inhalation Toxicity

Type: LC50
Species: rat
Sex:
Number of Animals: 10
Vehicle:
Exposure time: 1 hour(s)
Value: > 165 mg/l
Method: other: United States CFR Title 16, Federal Hazardous Labeling Act, Part 1500.4 (1975)
Year: 1975 **GLP:** no
Test substance: as prescribed by 1.1 - 1.4
Method: 10 male albino rats, initially weighing between 214 and 239 grams were exposed under dynamic conditions in a 38-liter glass inhalation chamber for one hour to an approximate 200 mg/liter concentration of the test material. Exposure to the test substance was accomplished through the use of a pulse-puff generator through which a constant airflow of 10 liters per minute was passed into the chamber. Total airflow through the chamber was 10 liters/minute. The nominal concentration was determined from the ratio of the total quantity (mg) of the test material aerosolized in one hour to the total airflow (liters) through the chamber during that hour. The animals were observed for pharmacotoxic

manifestations and mortality during the exposure and during the 14-day post exposure observation period.

Remark: Exposure for one-hour to a nominal concentration of 165 mg of the test substance/liter of air (18.4 % percent under the desired 200 mg/liter) was not lethal to rats. At the end of the 14 day observation period, no animals had died.

Result: At the beginning of the exposure, all rats were hyperactive and several rats were preening and appeared to be coughing or sneezing. This condition was followed by nasal discharge in several rats. After 35 minutes of exposure, the fur of all the rats was covered with the test substance. After 40 minutes, the rats could not be observed due to the density of the aerosol achieved. Upon removal from the exposure chamber, all rats exhibited a slight nasal discharge and their fur was saturated with the test substance. No deaths occured. On Day 1 post exposure, all rats were hyperactive and exhibited a red nasal discharge. On Day 2 post exposure, several rats exhibited a red crusty exudate and hair loss around the eyes and nose. At the end of the 14-day observation period, several rats still exhibited a slight red exudate and hair loss around the eyes and nose. No animals died.

Reliability: (2) valid with restrictions
Although the study was old and was probably not conducted to GLP, the test parameters were based on an estblished procedure for that time period and was conducted by a well known laboratory.

(6)

5.1.3 Acute Dermal Toxicity

Type: LD50
Species: rabbit
Sex: male/female
Number of Animals:
Vehicle:
Value: > 5010 mg/kg bw
Method: other: No data
Year: 1986 **GLP:** yes
Test substance: as prescribed by 1.1 - 1.4
Remark: Method: 2 male/2 female/per dose level
Reliability: (1) valid without restriction

(11)

5.1.4 Acute Toxicity, other Routes

-

5.2 Corrosiveness and Irritation

5.2.1 Skin Irritation

Species: rabbit
Concentration: .5 other: grams

Exposure: Occlusive
Exposure Time: 24 hour(s)
Number of Animals: 6
PDII:
Result: not irritating
EC classificat.: not irritating
Method: other: United States Federal Hazardous Substances Act, 16CFR1500.41 (1974)
Year: 1974 **GLP:** no
Test substance: as prescribed by 1.1 - 1.4
Method: A single 24-hour dermal application of 0.5 grams of the test substance was applied to clipped and premoistened intact and abraded skin sites on the back of six (6) New Zealand White rabbits. The areas were covered with one-inch square gause patches. The rabbits were immobilized in restrainers and their trunks were wrapped in nonabsorbent binders for the 24-hour exposure period. Observations were made at 24 and 72 hours.
Remark: Did not produce primary skin irritation in a standard assay conducted with New Zealand White rabbits.
The primary irritation score was 0.25.
Reliability: (2) valid with restrictions
Although the study was old and was probably not conducted to GLP, the test parameters were based on an estblished procedure for that time period and was conducted by a well known laboratory.

(9)

Species: rabbit
Concentration: .5 other: grams

Exposure: Occlusive
Exposure Time: 4 hour(s)
Number of Animals: 6
PDII:
Result: not irritating
EC classificat.: not irritating
Method: other: United States EPA

Year: 1986 **GLP:** yes
Test substance: as prescribed by 1.1 - 1.4
Remark: Method: United States Environmental Protection Agency-0.5 gm applied to intact skin for 4 hours to 6 albino rabbits. Score: 0.0/8.0
Reliability: (1) valid without restriction

(14)

Species: rabbit
Concentration: 500 other: mg/site

Exposure: Occlusive
Exposure Time: 4 hour(s)
Number of Animals: 6
PDII:
Result: slightly irritating
EC classificat.: not irritating
Method: Draize Test
Year: 2000 **GLP:** yes
Test substance: as prescribed by 1.1 - 1.4
Method: The test substance (at 500 mg/site) was applied to each of three sites on the clipped dorsal trunk of six (6) New Zealand White rabbits (3 male and 3 female). The upper dorsal sites were exposed to the test article for 3- and 60-minutes. The exposure period for the mid dorsal site was 4-hours. Observations for dermal irritation were recorded immediately after patch removal and daily throuh Day 15 for the 3-minute and 60-minute exposure sites. The 3-minute site was also scored at 60-minutes after patch removal. Observations of the 4-hour exposure sites were recorded immediately , 24, 48 and 72 hours after patch removal and daily thereafter. Grading of irritation was according to the Draize method.
Result: Rabbit sites in the 3-minute exposure group showed no erythema and no edema. Rabbit sites in the 60-minute exposure group showed very slight erythema and no edema. Rabbit sites in the 4-hour exposure group showed very slight erythema and no edema. The Primary Irritation Index (4-hour exposure) was calculated to be 0.2.
Reliability: (1) valid without restriction

(15)

5.2.2 Eye Irritation

Species: rabbit
Concentration: .1 other: grams

Dose:
Exposure Time: 24 hour(s)
Comment:
Number of Animals: 6
Result: slightly irritating
EC classificat.: not irritating
Method: other: United States EPA
Year: 1986 **GLP:** yes
Test substance: as prescribed by 1.1 - 1.4
Remark: Method: United States Environmental Protection Agency-0.1 gm applied for 24 hours to 6 albino rabbits. Score: 1.3/110
Reliability: (1) valid without restriction

(13)

5.3 Sensitization

Type:	Guinea pig maximization test			
Species:	guinea pig			
Concentration:	Induction	5	% active substance	intracutaneous
	Induction	25	% active substance	occlusive epicutaneous
	Challenge	5	% active substance	occlusive epicutaneous

Number of Animals: 36
Vehicle:
Result: sensitizing
Classification: sensitizing
Method: OECD Guide-line 406 "Skin Sensitization"
Year: 2000 **GLP:** yes
Test substance: as prescribed by 1.1 - 1.4
Method: For the intradermal induction phase of the study, the vehicle control and test article groups (10 animals/sex/group) and a positive control group (3 animals/sex) were administered intradermal injections (0.1 ml each) at three (3) clipped sites between the shoulders of each guinea pig. One week later, the injection sites were reclipped.

For the topical induction phase, the test sites were occluded with 25 % of the test substance for 48-hours. The vehicle control and positive control groups were topically induced in the same manner with 100% petrolatum or 0.1% DNCB in petrolatum, respectively.

Two weeks after the topical induction, all test article and

vehicle control animals were dermally challenged with occluded patches of 5% test substance in petrolatum on the left flank and 100 % petrolatum on the right flank. After 24-hours, the sites were unwrapped and cleaned. Challenged sites were graded for skin reactions at 24- and 48-hours after unwrapping. Positive control animals were challenged in the same manner with 0.01% DNCB in petrolatum on the left flank and 0.05% DNCB on the right flank.

Based upon the results of the primary challenge, the animals in the test article groups were rechallenged six (6) days later with the test substance at 5% (w/v).

Result: The test substance demonstrated a potential to produce mild dermal sensitization when administered to Hartley guina pigs. Based on the observations made in the study, the test substance intradermally induced at 5% and topically induced at 25 % did elicit a mild sensitization response (Grade II) when challenged and rechallenged at 5% of the test substance.

Reliability: (1) valid without restriction

(18)

5.4 Repeated Dose Toxicity

Species: rat **Sex:** male/female
Strain: other: Cr/CD BR Rat
Route of admin.: oral feed
Exposure period: 28 day
Frequency of treatment: daily
Post. obs. period:
Doses: 0,1000,5000,10000,25000, or 50000 ppm in the diet
Control Group: yes, concurrent no treatment
NOAEL: 1000 ppm
LOAEL: 5000 ppm
Method: other
Year: 1989 **GLP:** yes
Test substance: as prescribed by 1.1 - 1.4
Remark: In the 25,000 and 50,000 ppm groups, treatment was discontinued due to severe systemic toxicity after 10 days of exposure. During the first week of test materials administration, 1/5 males and 0/5 females died at 25,000 ppm and 2/5 males and 1/5 females died at 50,000 ppm. Observations included decreased body weight and food consumption. Internal hemorrhaging was observed at necropsy.
No animals in the 1,000 and 5,000 ppm dose level groups died.

In the 10,000 ppm group, one (1) male and one (1) female died during the treatment period. Internal hemorrhage was observed in these animals. Higher prothrombin and activated partial thromoplastin times were observed in a dose-related manner in males at 5,000 and 10,000 ppm. Mean liver weights relative to final body weights were significantly increased in the 5,000 and 10,000 ppm group females compared to those of the controls. No microscopic evaluation of tissues was done in this dose-range finding study.

Result: Based on the data from this study, dose levels of 500, 1,500 and 4,500 ppm were selected for evaluation in a definitive 90-day dietary study.

Reliability: (2) valid with restrictions
This study was not intended to be a guideline study. It was designed to be a dose-range finding study for the 90-day feeding study and gave useful data for dose selection.

(22)

Species: rat **Sex:** male/female
Strain: other: CrL/CD BR Rat
Route of admin.: oral feed
Exposure period: 90 days
Frequency of treatment: daily
Post. obs. period:
Doses: 0, 500, 1500, or 4500 ppm in diet
Control Group: yes, concurrent no treatment
NOAEL: 500 ppm
LOAEL: 1500 ppm
Method: OECD Guide-line 408 "Subchronic Oral Toxicity - Rodent: 90-day Study"
Year: 1989 **GLP:** yes
Test substance: as prescribed by 1.1 - 1.4
Method: Test material was added to the diets of 15 male and 15

female rats at 0, 500, 1500 or 4500 ppm test material for 90 days. Animals were observed for body weight gains, food consumption, blood effects. clinical changes, ophthalmic lesions and gross/microscopic pathology.

Result: No test chemical effects on survival body weights, food consumption (except week-1 females likely due to poor palatability) or clinical obervations were seen. Likewise, no changes were seen in 10 hematological parameters except for increases in protimes and partial thrombo-plastin times in high dose males (slight decrease protime-females). Leukocytes counts and differentials were unaffected as were 18 serum chemistry parameters except for elevated cholesterol (high dose females). No eye changes were seen. Liver weights of both genders were significantly increased in the high dose groups without evidence of microscopic changes, and non significant increases in mid-dose groups. Female adrenal weights were slightly increased at the mid-dose and significantly increased at the high dose while testes weights were decreased in the high dose groups, all without associated microscopic pathology.

Reliability: (1) valid without restriction

(23)

5.5 Genetic Toxicity 'in Vitro'

Type: Ames test
System of testing: Salmonella typhimurium TA-98, 100, 1535, 1537, and 1538 (In triplicate)
Concentration: 50, 167, 500, 1670, 5000 ug/plate
Metabolic activation: with and without
Result: negative

Method: other
Year: 1986 **GLP:** yes
Test substance: as prescribed by 1.1 - 1.4
Reliability: (1) valid without restriction

(10)

Type: Cytogenetic assay
System of testing: Chromosomal Aberrations Assay in CHO Cells
Concentration: Nonactivation-25 and 50 micrograms/ml of test article solution in 10 hour aberrations assay with 50 and 300 micrograms in 20 hour aberrations. Activation-100 to 1000 micrograms/ml in 10 and 20 hour aberrations.
Metabolic activation: with and without
Result: negative
Method: other
Year: 1991 **GLP:** yes
Test substance: as prescribed by 1.1 - 1.4
Method: Target concentrations of 0.0333ug/ml to 1000 ug/ml in half-log series were tested in range finding assays with and without metabolic activation. Total cellular toxicity was observed in the culture dosed with 1010 ug/ml and severe cell cycle delay was evident in the cultures dosed with 101 and 337 ug/ml in the range finding assay without metabolic activation. Also, severe reduction in the mititic index were observed in cultures dosed with 99.7, 332 and 997 ug/ml. No cell cycle delays or signicant reductions in mitotic index were evident in cultures with metabolic activation. Based on these results, replicate cultures of CHO cells were incubated with target concentrations of 25 and 50 ug/ml of the test substance in a 10-hour aberrations assay and with 50 and 300 ug/ml of the test substance in a 20-hour aberrations assay for the nonactivated conditions. Target concentrations of 100 to 1000 ug/ml were tested in 10- and 20-hour aberrations assays with metabolic activation.
Remark: No significant increase in cells with chromosomal aberrations were observed at the concentrations analyzed.
Result: The test substance was considered negative for inducing chromosomal aberrations in Chinese hamster ovary cells under both nonactivation and activation conditions.
Test substance: The test substance was dissolved in dimethyl sulfoxide.
Reliability: (1) valid without restriction

(8)

Type: DNA damage and repair assay
System of testing: E. coli Pol A+ and Pol A1- Assay
Concentration: 10, 100, 320, 1000 micrograms/liter

Metabolic activation: with and without
Result: negative
Method: other
Year: 1980 **GLP:** no
Test substance: as prescribed by 1.1 - 1.4
Method: The DNA Damage Study in E. coli was conducted following The Goodyear Tire & Rubber Company's, Health, Safety and Government Compliance Test Method 79-11.

Cultures of Escherichia coli strains W 3110 (pol A+) and p 3478 (pol A1-) were cultured overnight and diluted to a practical density of approximately 2000 cells/ml. Replicate 100 ul aliquots of these diluted cultures were distributed into separate sterile tubes. Each tube then received 10 ul of diluted test chemical or solvent. For metabolic activation assays, 50 ul aliquots of S-9 microsomal preparation were added to each applicable tube. The suspensions were incubated for one hour (activation assays) and two hours (non-activation assays) at 37 degrees C. Results were expressed as the Survival Index which is the % of Pol A1- survivors/plate as compared to its negative control divided by the % of Pol A+ survivors/plate as compared to its negative control.

Remark: A test for the ability of the chemical to damage cellular DNA in the E. coli POL A1- Assay.
Result: The test substance was negative in the E coli. Pol A1- Assay for DNA damage.
Reliability: (2) valid with restrictions
Although the study was old and was not conducted to GLP, the test parameters were based on a scientifically sound procedure for that time period and the study was properly conducted.

(20)

Type: HGPRT assay
System of testing: CHO/HGPRT Forward Mutation Assay
Concentration: Six dose levels from 100-1000 micrograms/liter
Metabolic activation: with and without
Result: negative
Method: other
Year: 1991 **GLP:** yes
Test substance: as prescribed by 1.1 - 1.4
Method: The test substance was determined to be soluble in DMSO up to 392 mg/ml. Dilution stocks of the test substance were prepared using DMSO. Treatment media were prepared by making 1:100 dilutions of dilution stocks into F12 tissue culture medium. Preliminary cytotoxicity testing showed the

test substance to be moderately toxic to CHO cells up to 1000 ug/ml without activation and weakly toxic in the presence of S9 metabolic activation test conditions. In the activation and nonactivation assays, six dose levels were used that included treatments from 100-1000 ug/ml.

Remark: The substance was considered negative for inducing forward mutations at the HGPRT locus in CHO cells under both nonactivation and activation conditions.

Result: The test substance was moderately toxic without activation at the higher dose levels and demonstrated weak toxicity with activation at all dose levels. The mutant frequenices of treated cultures varied randomly with dose within the range acceptable for background mutant frequencies which were 0 to 15 10-6.

Reliability: (1) valid without restriction

(7)

Type: other: Salmonella typhimurium/Escherichia coli Preincubation Assay

System of testing: Salmonella typhimurium/Escherichia coli Plate Incorporation/Preincubation Mutation Assay

Concentration: 100, 250, 500, 750, and 1000 micrograms/plate

Metabolic activation: with and without

Result: negative

Method: other

Year: 1995 **GLP:** yes

Test substance: as prescribed by 1.1 - 1.4

Method: The test substance was determined to be soluble in DMSO up to 0.5 mg/ml. Dilution stocks were prepared using DMSO and the test substance was tested at 5, 10, 50, 100, 500, 1000 and 5000 ug/plate in the range finding test. There was heavy precipitation in the 5000 ug plates and slight precipitation in the 1000 ug plates. Based on the range finding test, the first mutation assay was performed at the test substance concentrations of 100, 250, 500, 750 and 1000 ug/plate with and without S-9 activation.

Remark: All strains treated with the material exhibited a mean reversion frequency that was similar to the corresponding solvent control, and there was no evidence of a dose-response relationship. A preincubation assay was performed using the same doses as the first assay. The results of the confirmatory assay agreed with the first assay results.

Result: The test substance was considered negative for inducing reverse mutations in the Salmonella typhimurium/Escherichia coli Plate Incorporation/Preincubation Mutation Assay under both nonactivation and activation conditions.

Reliability: (1) valid without restriction

(17)

5.6 Genetic Toxicity 'in Vivo'

-

5.7 Carcinogenicity

-

5.8 Toxicity to Reproduction

-

5.9 Developmental Toxicity/Teratogenicity

Species: rat **Sex:** female
Strain: Sprague-Dawley
Route of admin.: gavage
Exposure period: 14 days (on gestational days 6 through 19)
Frequency of treatment: Daily
Duration of test: 20 days
Doses: 0, 1000, 2000 or 3000 mg/kg/day
Control Group: yes, concurrent vehicle
NOAEL Maternalt.: 1000 mg/kg bw
NOAEL Teratogen.: < 1000 mg/kg bw
Method: OECD Guide-line 414 "Teratogenicity"
Year: 1998 **GLP:** yes
Test substance: as prescribed by 1.1 - 1.4
Method: Timed-pregnant CD (Spraque-Dawley) rats were exposed to the test substance dissolved in corn oil and administered by oral gavage, once daily, on gestational days 6 through 19 at doses of 0, 1000, 2000, or 3000 mg/kg/day. The dosing volume was 10 ml/kg. The volume was adjusted based on each animal's most recent body weight.

There were 25 sperm-positive females per each group. Clinical observations were taken daily, except during the dosing period when they were made at least twice daily. At scheduled sacrifice on gestation day 20, the dams were evaluated for body, liver and gravid uterine weights. Ovarian corpora lutea were counted and fetuses were dissected from the uterus, counted, weighed, sexed and examined for external abnormalities. Approximately one half of the live fetuses in each litter were examined for visceral malformations and variations. These fetuses were decapitated and the heads fixed in Bouin's solution. Intact fetuses were examined for skeletal malformations and variations.
Remark: All fetal malformation and variation findings in this study were those commonly observed in historical control CD rat fetuses in the performing laboratory and in published control databases.

The material was placed in corn oil and administered via gavage at dosages of 0,1000, 2000 and 3000 mg/kg/day. There

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were 25 sperm positive female rats in each test group.

Result: Pregnancy rates were high and equivalent across all groups. Four (4) females were not pregnant. No dams died, aborted or delivered early. One (1) female was removed from the study due to intubation (dosing) errors. All pregnant animals had one (1) or more live fetuses at sacrifice.

Maternal body weights were equivalent across all groups for all time points examined. Maternal weight gain was significantly reduced in the 3000 mg/kg/day group for gestational days 6-9. Maternal absolute and relative liver weights were significantly increased at all doses. There were no specific treatment-related clinical signs.Maternal feed consumption was reduced in the 3000 mg/kg/day group for gestational days 6-9 and significantly increased for gestational days 18-20. There were no treatment-related effects on any gestational parameters.

There were no treatment-related statistically or biologically significant changes in the incidence of pooled external, visceral, skeletal or total fetal malformations in this study. Percent fetuses with variations per litter was significantly increased at all doses, when sexes were combined, due to treatment-related increases in the incidence of two (2) common fetal skeletal variations; rudimentary rib on lumbar 1 (bilateral, right or left) and reduced ossification in the thoracic centra (normal cartilage, bipartite ossification center and dumbbell cartilage, bipartite ossification center). The number of fetuses (and litters) with skeletal variations were 34 (18) at 0 mg/kg/day, 65 (20) at 1000 mg/kg/day, 72 (22) at 2000 mg/kg/day and 94 (25) at 3000 mg/kg/day. The consequences, if any, of these findings are not known, especially in the absence of any effects on the fetal body weight, an usually very sensitive indicator of developmental toxicity.

The test substance administered by gavage during major organogenesis in CD (Spraque-Dawlwy) rats resulted in no indication of teratogenicity, but did result in increased incidences of common fetal skeletal variations at 1000, 2000 and 3000 mg/kg/day in the absence of any other indicators of developmental toxicity. The NOAEL for maternal toxicity was 1000 mg/kg/day and the NOAEL for developmental toxicity was at or below 1000 mg/kg/day in rats.

Reliability: (1) valid without restriction

(4)

5.10 Other Relevant Information

Type: other: Absorption, Distribution and Excretion
Method: OECD Guide-line 417

The study was designed following OECD Guidelines for Testing of Chemicals: No. 417, April 1984 and ECETOC, Technical Report No. 46, May 1992. This study was conducted in compliance with Good Laboratory Practices (GLP) following OECD and Swiss Guidelines.

The effective average doses administered were 29.3 mg/kg for the males and 29.9 mg/kg for the females. The specific radioactivity and the concentration of the administration solution were determined by liquid scintillation counting (LSC) to be 3.87 uCi/mg (0.14 MBq/mg) and 3.01 mg/ml, respectively.

Prior to administering the dose by gavage, the rats were fasted overnight. Four males and 4 female BRL-HAN, Wister rats that were 6-8 weeks old were used for the study. Levels of radioactivity in urine and feces were followed for 168 hours after a single oral administration. Additionally, at sacrifice (168 hours after administration) the residual radioactivity in the blood, plasma and organs/tissues (gastro-intestional tract, liver, kidney, adrenal gland, epididymes, ovaries, eyes, bone, brain, lung, muscle, spleen, thyroid gland, other tissues/organs and carcass) was determined.

Remark: The majority of the WINGSTAY L was not absorbed and passes through the gastrointestinal tract. Within 48 hours of dosing, approximately 90% of the dose was excreted in the feces.

Very small amounts were absorbed and excreted in the urine. Excreted in the urine was 0.1% to 0.2% of the administered dose over the seven (7) day period.

The low level of additional excretion in the feces 48 hours after dosing suggests that part of the absorbed dose may be excreted in the bile.

Small percentage is retained in the body seven (7) days after a single dose. Only 1.5% to 2.4% of the radioactivity remained in the tissue, As expected, the highest concentration (ug-eq WINGSTAY L/g of tissue) of the radiolabeled material was in the fat.

Result: Total mean radioactivity recovered was males: 94.02 = or - 1.14% and females: 96.34 + or - 3.42%.

The total amount of radioactivity recovered in feces at 168 hours was 91.90 + or - 1,41% of the radioactivity administered in the males and 93.32 + or - 3.31% in the females. The majority was accounted for within 48 hours

(males: 90.05 + or - 1.21%, females: 90.43 + or - 2.35%), indicating tht WINGSTAY L was poorly absorbed.

Excretion via urine was very low, in total amounting to only 0.1 + or - 0.07% in the males and 0.20 + or - 0,12% in the females. Radioactivity was mainly excreted within the first 48 hours after administration, representing on average 0.0 + or - 0.07% of the radioactivity administered in the males and 0.16 + or - 0.11% in the females.

The total excreted radioactivity (total from feces, urine and cage waste) amounted to 92.50 + or - 0.79% in the males and to 93.94 + or - 3.2% in the females.

14C-WINGSTAY L was rapidly eliminated from the body. During the first 48 hours an average of 90% of the administered dose was excreted via the feces. An additional 1.9 70 2.9% was excreted in feces over the next 5 days. 0.1 to 0.2 % of the administered dose was excreted via urine over 7 days while 1.5 to 2.4% was recovered in rat tissues at end of 7 days.

Reliability: (1) valid without restriction

(1)

Type: other: Benchmark Dose (BMD) for "Developmental Toxicity"

Method: Reference Study: "Developmental Toxicity Evaluation with WINGSTAY L Administered by Gavage to CD (Sprague-Dawley) Rats", Research Triangle Institute Study Number 65C-6503-600/300/700 (Final Report April 13, 1998).

The developmental study concluded that WINGSTAY L was not

teratogenic, but that there was a test article related increase in the incidence of common fetal skeletal variations. A NOAEL for this observation was not established experimentally. The purpose of this project was to estimate the NOAEL for this fetal effect using the benchmark dose modeling.

The dose-response modeling was performed using U.S. EPA Benchmark Dose (BMD) software (Version 1.2). The Nested Logistic Dose-Response Model was used to calculate the BMD. The model estimated the Benchmark Response (BMR) at the 5% effect level (ED05) and its lower confidence limit (LED05).

Result: The BMD at the ED05 was determined to be 740 mg/kg/day for common fetal variations. The 95% lower confidence limit for the ED05 was 530 mg/kg/day.

For the developmental study in rats with WINGSTAY L, the BMD at the ED05 was estimated to be 740 mg/kg/day for the common fetal variations.

Reliability: (1) valid without restriction

(3)

5.11 Experience with Human Exposure

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(1) 14C-WINGSTAY L: Absorption, Distribution, and Excretion after Single Oral Administration to Rats, Report #: 756145, RCC Ltd., 5/4/00

(2) Acute Oral Exposure Toxicity Study (LD50) in Rats Using WINGSTAY L as the Test Chemical, Report Number:0402XG05.002, Chrysalis Labs, 2000

(3) Benchmark Dose (BMD) Calculations for "Developmental Toxicity Evaluation with WINGSTAY L Administered by Gavage to CD (Sprgue-Dawley) Rtas", Research Triangle Institute Study Number 65C-6503-600/300/700 (Final Report April 13, 1998), The Sapphire Group, 5/4/2000

(4) Developmental Toxicity Evaluation of Wingstay L Administered by Gavage to CD (R) Sprague-Dawley Rats, Report # 65C-6503-600/300/700, Research Triangle Institute, April 13, 1998

(5) Food and Drug Research Laboratories, Inc., Approximate Acute Oral LD50 in Rats, Report No.85320 to The Goodyear Tire & Rubber Company, 1964

(6) Hazelton Laboratories America, Inc., Acute Inhalation Exposure in Rats-WINGSTAY L to The Goodyear Tire & Rubber Company, 1975.

(7) Hazelton Laboratories America, Inc., Mutagenicity Test on WINGSTAY L in the CHO/HGPRT Forward Mutation Assay, Project No. 12638-0-435R to The Goodyear Tire & Rubber Company, 1991.

(8) Hazelton Laboratories America, Inc., WINGSTAY L-Measuring Chromosomal Aberrations in Chinese Hamster Ovary (CHO) Cells: Multiple Harvests under Conditions of Metabolic Activation with a Confirmatory Assay, Project No. 12638-0-437CR to The Goodyear Tire & Rubber Company, 1991.

(9) Hazelton Laboratories, Inc., Primary Skin Irritation in Rabbits-WINGSTAY L to The Goodyear Tire & Rubber Company, 1974 h

(10) Monsanto (1986)-Ames/Salmonella Plate Incorporation Assay (PH-301-MO-008-86) Santowhite ML Lot#001, Pharmcopathic Research Labs, December 17, 1986.

(11) Monsanto-Acute Dermal Toxicity Study, No. Y-86-399, Younger Laboratories, November 13, 1986.

(12) Monsanto-Acute Oral Toxicity Study, No. Y-88-399, Younger Laboratories, November 13, 1986

(13) Monsanto-Primary Eye Irritation, No. Y-86-399, Younger Laboratories, November 13, 1986.

(14) Monsanto-Primary Skin Irritation, No. Y-86-399, Younger Laboratories, November 13, 1986.

(15) Primary Dermal Irritation (D.O.T.) Using WINGSTAY L as the Test Chemical, Report Number:0402XG0.001, Chrysalis Labs, 2000

(16) Ricerca, Inc., Report No. 5797-93-0200-TX-001 to The Goodyear Tire & Rubber Co., 1993

(17) SITEK Research Laboratories, Evaluation of WINGSTAY L-HLS in the Salmonella typhimurium/Escherichia coli Plate Incorporation/Preincubation Mutation Assay in the Presence and Absence of Aroclor-induced Rat Liver S-9 with a Confirmatory Study, Project No. 0338-2140 to The Goodyear Tire & Rubber Company, 1995.

(18) Skin Sensitization "Guina Pig Sensitization-Maximization Test" (Magnusson-Kligman) Using WINGSTAY L as the Test Chemical, Report Number:0423XG05.001, Chrysalis Labs, 2000

(19) The Goodyear Tire & Rubber Company's Data

(20) The Goodyear Tire & Rubber Company, DNA Damage by WINGSTAY L in the E. coli Pol A1- Assay, Goodyear Laboratory Report No. 80-11-2, 1980.

(21) The Goodyear Tire & Rubber Company, Material Safety Data Sheet, 1997

(22) Wil Research Laboratories, Inc., 28-Day Dietary Study in Rats with WINGSTAY L, Project Number: WIL-140001 to The Goodyear Tire & Rubber Company, 1989.

(23) Wil Research Laboratories, Inc., 90-Day Dietary Study in Rats with WINGSTAY L, Project Number: WIL-140002 to The Goodyear Tire & Rubber Company, 1989.

(24) WINGSTAY L-HLS-Acute Toxicity to Daphnia magna, Report # 1515/2-1018, Covance Laboratories, 3/26/1998.

(25) WINGSTAY L-HLS-Acute Toxicity to Oncorhynchus mykiss (Trout), Report # 1515/1-1018, Covance Laboratories, 3/26/1998.

(26) WINGSTAY L-HLS-Determination of the N-Octanol/Water Coefficient, Report #: 95-5-5844, Springborn Laboratories (Wareham), 6/14/95

(27) WINGSTAY L-HLS-Inhibition of Growth to the Alga Selenastrum capricornutum, Report # 1515/3-1018, Convance Laboratories, 3/26/1998.

(28) WINGSTAY L-HLS: Evaluation of the Partition Coefficient, Report # 115/10-D2141, Covance Laboratories (Harrogate), 2/2000

(29) Wingstay L-HLS:Assessment of Inherent Biodegradability by Measuring Carbon Dioxide Envolved by Pre-Acclimatised Inoculum, Report # 1515/4-D2145, Covance Laboratories, March, 1998

(30) Wingstayl L-HLS Determination of Physical Properties (Tests A1,A3,A4,A6 and A10), Report # 1515/5-1014, Covance Laboratories, April, 1997

(31) Wingstayl L-HLS Determination of the Solubility in Water, Report # 1515/9-D2141, Covance Laboratories, Januray, 2000

(32) Wingstayl-HLS Determination of Physical Properties (Tests A1,A3,A4,A6 and A10), Report # 1515/5-1014, Covance Laboratories, April, 1997

7.1 Risk Assessment

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IRGANOX 3114

1,3,5 –tris(3,5-di-tert-butyl-4-hydroxybenzyl)-1,3,5-triazine-2,4,6 (1H,3H,5H) -trione

CAS No. 27676-62-6

CONTENTS

SUMMARY TABLE

CAS No. 27676-62-6 **PHYSICAL/CHEMICAL ELEMENTS**	**DATE**	**RESULTS**	**FULFILLS REQUIREMENT**
Melting Point	2000	219.5-225.5 °C	Yes
Boiling Point	2001	960.98 °C	Yes
Vapor Pressure	2000	5×10^{-15} mm Hg	Yes
Partition Coefficient	2000	log P > 6.0	Yes
Water Solubility	2000	< 1 ppm	Yes
ENVIRONMENTAL FATE ELEMENTS			
Photodegradation	2001	For reaction with hydroxyl radical, predicted rate constant = 66.5×10^{12} cm^3/molecule-sec predicted half-life = 1.93 h	Yes
Stability in Water	2001	Hydrolysis rate extremely slow	Yes
Fugacity	2001	Predicted distribution using Level III fugacity model Air 0.02 % Water 1.15 % Soil 38.4 % Sediment 60.4 % Persistence = 6.4×10^3 h	Yes
Biodegradation	1985	Not biodegradable 0 -7 % after 28 days	Yes
Bioaccumulation	2001	Estimated log BCF = 0.500 (BCF = 3.162)	
ECOTOXICITY ELEMENTS			
Acute Toxicity to Fish	1988	Zebra fish (Brachydanio rerio): LC_{50} (24 – 96 h) => 100 mg/L	Yes
Toxicity to Aquatic Plants	1992	Green algae (Scenedesmus subspicatus): EC_{50} (0 – 72 h) => 100 mg/L NOEC (0 – 72 h) = 33 mg/L	Yes
Acute Toxicity to Aquatic Invertebrates	1988	Daphnia magna: EC_0 (24 h) = > 100 mg/L EC_{50} (24 h) = 32 mg/L EC_{100} (24 h) => 100 mg/L	Yes

SUMMARY TABLE (CONTINUED)

CAS No. 27676-62-6 HEALTH ELEMENTS	DATE	RESULTS	FULFILLS REQUIREMENT
Acute Toxicity	1986	Rat: LD_{50} (Oral) > 5000 mg/kg	Yes
	1992	Rabbit: LD_{50} (Dermal) > 2000 mg/kg	Yes
Genetic Toxicity in vivo	1987	Chinese hamster: Nonmutagenic in somatic mutation assay (exposed by gavage 5000 mg/kg)	Yes
Genetic Toxicity in vitro	1986	Salmonella typhimurium: No increase in mutations with or without metabolic activation (at doses of 20 – 5000 µg/0.1 mL)	Yes
	1978	Salmonella typhimurium: No increase in mutations with or without metabolic activation (at doses of 25 – 2025 µg/0.1 mL)	Yes
Genetic Toxicity in vitro (non-bacterial)	1991	Chinese hamster V79 cells: No increase in mutations with or without metabolic activation (at doses of 27.5 – 550 µg/0.1 mL)	Yes
Cytogenetic test	1991	Chinese hamster ovary cells: No clastogenic effects	Yes
Repeated Dose Toxicity	1990	Albino Rats: NOEL = 3000 ppm (males) NOEL = 800 ppm (females) (90 days exposure, diet)	Yes
	1970	Albino Rats: NOEL = 10,000 ppm (92-93 days exposure, diet)	Partially
	1970	Dog: NOEL = 10,000 ppm (90 days exposure, diet)	Partially
Chronic Toxicity / Carcinogenicity	1978	2 year rat study: Not carcinogenic at 100 ppm	Partially

1. 0 GENERAL INFORMATION

1.0.1 SUBSTANCE INFORMATION

A. CAS Number 27676-62-6

Name *(IUPAC name)* 1,3,5–tris(3,5-di-tert-butyl-4-hydroxybenzyl)-1,3,5-triazine-2,4,6 (1H,3H,5H) -trione

B. Molecular Formula C48 H69 N3 O6

C. Structural Formula *(indicate the structural formula in smiles code, if available)*

n1(C(c2cc(C(C)(C)C)c(O)c(C(C)(C)C)c2))c(=O)n(C(c3cc(C(C)(C)C)c(O)c(C(C)(C)C)c3))c(=O)n(C(c4cc(C(C)(C)C)c(O)c(C(C)(C)C)c4))
c1(=O)

D. Molecular Weight 784

E. Type of Substance

element [ ]; inorganic [ ]; natural substance [ ]; organic [X]; organometallic [ ]; petroleum product [ ]

F. Physical State *(at 20°C and 1.013 hPa)*

gaseous [ ]; liquid [ ]; solid [X]

2.0 PHYSICAL-CHEMICAL DATA

2.0.1 MELTING POINT

Value:	219.5 – 225.5 °C
Decomposition:	Yes **[X]** No **[ ]** Ambiguous **[ ]** > 350 °C
Sublimation:	Yes **[ ]** No **[X]** Ambiguous **[ ]**
Method:	Not reported
GLP:	Yes **[ ]** No **[X]** ? **[ ]**
Remarks:	The melting point was reported in the MSDS from Ciba Specialty Chemicals Corp. The method of determination by Ciba was not reported. The melting point was assigned a reliability code of 2g (data from handbook or collection of data)[2].
Reference:	[1]MSDS No. 85, September 28, 2000, Ciba Specialty Chemicals, Tarrytown, New York. [2]Klimisch, H.J., Andreae, M and Tillman, U. A systemic approach for evaluating the quality of experimental toxicological and ecotoxicological data. *Regulatory Toxicology and Pharmacology*. 25:1-5, 1997.

2.0.2 BOILING POINT

Value: 960.9 °C

Method: Estimated by the MPBPWIN Program (v. 1.40) [1,2] using the adapted Stein and Brown method.

GLP: Yes **[ ]** No **[X]** ? **[ ]**

Remarks: In the absence of reliable experimental data, the boiling point was calculated using an accepted method and assigned a reliability code of 2f [3] (Accepted calculation method).

Reference:

[1]Syracuse Research Corporation, Syracuse, NY.

[2]Pollution Prevention (P2) Assessment Framework, U.S. Environmental Protection Agency, Office of Pollution Prevention and Toxics (Draft), 1998.

[3]Klimisch, H.J., Andreae, M and Tillman, U. A systemic approach for evaluating the quality of experimental toxicological and ecotoxicological data. *Regulatory Toxicology and Pharmacology*. 25:1-5, 1997.

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2.0.3 VAPOR PRESSURE

Value: 5×10^{-15} mm Hg at $25^{o}C$

Temperature: 25 °C

Method: calculated **[ ]**; measured **[X]**
The vapor pressure was reported from the Ciba MSDS. [1]

GLP: Yes **[ ]** No **[X]** ? **[ ]**

Remarks: The vapor pressure of 4.68E-028 mm Hg was also estimated by the MPBPWIN Program (v.1.40) using the modified Grain method.[2,3] This calculation confirmed the low vapor pressure reported on the MSDS. The MSDS value was assigned a reliability code of 2g (data from handbook or collection of data)[4].

References:

[1]MSDS No. 85, September 28, 2000, Ciba Specialty Chemicals, Tarrytown, New York.

[2]Syracuse Research Corporation, Syracuse, NY.

[3]Pollution Prevention (P2) Assessment Framework, U.S. Environmental Protection Agency, Office of Pollution Prevention and Toxics (Draft), 1998.

[4]Klimisch, H.J., Andreae, M and Tillman, U. A systemic approach for evaluating the quality of experimental toxicological and ecotoxicological data. *Regulatory Toxicology and Pharmacology.* 25:1-5, 1997.

2.0.4 PARTITION COEFFICIENT $log_{10}P_{ow}$

Log Pow: > 6.0

Method: calculated **[ ]**; measured **[X]**
Ciba MSDS report[1]

GLP: Yes **[ ]** No **[X]** ? **[ ]**

Remarks: A log P value of 15.18 was also estimated by KOWWIN (v. 1.66).[2,3] The calculated log P confirms the high value of the MSDS. The partition coefficient was assigned a reliability code of 2g (data from handbook or collection of data)[4].

Reference:

[1]MSDS No. 85, September 28, 2000, Ciba Specialty Chemicals, Tarrytown, New York.

[2]Syracuse Research Corporation, Syracuse, NY.

[3]Pollution Prevention (P2) Assessment Framework, U.S. Environmental Protection Agency, Office of Pollution Prevention and Toxics (Draft), 1998.

[4]Klimisch, H.J., Andreae, M and Tillman, U. A systemic approach for evaluating the quality of experimental toxicological and ecotoxicological data. *Regulatory Toxicology and Pharmacology*. 25:1-5, 1997.

2.0.5 WATER SOLUBILITY

Value: < 1 ppm

Temperature: 25 °C

Description: Miscible **[ ]**; Of very high solubility **[ ]**;
Of high solubility **[ ]**; Soluble **[ ]**; Slightly soluble **[ ]**;
Of low solubility **[X]**; Of very low solubility **[ ]**; Not soluble **[ ]**

Method: calculated **[ ]**; measured **[X]**
Ciba MSDS report.[1]

GLP: Yes **[ ]** No **[X]** ? **[ ]**

Remarks: Ciba MSDS reported the solubility as < 1 ppm in water at 20 °C. The water solubility value was 3.998e-012 mg/L when estimated by WSKOW Program (v. 1.37) [2,3] which confirms the low solubility. The MSDS value was assigned a reliability code of 2g (data from handbook or collection of data)[4].

Reference:

[1]MSDS No. 85, September 28, 2000, Ciba Specialty Chemicals, Tarrytown, New York.

[2]Syracuse Research Corporation, Syracuse, NY.

[3]Pollution Prevention (P2) Assessment Framework, U.S. Environmental Protection Agency, Office of Pollution Prevention and Toxics (Draft), 1998.

[4]Klimisch, H.J., Andreae, M and Tillman, U. A systemic approach for evaluating the quality of experimental toxicological and ecotoxicological data. *Regulatory Toxicology and Pharmacology*. 25:1-5, 1997.

3.0 ENVIRONMENTAL FATE AND PATHWAYS

3.0.1 PHOTODEGRADATION

Type: Air **[X]**; Water **[ ]**; Soil **[ ]**; Other **[ ]**

Half life: 1.93 hours.

Rate constant (radical): 66.5 E-12 cm^3/molecule*sec

Method: calculated **[X]**; measured **[ ]**
Estimated by the AOP program (v. 1.90) [1,2] which estimates rate constants
and half-lives of atmospheric reactions of organic compounds with hydroxyl radicals and ozone in the atmosphere.

GLP: Yes **[ ]** No **[X]** ? **[ ]**

Test substance: 1,3,5-tris(3,5-di-tert-butyl-4-hydroxybenzyl-)-1,3,5-triazine-2,4,6(1H,3H,6H)-trione.

Remarks: In the absence of reliable experimental data, the photodegradation was
calculated using an accepted method and assigned a reliability code of 2f.[3]
(Accepted calculation method)

Reference: [1]Syracuse Research Corporation, Syracuse, NY.

[2]Pollution Prevention (P2) Assessment Framework, U.S. Environmental Protection Agency, Office of Pollution Prevention and Toxics (Draft), 1998.

[3]Klimisch, H.J., Andreae, M and Tillman, U. A systemic approach for evaluating the quality of experimental toxicological and ecotoxicological data. *Regulatory Toxicology and Pharmacology*. 25:1-5, 1997.

3.0.2 STABILITY IN WATER

Type:	Abiotic (hydrolysis) **[X]**; biotic (sediment)**[ ]**
Results:	"Hydrolysis rate is extremely slow". Model did it not provide numerical estimate.
Method:	Estimated by the HYDROWIN Program (v. 1.67) [1,2]
GLP:	Yes **[ ]** No **[X]** ? **[ ]**
Test substance:	1,3,5-tris(3,5-di-tert-butyl-4-hydroxybenzyl-)-1,3,5-triazine-2,4,6(1H,3H,6H)-trione.
Remarks:	The stability in water was calculated using an accepted method and assigned a reliability code of 2f.[3] (Accepted calculation method)
References:	[1]Syracuse Research Corporation, Syracuse, NY
	[2]Pollution Prevention (P2) Assessment Framework, U.S. Environmental Protection Agency, Office of Pollution Prevention and Toxics (Draft), 1998.
	[3]Klimisch, H.J., Andreae, M and Tillman, U. A systemic approach for evaluating the quality of experimental toxicological and ecotoxicological data. *Regulatory Toxicology and Pharmacology*. 25:1-5, 1997.

3.0.3 THEORETICAL DISTRIBUTION (FUGACITY CALCULATION)

Media: Air-biota [ ]; Air-biota-sediment-soil-water [ ]; Soil-biota [ ]; Water-air [ ]; Water-biota [ ]; Water-soil [ ]; Other [ ]

Method: Fugacity level I [ ]; Fugacity level II [ ]; Fugacity level III [X]; Fugacity level IV [ ]; Other (calculation) [X]; Other (measurement)[ ]

Estimated by EPIWIN Level III Fugacity Model [1, 2]

Results: Distribution using level III fugacity model

Air	0.02 %
Water	1.15 %
Soil	38.4 %
Sediment	60.4 %

Persistence Time: 6.4×10^3 hr.

Remarks: In the absence of reliable experimental data, the fugacity was calculated using an accepted method and assigned a reliability code of 2f.[3] (Accepted calculation method).

References:

[1]Syracuse Research Corporation, Syracuse, NY

[2]Pollution Prevention (P2) Assessment Framework, U.S. Environmental Protection Agency, Office of Pollution Prevention and Toxics (Draft), 1998.

[3]Klimisch, H.J., Andreae, M and Tillman, U. A systemic approach for evaluating the quality of experimental toxicological and ecotoxicological data. *Regulatory Toxicology and Pharmacology*. 25:1-5, 1997

3.0.4 BIODEGRADATION

Type:	aerobic **[X]**; anaerobic **[ ]**
Concentration of the chemical:	10 mg and 20 mg of test substance /l.
Medium:	water [ ]; water-sediment [ ]; soil [ ]; sewage treatment [X]
Vehicle:	Water as specified in the guideline containing 0.5 ml of the Nonylphenol 10E05P0 solution.
Inoculum:	Fresh sewage treatment plant sample (per guideline)
Degradation:	The biodegradation calculated as percentage of measured amount of carbondioxide was: 10 mg test substance/ L = 7 % in 28 days (time) 20 mg test substance/ L = 0 % in 28 days (time)
Results:	Readily biodeg. **[ ];** inherently biodeg. **[ ]**; under test condition no biodegradation observed **[X]**, other **[ ]**
Method:	*OECD Guideline for testing of Chemicals No. : 301B (May 1981)* The EEC Directive 79/831 Annex V part C 5.2 was established according to the OECD Guideline for testing of chemicals No. : 301 E (May 1981). The only deviation from the guideline method is the volume of the test solution was reduced from 3.0 L to 1.5L. The carbon dioxide formed by biodegradation was absorbed with NaOH and determined on a carbon analyser. Due to the poor solubility of the test material in water, an emulsifier was used to achieve a better distribution in the medium. [1]
GLP:	Yes **[ ]** No **[X]** ? **[ ]**
Test substance:	1,3,5-tris(3,5-di-tert-butyl-4-hydroxybenzyl-)-1,3,5-triazine-2,4,6(1H,3H,6H)-trione.
Remarks:	This study was assigned a reliability code of 2b[2] (guideline study with acceptable restrictions) according the criteria established by Klimisch *et al* (1997).
Reference:	[1]Report on the test for ready biodegradability of Irganox 3114 in the modified sturm test. Project No.: 88 43 81, November 01, 1988. Ciba-Geigy Ltd., Basle, Switzerland. [2]Klimisch, H.J., Andreae, M and Tillman, U. A systemic approach for evaluating the quality of experimental toxicological and ecotoxicological data. *Regulatory Toxicology and Pharmacology*. 25:1-5, 1997.

3.0.5 BIOACCUMULATION

BCF: Estimated log BCF = 0.500 (BCF = 3.162)

Elimination: Yes **[ ]** No **[ ]** ? **[ ]**

Method: Estimated by EPIWIN BCF Program (v2.14) [1,2]

Type of test: calculated **[X]**; measured **[ ]**
static **[ ]**; semi-static **[ ]**; flow-through **[ ]**; other *(e.g. field test)* **[ ]**

GLP: Yes **[ ]** No **[X]** ? **[ ]**

Test substance: 1,3,5-tris(3,5-di-tert-butyl-4-hydroxybenzyl-)-1,3,5-triazine-2,4,6(1H,3H,6H)-trione.

Remarks: In the absence of reliable experimental data, the bioaccumulation was calculated using an accepted method and assigned a reliability code of 2f.[3]
(Accepted calculation method).

References:

[1]Syracuse Research Corporation, Syracuse, NY

[2]Pollution Prevention (P2) Assessment Framework, U.S. Environmental Protection Agency, Office of Pollution Prevention and Toxics (Draft), 1998.

[3]Klimisch, H.J., Andreae, M and Tillman, U. A systemic approach for evaluating the quality of experimental toxicological and ecotoxicological data. *Regulatory Toxicology and Pharmacology.* 25:1-5, 1997

4.0 ECOTOXICITY ELEMENTS

4.0.1 ACUTE/PROLONGED TOXICITY TO FISH

Type of test:	static **[X]**; semi-static **[ ]**; flow-through **[ ]**; other *(e.g. field test)* **[ ]** open-system **[ ]**; closed-system **[ ]**
Species:	Zebra-Fish (Brachydanio rerio)
Number of fishes:	20 fishes in test concentration, tested in 2 separate tanks 10 fishes in control 10 fishes per aquarium
Control:	Water
Vehicle:	4 mg alkylphenol-polyglykol-ether per liter water
Exposure period:	96 - hours
Results:	LC_{50} (24h) = > 100 mg/l LC_{50} (48h) = > 100 mg/l LC_{50} (72h) = > 100 mg/l LC_{50} (96h) = > 100 mg/l Values are based on nominal concentrations.
Analytical monitoring:	Yes **[ ]** No **[X]** ? **[ ]**
Method:	OECD-Guideline No. 203, Paris 1984 (static procedure) Test solution containing 5.0 g of test material and 200 mg alkylphenol-polyglykol-ether were mixed with and made up to 1 L with water and stored at room temperature. Glass aquaria of 20 litres was filled with 15 litres of dechlorinated tap water. The temperature is maintained at 23 ± 1° C and was lighted for 16 hours with fluorescent light. Daily measurements of oxygen, pH, temperature were taken. Desired test concentrations were homogeneously distributed into the water. A slight deposit was observed at concentration of 100 mg/ L (nominal) after 24 hour exposure[1].
GLP:	Yes **[ ]** No **[X]** ? **[ ]**
Test substance:	1,3,5-tris(3,5-di-tert-butyl-4-hydroxybenzyl-)-1,3,5-triazine-2,4,6(1H,3H,6H)-trione. Purity: commercial grade
Remarks:	This study was assigned a reliability code of 2b (guideline study with acceptable restrictions) according the criteria established by Klimisch *et al* (1997) [2].

Reference: [1]Test for Acute Toxicity of TK 10730 to Zebra Fish (Brachydanio rerio), Project No.: 884382, Ciba-Geigy Ltd., Basel, Switzerland, December 2, 1988.

[2]Klimisch, H.J., Andreae, M and Tillman, U. A systemic approach for evaluating the quality of experimental toxicological and ecotoxicological data. *Regulatory Toxicology and Pharmacology.* 25:1-5, 1997

4.0.2 ACUTE TOXICITY TO AQUATIC INVERTEBRATES

Type of test:	static **[X]**; semi-static **[ ]**; flow-through **[ ]**; other *(e.g. field test)* **[ ]**; open-system **[ ]**; closed-system **[ ]**
Species:	Daphnia Magna Straus 1820
Number of Daphnia:	20 daphnia per concentration and control. 4 replicates of 5 daphnia each
Control:	Blank: water Vehicle: 4 mg alkylphenol-polyglykol-ether per litre water
Test Concentration:	10, 18, 32, 58, 100 mg/L
Exposure period:	24 hours
Results:	EC_{50} (24h) = > 100 mg/l EC_0 (24h) = 32 mg/l EC_{100} (24h) = > 100 mg/l
Analytical monitoring:	Yes **[ ]** No **[X]** ? **[ ]**
Method:	OECD Guideline No. 202, Paris 1984. Tests were conducted in beakers containing 100 mL solution. Reconstituted water was prepared by dissolving 65 mg $NaHCO_3$, 294 mg $CaCl_2$ (2 H_2O), 123 mg $MgSO_4$ (7H_2O), 6 mg KCl per liter bidistilled water. Total hardness was 240 mg $CaCO_3$/L; pH ranged from 7.2 to 7.9; O_2 ranged from 87 to 96% saturation; temperature was 20 $\pm$ 1 ^oC.). The nominal concentrations of the test compound were 10, 18, 32, 58 and 100 mg/L. The test substance appeared homogeneously distributed at all test concentrations except at 58-100 mg/L, where a slight deposit was observed. Samples for analysis were taken after 0 and 24 h exposure.[1]
GLP:	Yes **[ ]** No **[X]** ? **[ ]**
Test substance:	1,3,5-tris(3,5-di-tert-butyl-4-hydroxybenzyl-)-1,3,5-triazine-2,4,6(1H,3H,6H)-trione
Remarks:	This study was assigned a reliability code of 2b (guideline study with acceptable restrictions) according the criteria established by Klimisch *et al* (1997) [2].

Reference: [1]Test for Acute Toxicity to Daphnia magna, Project No.: 884383, Ciba-Geigy Ltd., Basel, Switzerland, November 16, 1988.

[2]Klimisch, H.J., Andreae, M and Tillman, U. A systemic approach for evaluating the quality of experimental toxicological and ecotoxicological data. *Regulatory Toxicology and Pharmacology*. 25:1-5, 1997

4.0.3 TOXICITY TO AQUATIC PLANTS

Species: Green Algae (Scenedesmus subspicatus)

Endpoint: Biomass **[X]**; Growth rate **[ ]**; Other **[ ]**

Exposure period: 72 hours

Test concentrations: 1.23, 3.7, 11, 33 and 100 mg/ L (nominal)

Controls: Blank: water
Vehicle: 4.0 mg Arkopal/L (alkylphenol-polyglykolether)

Results: EC_{50} (72 h) = > 100 mg/l
NOEC (72 h) = 33 mg/l

Analytical monitoring: Yes **[ ]** No **[X]** ? **[ ]**

Method: 87/302/EEC, Algal growth inhibition test.

Tests were conducted in 100 mL Erlenmeyer flasks containing 50 mL test solution. The vehicle contained 4 mg alkylphenol-polyglycolether (ARKOPAL)/L. Nominal test concentrations were 1.23, 3.7, 11, 33, and 100 mg/L. Each test concentration was tested in 3 replicates and the blank control in 6 replicates. Samples for analysis were taken immediately before exposure and after 72 h exposure. The temperature was 23 $\pm$ 2 ^{o}C, other information, such as pH, water hardness, TOC and O_2 was not provided. Continuous illumination was provided by cold white fluorescent light (117 µE/m2 sec). Cell densities were measured at 24, 48, and 72 h, and the EC values calculated.[1]

GLP: Yes **[ ]** No **[X]** ? **[ ]**

Test substance: 1,3,5-tris(3,5-di-tert-butyl-4-hydroxybenzyl-)-1,3,5-triazine-2,4,6(1H,3H,6H)-trione, Purity: > 95%

Remarks: This study was assigned a reliability code of 2b (guideline study with acceptable restrictions) according the criteria established by Klimisch *et al* (1997).[2]

Reference: [1]Report on the growth inhibition test of Irganox 3114 to green algae (Scenedesmus subspicatus), Test No.: 928149, Ciba-Geigy Ltd., Basel, Switzerland, december 17, 1992.

[2]Klimisch, H.J., Andreae, M and Tillman, U. A systemic approach for evaluating the quality of experimental toxicological and ecotoxicological data. *Regulatory Toxicology and Pharmacology*. 25:1-5, 1997

5.0 HEALTH ELEMENTS

5.1 ACUTE TOXICITY

5.1.1 ACUTE ORAL TOXICITY

Type: LD_0 **[ ]**; LD_{100} **[ ]**; LD_{50} **[X]**; LDL_0 **[ ]**; Other **[ ]**

Species/strain: Rat, Tif : Raif (SPF), F3 – hybrid of RII 1/ Tif x RII 2/ Tif

Dose Level: 5000 mg/kg bw. (limit test)

Number of animals: 5 males and 5 females

Initial age: 7 – 8 weeks

Body weight: 168 to 201 g

Vehicle: distilled water containing 0.5% carboxymethylcellulose and 0.1% polysorbate 80

Administration: oral, by gastric intubation (gavage)

Observation period: 14 days

Results: LD50 > 5000 mg/kg b.w.

There were no mortalities during the study. Dyspnea, ruffled fur, and curved body position were noted. These are common symptoms in acute tests. The animals recovered within 11 days. Treated rats had a slight loss of body weight. The results are summarized in table 1and 2.

Signs and Symptoms

Table 1

Observations	Exposure day: Hours				Days of post-exposure period													
	1	2	3	5	1	2	3	4	5	6	7	8	9	10	11	12	13	>13
Dose	5000 mg / kg																	
Dyspnea	X	X	X	X	X	X	X	X	X	X	X							
Ruffled fur	X	X	X	X	X	X	X	X	X	X	X	X	X	X				
Body position - curved	X	X	X	X	X	X	X	X	X									

X = slight, XX = moderate, XXX = marked

Body weights and Standard deviations

Table 2

Dose mg/ kg	Males			Females		
	Day 1	Day 7	Day 14	Day 1	Day 7	Day 14
5000	193/ 6.6*	260/ 7.6*	307/11.7*	179/10.1*	211/10.1*	222/ 4.3*

* mean / standard deviation

Method: OECD Guideline No. 401

The animals were caged in groups of 5. The animal room was air conditioned at a temperature of 22 ± 3 °C, relative humidity of 55 ± 15 %, 12 hours light / day, with approximately 15 air changes/h. Food and water were provided ad libitum. The animals were observed for body weight changes, clinical symptoms, and mortalities for 14 days. Necropsy was performed at the end of the observation period.[1]

GLP: Yes [ ] No [X] ? [ ]

Testsubstance: 1,3,5-tris(3,5-di-tert-butyl-4-hydroxybenzyl-) -1,3,5-triazine-2,4,6(1H,3H,6H)-trione

Remarks: The study is assigned a reliability code of 2b (guideline study with acceptable restrictions).[2]

Reference: [1]Acute Oral Toxicity in the Rat, GU Project No.: 860786, Ciba–Geigy Limited, Basle, Switzerland, September 8, 1986.

[2]Klimisch, H.J., Andreae, M and Tillman, U. A systemic approach for evaluating the quality of experimental toxicological and ecotoxicological data. *Regulatory Toxicology and Pharmacology*. 25:1-5, 1997.

5.1.2 ACUTE DERMAL TOXICITY

Type: LD_0 [ ]; LD_{100} [ ]; LD_{50} [X]; LDL_0 [ ]; Other [ ]

Species/strain: Albino rats / Tif: RAI f (SPF)

Number of animals: 5 males and 5 female / dose level

Initial age: 7 – 8 weeks

Body weight: 207 to 273 g

Dose Level: 2000 mg/kg bw. (limit test)

Vehicle: 0.5% carboxymethylcellulose in 0.1% (w/v) aqueous polysorbate 80

Observation period: 14 days

Results: LD50 > 2000 mg/kg b.w.

No mortalities occurred in this study. Piloerection and hunched posture were seen, being common symptoms in acute dermal tests. The animals recovered within 2 days. No mortalities occurred in this study. At necropsy, no deviations from normal morphology were found. Individual body weights, their group means and standard deviations are shown in table 1.

Table 1

Body Weight and Necropsy Findings

Animal number (male)	Body weights (g)			Necropsy findings
	Day 0	Day 7	Day 14	
1	264	307	350	No abnormalities
2	273	301	333	No abnormalities
3	256	290	319	No abnormalities
4	265	291	317	No abnormalities
5	260	288	316	No abnormalities
Mean deviation	**264**	**295**	**327**	
Standard deviation	**6.3**	**8.2**	**14.6**	

Table 1 (continued)

Body Weight and Necropsy Findings

Animal number (female)	Body weights (g)			Necropsy findings
	Day 0	Day 7	Day 14	
1	254	253	291	No abnormalities
2	232	241	252	No abnormalities
3	229	247	240	No abnormalities
4	207	212	235	No abnormalities
5	221	226	235	No abnormalities
Mean deviation	**229**	**236**	**251**	
Standard deviation	**17.2**	**16.7**	**23.6**	

Method: OECD Guideline 402/ 84/ 449 EEC, B.3, "Acute Dermal Toxicity", adopted February 24,1987. The animals were kept in an air conditioned room, at a temperature of 22 ± 3 °C, relative humidity of 55 ± 15 %, with 12 hours light /day, and approximately 15 air changes/h. Food and water were provided ad libitum. The dose group consisted of 10 rats. During and after exposure, the animals were placed in their cages. The test article was evenly dispersed on the skin. The only deviation from the protocol is, due to the physical-chemical properties, test material had to be applied by weight.[1]

GLP: Yes **[X]** No **[ ]** ? **[ ]**

Test substance: 1,3,5-tris(3,5-di-tert-butyl-4-hydroxybenzyl-)-1,3,5-triazine-2,4,6(1H,3H,6H)-trione

Remarks: The study is assigned a reliability code of 2b (guideline study with acceptable restrictions).[2]

Reference: [1]Acute Dermal Toxicity in the Rat, Test No. 924064, Ciba-Geigy Limited, Basle, Switzerland, June 22, 1992.

[2]Klimisch, H.J., Andreae, M and Tillman, U. A systemic approach for evaluating the quality of experimental toxicological and ecotoxicological data. *Regulatory Toxicology and Pharmacology*. 25:1-5, 1997.

5.2 GENETIC TOXICITY IN VITRO

A. BACTERIAL TEST

Type: *Bacterial reverse mutation assay*

System of testing: Salmonella typhimurium TA 98, TA 100, TA 102, TA 1535 and TA 1537

Concentrations: 0.08 – 5000 ug/ 0.1 ml, range in the toxicity test
20, 78, 313,1250 and 5000 ug/ 0.1 ml in the mutagenicity test

Metabolic activation: With **[ ]**; Without **[ ]**; With and Without **[X]**; No data **[ ]**

Vehicle: Acetone

Results:

Precipitation conc: 1250 ug/ 0.1 ml

Genotoxic effects:	+	?	-
With metabolic activation:	**[ ]**	**[ ]**	**[X]**
Without metabolic activation:	**[ ]**	**[ ]**	**[X]**

In the experiments performed without and with microsomal activation, comparison of the number of back-mutants in the controls and the cultures treated with the various concentrations of test material revealed no marked deviations. No evidence of the induction of point mutations in the strains of S.typhimurium by the test substance or by the metabolites.

Table 1. Mean number of revertant colonies from experiments without metabolic activation

Strain	TA 98	TA 100	TA 102	TA 1535	TA 1537
Control (Acetone)	37	160	322	17	7
20 µg/0.1 mL	25	140	311	17	7
78	28	152	329	15	7
313	26	133	282	16	7
1250	26	158	217	16	7
5000	18	111	245	13	3

Table 2. Mean number of revertant colonies from experiments with metabolic activation (without/with pre-incubation)

Strain	TA 98	TA 100	TA 102	TA 1535	TA 1537
Control (Acetone)	37	135	334	20	13
20 µg/0.1 mL	44	115	348	11	16
78	56	113	253	15	12
313	39	115	237	16	9
1250	39	110	286	16	7
5000	31	109	256	10	5

Method:	OECD Guideline 471 (with the exception of statistical analysis) and methods described by Ames *et al* [2,3,4] A preliminary toxicity test was carried out with the concentrations ranging from 0.08 to 5000 ug/ 0.1 ml. Thereafter, the concentration range of 20 to 5000 ug/ 0.1 ml was used in the mutagenicity test. The substance was dissolved in acetone. Positive control experiments were carried out simultaneously. Positive controls included sodium azide (TA 1535), 9(5)-aminoacridine hydrochloride monohydrate (TA 1537), daunorubicin (TA 98), 4-nitroquinoline-N-oxide (TA 100), mytomycin (TA 102). In the experiments without and with the addition of microsomal activation mixture, three petri dishes were prepared per strain and per group (i.e. per concentration or per control group). The plates were incubated for about 48 hours at 37 ± 1.5 ^{0} C in darkness. [1]
GLP:	Yes **[ ]** No **[** X**]** ? **[ ]**
Test substance:	1,3,5-tris(3,5-di-tert-butyl-4-hydroxybenzyl-)-1,3,5-triazine-2,4,6(1H,3H,6H)-trione
Remarks:	The study was assigned a reliability code of 2b (guideline study with acceptable restrictions).[5]
References:	[1]"Salmonella/Mammalian Microsome Mutagenicity Test with TKA 10730." Test No.: 860790, Ciba Geigy, Limited, Basel, Switzerland. August 13, 1986. [2]Ames, B.N., Lee, F.D., and Durston, W.E., "An improved bacterial test system for the detection and classification of mutagens and carcinogens, Proc. Natl. Acad. Sci. USA, 70, 782-786, 1973. [3]Ames, B.N., Durston, W.E., Yamasaki, E., and Lee, F.D., "Carcinogens are mutagens: a simple test system combining liver homogenates for activation and bacteria for detection," Proc. Natl. Acad. Sci. USA, 70, 2281-2285, 1973. [4]Ames, B.N., McCann, J., and Yamasaki, E., "Methods for detectingcarcinogens and mutagens with the Salmonella/mammalian-microsome mutagenicity test, Mutat. Res., 31, 347-364, 1975. [5]Klimisch, H.J., Andreae, M and Tillman, U. A systemic approach for evaluating the quality of experimental toxicological and ecotoxicological data. *Regulatory Toxicology and Pharmacology*. 25:1-5, 1997.

B. NON-BACTERIAL IN VITRO TEST

Type: *Gene mutation test with V79 Chinese Hamster Cells*

System of testing: Chinese hamster V79 cells

Concentration: Cytotoxicity test: 0.27 – 550.0 ug/mL
Mutagenicity test: 27.5 – 550.0 ug/mL

Vehicle: Dimethylsulfoxide

Metabolic activation: With **[ ]**; Without **[ ]**; With and Without **[X]**; No data **[ ]**

Results:

Mutagenic effects: **+ ? -**
With metabolic activation: **[ ] [ ] [X]**

Without metabolic activation: **[ ] [ ] [X]**

In mutagenicity test, both original and confirmatory experiment were performed with and without microsomal activation. In both experiments comparison of the number of mutant colonies in the controls and in the cultures treated with the various concentrations of the test material revealed no significant deviations of the mutant frequencies. Hence test material and its metabolites are non- mutagenic.

Summary of Mutagenic Experiment with microsomal activation

Treatment	Mean of Survivor II colonies per dish	Mean of mutants per dish	Normalized mean of Mutants/dish
Negative control	56.83	0.17	0.29
Negative control	66.0	0.28	0.42
Positive control DMN, 1.00 ul/ml	35.67	7.33	20.56
Test substance: (ug/ml)			
550.00	75.83	0.44	0.59
440.00	76.67	0.39	0.51
330.00	67.17	0.28	0.41
220.00	70.00	0.11	0.16
110.00	74.67	0.22	0.30
55.00	54.50	0.39	0.71
27.50	70.67	0.33	0.47

Summary of Mutagenic Experiment without microsomal activation

Treatment	Mean of Survivor II colonies per dish	Mean of mutants per dish	Normalized mean of Mutants/dish
Negative control	71.50	0.33	0.47
Negative control	66.83	0.33	0.50
Positive control EMS, 300.00 ul/ml	31.17	32.00	102.67
Test substance: (ug/ml)			
550.00	61.50	0.22	0.36
440.00	59.33	0.44	0.75
330.00	87.67	0.50	0.57
220.00	71.33	0.39	0.55
110.00	68.00	0.17	0.25
55.00	69.50	0.22	0.32
27.50	84.83	0.17	0.20

Method: *OECD Guideline 476 (April 4, 1984)*[2]
EPA Guidelines (1987)[3]
EPA Guidelines (1988)[4]

A cytotoxicity test was performed on V79 cells as a preliminary test to determine the highest concentration of the test substance. In the microsomal activated and non-activated cultures 7 concentrations of test substance, 2 negative controls and 1 positive control were included. The high density cultures were subjected to mutant selection procedure. The number of colonies formed in these dishes after a period of 7–8 days were measured with Fisher Count-All^{TM} colony counter. [1]

GLP: Yes **[X]** No **[ ]** ? **[ ]**

Test substance: 1,3,5-tris(3,5-di-tert-butyl-4-hydroxybenzyl-)-1,3,5-triazine-2,4,6(1H,3H,6H)-trione , purity: 98.2 %

Remarks: The study is assigned a reliability code of 2b (guideline study with acceptance restrictions) [5]

Reference:

[1]Gene Mutation Test with Chinese Hamster Cells V79 in Vitro, Test No.: 904299, Ciba –Geigy Limited, Basle, Switzerland, , March 26, 1991.

[2] OECD (April 1984), Genetic Toxicology: In vitro Mammalian Cell Gene Mutation Tests. OECD Guideline for testing of chemicals 476.

[3]EPA (May 20, 1987), Detection of gene mutations in somatic cells in culture. Environmental Protection Agency Health Effects Testing Guidelines, 52 FR 19072 (Corr. 52 FR 26150, July 13, 1987) ; 798.5300.

[4]EEC (May 30, 1988), Mutagenicity testing and screening for carcinogenicity – In vitro mammalian cell gene mutation test. Official Journal of the European Comm. No L 133 61-63.

[5]Klimisch, H.J., Andreae, M and Tillman, U. A systemic approach for evaluating the quality of experimental toxicological and ecotoxicological data. *Regulatory Toxicology and Pharmacology*. 25:1-5, 1997.

C. CYTOGENETIC TEST

Type:	*Chromosomal studies on Chinese hamster ovary cell line in vitro*
System of testing:	Cell line: ATCC (American Type Culture Collection) CCL 61 (ovary, Chinese hamster)
Concentration:	Cytotoxicity test: 0.22 – 28.0 ug/mL Mutagenicity test: 0.22 – 28.0 ug/mL
Vehicle:	Dimethylsulfoxide
Metabolic activation:	With **[ ]**; Without **[ ]**; With and Without **[X]**; No data **[ ]**
Results:	The chemical was tested for clastogenic effects on Chinese hamster ovary cells in vitro. In the studies performed without microsomal activation using 18 and 42 hours incubation no significant increase in the number of chromosome aberrations was observed. In the studies performed in the presence of metabolic activation system (3 hours treatment and harvest time after treatment is 15 and 39 hours), there were no marked increase in the number of specific chromosome aberrations observed. The number of chromosome aberrations was within the historical control range at all doses assessed. Hence the test substance is considered to be non-clastogenic.

Table 1 - The effect on Chinese Hamster Ovary Cells without Metabolic Activation (18 h Treatment)

	Vehicle Control	Test substance* (ug/ml) 7.0	14.0	28.0	Positive control Mitomycin-C 0.2 ug/ml
Percent of metaphases with specific aberrations	**1**	**1**	**1**	**0**	**50**
Metaphases with					
Chromatid breaks			**1**		**14**
Iso-chromatid breaks					**1**
Deletions					
Iso-chromatid deletions					
Chromatid exchanges					**7**
Di-, polycentrics					
Ring chromosomes					**1**
Acentric rings					
Chromatid fragments					**1**
Iso-chromatid fragments	**1**	**1**			**5**
Percent of metaphases with unspecific aberrations	**2**	**2**	**2**	**3**	**18**
Metaphases with					
Chromatid gaps	**1**	**2**	**2**	**3**	**6**
Iso-chromatid gaps	**1**				**4**
Chromosome decay (partial)					
Chromosomal decay (complete)					
Premature chromosome condensation (PCC)					

The effect of test substance on Chinese Hamster Ovary Cells with Metabolic Activation

Table 2

Treatment 3 h Harvest time after treatment 15 h

** D	Vehicle Control	Test substance* (ug/ml) 7.0 14.0 28.0			Positive control Mitomycin-C 0.2 ug/ml
Percent of a metaphases with specific aberrations	**0**	**2**	**1**	**1**	**36**
Metaphases with					
Chromatid breaks		**1**	**1**		**12**
Iso-chromatid breaks					
Deletions					
Iso-chromatid deletions					
Chromatid exchanges					**1**
Di-, polycentrics		**1**			
Ring chromosomes					
Acentric rings					
Chromatid fragments				**1**	
Iso-chromatid fragments				**1**	**8**
Percent of metaphases with unspecific aberrations	**1**	**2**	**0**	**2**	**18**
Metaphases with					
Chromatid gaps	**1**	**2**	**0**	**2**	**6**
Iso-chromatid gaps	**1**				**3**
Chromosome decay (partial)					
Chromosomal decay (complete)					
Premature chromosome condensation (PCC)					

ations (for table 1 and 2)

In the experiment performed without microsomal activation (table 1), in the negative control, 1% of metaphases with specific chromosomal aberrations were detected. At the concentration of 7.0, 14.0, 28.0 ug/ml of test material, 1%, 1%, and 0% of cells with specific chromosomal aberrations were found.

In the experiment performed with microsomal activation (table 2), in the negative control, 0% of metaphases with specific chromosomal aberrations were detected. At the concentration of 7.0, 14.0, 28.0 ug/ml of test material, 2%, 1%, and 1% of cells with specific chromosomal aberrations were found.

Mutagenic effects: + ? -

with metabolic activation: **[ ] [ ] [X]**

without metabolic activation: **[ ] [ ] [X]**

Method:	*OECD Guidelines 473 (May 26, 1983)*[2] *EPA Guidelines (May 20, 1987)*[3] *EPA Guidelines (September 19, 1984)*[4]
	Chinese hamster ovary cells were exposed to eight concentrations of the test substance ranging from 0.22 to 28.0 ug/ml in four different experiments, with and without metabolic activation. Two hours prior to harvesting, the cultures were treated with Colcemide, 0.4 ug/ml. The experiment was terminated by hypotonic treatment followed by fixation. For the dtermination of mitotic index the preparations from the various cultures were examined first, uncoded. The percentages of mitotic suppression in comparison with the controls were evaluated by counting at least 2000 cells per concentration. The determination of the mitotic coefficient was performed for all four experiments separately.[1]
GLP:	Yes **[X]** No **[ ]** ? **[ ]**
Test substance:	1,3,5-tris(3,5-di-tert-butyl-4-hydroxybenzyl-)-1,3,5-triazine-2,4,6(1H,3H,6H)-trione, purity: 98.2 %
Remarks:	The study is assigned a reliability code of 2b (guideline study with acceptance restrictions)[5]
Reference:	[1]Cytogenetic Test on Chinese Hamster Cell in Vitro, Test No. 904298, Ciba – Geigy Limited, Basle, Switzerland, April 03, 1991.
	[2]OECD (May 26, 1983). Genetic Toxicology: In vitro Mammalian Cytogenetic Test. OECD Guideline for testing of chemicals 473.
	[3]EPA (May 20, 1987). In Vitro Mammalian Cytogenetics. Environmental Protection Agency Health Effects Testing Guidelines. § 798.5375
	[4]EEC (September 19, 1984). Mutagenicity - In vitro mammalian cytogenetic test. B 10/EEC.
	[5]Klimisch, H.J., Andreae, M and Tillman, U. A systemic approach for evaluating the quality of experimental toxicological and ecotoxicological data. *Regulatory Toxicology and Pharmacology*. 25:1-5, 1997.

5.3 GENETIC TOXICITY IN VIVO

Type: *Micronucleus test*

Species/strain: Chinese Hamster (Cricetulus griseus) random outbred strain

Sex: Female **[ ]**; Male **[ ]**; Male/Female **[X]**; No data **[ ]**

No.of animals: In tolerability test: 2 males and 2 females

In mutagenicity test: 24 females and 24 males in both the test substance and in the negative control group. 8 females and 8 males in the positive control group.

Weight: female: 22-34 g
males: 24-35 g

Age: females: 6-10 weeks
males: 4-9 weeks

Route of Administration: Oral by stomach tube

Exposure period: 16, 24, and 48 hours

Dosage: 5000 mg/ kg

Control: negative: carboxymethylcellulose 0.5%
positive: cyclophosphamide (64 mg/kg)

Results: There was no significant increase in the number of micronucleated polychromatic erythrocytes in the treated animals as compared to negative control animals. By contrast, the positive control (cyclophosphamide, 64 mg/kg) yielded a marked increase of the percentage of micronucleated cells.

The effect of test substance on bone marrow cells of chinese hamster are summarized in the following tables. Animals are sacrificed after 24 hour of application.

Number of Polychromatic erythrocytes with micronuclei and ratio of PCE to NCE

	Control (CMC 0.5 %)									
No. of animals	1	2	3	4	5	6	7	8	9	10
Sex of animals	M	M	M	M	M	F	F	F	F	F
Polychromatic erythrocytes (PCE)	365	424	525	492	443	440	422	451	462	412
Normochromatic erythrocytes (NCE)	635	576	475	508	557	560	578	549	538	588
Ratio of PCE to NCE	0.57	0.74	1.11	0.97	0.80	0.79	0.73	0.82	0.86	0.70
Number of PCE with micronuclei	0	0	1	0	0	1	0	1	0	1
Percent of PCE with micronuclei	0	0	0.1	0	0	0.1	0	0.1	0	0.1

Number of Polychromatic erythrocytes with micronuclei and ratio of PCE to NCE

	Test substance (5000 mg/ kg)									
No. of animals	1	2	3	4	5	6	7	8	9	10
Sex of animals	M	M	M	M	M	F	F	F	F	F
Polychromatic erythrocytes (PCE)	547	480	466	494	464	444	516	418	505	396
Normochromatic erythrocytes (NCE)	453	520	534	506	536	556	484	582	495	604
Ratio of PCE to NCE	1.21	0.92	0.87	0.98	0.87	0.80	1.07	0.72	1.02	0.66
Number of PCE with micronuclei	0	0	0	1	0	1	0	0	1	1
Percet of PCE with micronuclei	0	0	0	0.1	0	0.1	0	0	0.1	0.1

Number of Polychromatic erythrocytes with micronuclei and ratio of PCE to NCE

	Positive Control (Cyclophosphamide 64 mg/kg)									
No. of animals	1	2	3	4	5	6	7	8	9	10
Sex of animals	M	M	M	M	M	F	F	F	F	F
Polychromatic erythrocytes (PCE)	318	426	305	421	396	345	400	380	342	426
Normochromatic erythrocytes (NCE)	682	574	695	579	604	655	600	620	658	574
Ratio of PCE to NCE	0.47	0.74	0.44	0.73	0.66	0.53	0.67	0.61	0.52	0.74
Number of PCE with micronuclei	65	42	11	17	9	49	27	24	22	50
Percet of PCE with micronuclei	6.5	4.2	1.1	1.7	0.9	4.9	2.7	2.4	2.2	5.0

Genotoxic effects:	+ ? - **[ ] [ ] [X]**
Method:	This study was not conducted under OECD guidelines. A preliminary test was performed to determine the highest dosage of the test substance. In this experiment the dose of 5000 mg/kg was determined as the highest applicable in the mutagenicity assay. The animals were kept in air-conditioned room at a temperature of 22 ^{0}C and a relative humidity of 53-58 %. The room was illuminated for 12 hours daily. Animals were provided standard diet and tap water ad libitum. Treatment consisted of a single application. Animals were sacrificed after 16, 24, 48 hours of application. Bone marrow was harvested from the femurs and slides were stained with May-Grunwald solution. One thousand polychromatic erythrocytes were scored for the incidence of micronuclei per animal. [1]
GLP:	Yes [ ] No [X] ? [ ]
Test substance:	1,3,5-tris(3,5-di-tert-butyl-4-hydroxybenzyl-)-1,3,5-triazine-2,4,6(1H,3H,6H)-trione, purity: commercial grade
Remarks:	The study is assigned a reliability code of 2 (Valid with restrictions). [2]
Reference:	[1]Micronucleus Test (Chinese hamster) (screening test), Test No. 861286, Ciba -Geigy Limited, Basle, Switzerland. February 06, 1987. [2]Klimisch, H.J., Andreae, M and Tillman, U. A systemic approach for evaluating the quality of experimental toxicological and ecotoxicological data. *Regulatory Toxicology and Pharmacology*. 25:1-5, 1997.

5.4 REPEATED DOSE TOXICITY

A. 3-MONTH ORAL TOXICITY STUDY IN RATS

Species/strain:	Albino Rats / Tif: RAIf (SPF), hybrids of RII/1 x RII/2
Sex:	Female **[ ]**; Male **[ ]**; Male/Female **[X]**; No data **[ ]**
Route of Administration:	Orally in the diet.
Frequency of treatment:	92 - 93 days
No. of animals per group:	10 males and 10 females / group
Initial age:	4 - 5 weeks
Initial bodyweight:	111.0 – 129.9 g in males 95.3 – 124.0 g in females
Dose:	0, 150, 800, 3000 and 15000 ppm (mg/kg food)
Control group:	Yes **[X]**; No **[ ]**; No data **[ ]**; Concurrent no treatment [X]; Concurrent vehicle [ ]; Historical [ ]
NOEL:	3000 ppm (males) 800 ppm (females)
Results:	No relevant clinical symptoms and no signs of systemic toxicity were observed during this study.

No treatment related death occurred during the study. The mean body weight gain of all treated groups was similar to that of the control group. The mean food consumption of group 5 (15000 ppm) was increased from week 5 onwards, but with no toxic effect. Mean water consumption of all treated animals was comparable to the controls.

The macroscopical and microscopical examination of the treated animals did not reveal any abnormal findings.

No deviation from the control were observed in blood chemistry investigations, and urine analysis.

Under the conditions of this test, treatment with TK 10730 for 3 months resulted in a slight increase of food consumption and consumption ratios in group 5 males (15000 ppm) and in elevated platelet counts in females treated at 3000 and 15000 ppm, but with no toxic effect at these dose levels.

Based on the observations made during this study, it can be inferred that a “no observable effect level” for TK 10730 when offered to rats continuously in their food over a period of 3 months is 3000 ppm in males, corresponding to a mean daily intake of 201 mg/kg bw and 800 ppm in females, corresponding to a mean daily intake of 50.1 mg/kg bodyweight.

Mean organ weights and ratios are presented in the following summary tables.

Organ Weights (means): males week 14

Dose (ppm)	Group 1 0	Group 2 150	Group 3 800	Group 4 3000	Group 5 15000
Body (g)	479.7	488.5	488.7	475.5	481.7
Brain (g)	2.347	2.465	2.413	2.411	2.414
Heart (g)	1.450	1.460	1.451	1.401	1.450
Liver (g)	20.58	21.04	21.48	21.43	20.80
Kidney (both) (g)	2.850	3.003	2.998	2.939	2.901
Adrenal (both) (mg)	78.75	75.83	69.52	77.74	73.48
Thymus (mg)	533.5	575.8	581.0	534.7	536.7
Testis (both) (g)	4.088	4.114	4.147	4.221	4.225
Spleen (g)	0.776	0.855	0.852	0.790	0.791

Organ Weights (means): females week 14

Dose (ppm)	Group 1 0	Group 2 150	Group 3 800	Group 4 3000	Group 5 15000
Body (g)	291.6	276.7	291.8	304.4	290.8
Brain (g)	2.188	2.206	2.242	2.218	2.153
Heart (g)	1.038	0.972	0.976	1.009	0.965
Liver (g)	11.75	10.64	11.07	11.39	11.50
Kidney (both) (g)	1.856	1.758	1.777	1.956	1.895
Adrenal (both) (mg)	93.02	85.01	86.45	94.64	83.40
Thymus (mg)	393.3	354.5	415.6	403.6	388.6
Ovary (both) (mg)	178.6	174.4	187.0	186.9	184.1
Spleen (g)	0.553	0.526	0.563	0.598	0.539

Method: *OECD Guidelines No. 407 (May 12, 1981)*[2]
EPA Guidelines (May 30, 1988)[3]

A total of 100 albino rats were used, 10 males and 10 females per dose group. The test material was administered in the diet for 3 month at doses of 0, 150, 800, 3000, and 15000 ppm. The experiment was carried out under specified pathogen free (SPF) standard laboratory conditions. The animal room was air-conditioned at a temperature of 22 $\pm$ 2 ^{o}C and a humidity of 55 $\pm$ 10%. The room was illuminated for

12 hours daily with 16-20 air changes/hour. The test article was administered orally in the diet (admixed to pelleted food). The control animals were fed with similarly pelleted food without the test article. Animals were provided standard diet and tap water ad libitum. The study examined macroscopically and microscopically the following tissues: skin, spleen, mammary area, mesenteric lymph nodes, axillary lymph node, sternum with bone marrow, femur with joint, skeletal muscle, trachea, lung, heart, aorta, submandibular salivary gland, liver, pancreas, esophagus, stomach small and large intestine, kidney, urinary bladder, prostate, seminal vesicle, testis, epididymis, uterus, vagina, ovary, pituitary gland, adrenal gland, thyroid with parathyroid gland, thymus, peripheral nerve, brain, spinal cord, eye with optic nerve, orbital gland, extraorbital lacrimal gland, tongue, and any tissue with gross lesions. [1]

GLP: Yes **[X]** No **[ ]** ? **[ ]**

Test substance: 1,3,5-tris(3,5-di-tert-butyl-4-hydroxybenzyl-)-1,3,5-triazine-2,4,6(1H,3H,6H)-trione

Remarks: The study is assigned a reliability code of 2b (guideline study with acceptance restrictions) [4]

Reference:

[1]3-Month Oral Toxicity Study in Rats, Test No.: 884665, Ciba-Geigy Limited, Basle, Switzerland, December 19, 1990.

[2]OECD Guideline for testing of chemicals, No. 407, (May 12, 1981). "Repeated Dose Oral Toxicity – Rodent: 28-day or 14-day Study"

[3]EEC May 30, 1988). SubChronic Oral toxicity test: 90-day repeated oral dose (rodent species).

[4]Klimisch, H.J., Andreae, M and Tillman, U. A systemic approach for evaluating the quality of experimental toxicological and ecotoxicologic al data. *Regulatory Toxicology and Pharmacology.* 25:1-5, 1997.

B. 90-DAY SUBACUTE ORAL TOXICITY STUDY IN ALBINO RATS

Species/strain: Albino Rats / Charles River strain

Sex: Female **[ ]**; Male **[ ]**; Male/Female **[X]**; No data **[ ]**

Route of Administration: Orally in the diet.

Frequency of treatment: 90 days

No. of animals per group: 15 males and 15 females / group

Initial bodyweight: 112.0 g in males
108.0 g in females

Dose: 0, 1000, 3000 and 10000 ppm (mg/kg food)

Control group: Yes **[X]**; No **[ ]**; No data **[ ]**;
Concurrent no treatment **[X]**; Concurrent vehicle **[ ]**; Historical **[ ]**

Results: Three deaths occurred during the investigation. Two of these deaths were ascribed to an acute respiratory infection while the other resulted from trauma incurred during the collection of blood samples. No untoward behavioral reactions were noted among any of the animals employed in the study.

No outstanding differences between test and control rats were noted with respect to body weights, food consumption and hematological studies. Histopathology and blood biochemistry indicated no deviation from the control. The NOEC was 10,000 ppm, the highest level tested.

Method: A total of 120 Charles River strain albino rats were used. 15 males and 15 females per dose group of 0, 1000, 3000, and 10000 ppm. The diet for any given group was prepared by blending the appropriate amount of test material with standard rat ration in a Hobart Mixer. Fresh diets were prepared each week. Animals were provided standard diet and tap water ad libitum. The control animals were fed with similar food without the test article. Each animal was weighed on the first day of the test and at weekly intervals there after. Following 90 days of feeding, all surviving rats were sacrificed and autopsied. Histopathological examinations were conducted on lungs, liver, trachea, small intestine, caecum, kidney and adrenal gland. Whereas gross pathological examinations were done on liver, kidneys, spleen, gonads, heart, and brain.[1]

GLP: Yes **[ ]** No **[X]** ? **[ ]**

Test substance: 1,3,5-tris(3,5-di-tert-butyl-4-hydroxybenzyl-)-1,3,5-triazine-2,4,6(1H,3H,6H)-trione

Remarks: The study is assigned a reliability code of 2e (Meets generally accepted scientific standards) [2]

Reference: [1]90-Day Subacute Oral Toxicity in Albino Rats, IBT No. B7758, Industrial Bio-Test Laboratories, Inc., Northbrook, Illinois , March 11, 1970.

[2]Klimisch, H.J., Andreae, M and Tillman, U. A systemic approach for evaluating the quality of experimental toxicological and ecotoxicological data. *Regulatory Toxicology and Pharmacology*. 25:1-5, 1997.

C. 90-DAY SUBACUTE ORAL TOXICITY STUDY IN BEAGLE DOGS

Species/strain: Purebred Beagle dogs

Sex: Female **[ ]**; Male **[ ]**; Male/Female **[X]**; No data **[ ]**

Route of Administration: Orally in the diet.

Frequency of treatment: 90 days

No. of animals per group: 4 males and 4 females / group

Dose: 0, 1000, 3000 and 10000 ppm (mg/kg food)

Control group: Yes **[X]**; No **[ ]**; No data **[ ]**;
Concurrent no treatment **[X]**; Concurrent vehicle **[ ]**; Historical **[ ]**

Results: No significant abnormalities were observed in food consumption, body weights, mortality and hematologic studies. Histopathology and blood biochemistry indicated no deviation from the control.

Reactions:
No behavioral reactions were noted at any of the levels tested.

Mortality:
No fatalities occurred during the investigation.

Opthalmic Examinations:
Opthalmic examinations conducted prior to the inception of the test and after 45 and 90 days of testing revealed no significant abnormalities at any of the levels tested.

Hematologic Studies:
Values for the test dogs were comparable to those of the untreated control dogs.

Pathologic Studies:
In pathologic studies, organ weight data, and gross and histopathologic studies showed no significant abnormalities when compared to control group.

No treatment related effects were noted at any of the treatment levels, therefore, the NOEL was the highest dietary concentration tested (10,000 ppm).

Method: The beagle dogs were housed in kennels equipped with outside runs, four dogs of the same sex and group being accommodated in a single kennel. Test material was incorporated into a stock diet and fed to the dogs seven days a week. The body weight of each dog was determined initially and there after every week till the end of the experiment. Water was available to the animals at all times. The dogs were under observation during the investigation and were examined daily for clinical signs or symptoms indicative of systemic toxicity. At the conclusion of the investigation, the dogs from each group were sacrificed. All major tissues and organs were examined grossly and histopathological examinations were conducted on

lungs, liver, trachea, small intestine, caecum, kidney, thyroid glands, pituitary glands and adrenal glands.[1]

GLP: Yes **[X]** No **[ ]** ? **[ ]**

Test substance: 1,3,5-tris(3,5-di-tert-butyl-4-hydroxybenzyl-)-1,3,5-triazine-2,4,6(1H,3H,6H)-trione

Remarks: The study is assigned a reliability code of 2e (Meets generally accepted scientific standards) [2]

Reference: [1]90-Day Subacute Oral Toxicity Study in Beagle Dogs, IBT No. C7759, Industrial Bio-test Laboratories Inc., March 2, 1970.

[2]Klimisch, H.J., Andreae, M and Tillman, U. A systemic approach for evaluating the quality of experimental toxicological and ecotoxicological data. *Regulatory Toxicology and Pharmacology*. 25:1-5, 1997.

5.5 CHRONIC TOXICITY/ CARCINOGENICITY

Species/strain: Wistar Rats

Sex: Female **[ ]**; Male **[ ]**; Male/Female **[X]**; No data **[ ]**

Route of Administration: Orally in the diet

Frequency of treatment: 24 months

No. of animals: 40 rats in total, of 20 males and 20 females

Doses: 100 mg / kg of powdered feed.

Control group: Yes **[X]**; No **[ ]**; No data **[ ]**;
Concurrent no treatment **[x]**; Concurrent vehicle **[ ]**; Historical **[ ]**

Results: Body weights and gross analysis did not show differences between control and treated rats.

Histological studies related to lungs, liver, spleen, pancreas, stomach, caecum, sigmoid and rectum, salivary glands, kidneys, uterus, ovaries, thyroid, thymus, lymphatic ganglions, heart, and bone marrow revealed no abnormal developments.

No cardiac lesions were found.

Pulmonary Mycoplasmosis: A chronic mycoplasmic brancho-pneumopathy was seen in three of the animals and a chronic beginning bronchopneumonia on mycoplasmosis was seen in three of the animals. These pulmonary afflictions were also seen in the control animals.

Suppurative Otitis: A suppurative otitis without basilar abscess was seen in three animals. Meningeal diencephalons reactions were found in one animal which had suppurative otitis with basilar abscess. Similar findings were also seen in the control animals.

Digestive Tract: No lesions of the oesophagus or phrynx present. Intestinal valvulus observed.

Liver: Hepatic teatosis, hepatic inflammatory infiltration was found in two rats. Such hepatic afflictions are common in the control animals.

Spleen, Thymus, Lymphatic Ganglions: Spleen lymphoid hypertrophy, and splenitis was found in three rats. Similar spleen conditions were found in the control animals. No thymic lesions present. Mesentric cyst found in some rats. Similar findings occurred in the control animals.

Urinary Organs: Cystic nephrosis was found in three treated rats. Nephritis found in one rat. Similar conditions observed in the control animals.

Endocrine glands: Cortico-suprarenal hypertrophy in 5 rats and hyperplasia on the hypophysis principal cells in 2 rats. Similar findings in control animals.

Male and Female Genital Organs: Testicular aplasia and epididymis inflammatory testicular infiltration found in a treated male rat. Similar findings occurred in control group. Hydrosalpinx, pyometra, congested

uterus, benign ovarian cysts, benign mammary adenofibroid, atrophic genital tract, and salient follicles were found in various treated females. Such findings were also found on the control females.

Conclusion: Treatment with the test substance did not cause malignant tumors in wistar rats.

Method: Rats were held in metal cages in a heated and ventilated environment. Animals were segregated by sex and had free access to feed. All tissue specimens were stained with toluidene blue.

Six male animals died during the experiments and the other 14 animals were sacrificed at the end of the study. Three females were sacrificed for a preliminary report, one female died during the course of the experiment, and the remaining sixteen females were sacrificed at the end of the experiment.

All of the autopsies performed on the animals were part of a complete histopathological study. [1]

Reproduction evaluation:

Method: One male and five females from the 2-year carcinogenicity study were mated after seven months of treatment with 100 ppm of the test material. Their offspring (25 males and 27 females, first generation) were normal. Out of these 52 offspring of the first generation, 5 males and 5 females were treated with the test substance. These first generation rats were mated 6 months later to obtain a second generation. Their offspring (26 males and 22 females, second generation) were all normal. Of the 48 animals (second generation), 5 males and 5 females underwent treatment[1].

Results: No teratogenic or congenital malformations are seen. All new born animals from the second generation were carefully examined macroscopically. Autopsy was done on 10 animals of the first and second generation each. Neither the macropathologic examination of the whole body nor the histopathology (lung, liver, spleen and kidney) showed any deviation from the normal morphology. There were no anomalies present in cranial-cerebral, digestive, thorax-visceral, abdominal, and genital studies.

GLP: Yes **[ ]** No **[** X**]** ? **[ ]**

Test substance: 1,3,5-tris(3,5-di-tert-butyl-4-hydroxybenzyl-)-1,3,5-triazine-2,4,6(1H,3H,6H)-trione

Remarks: The study is assigned a reliability code of 4d[2] [not assignable - original reference in a foreign language (French)]. Provides supplementary information.

Reference: [1]Chronic Toxicity / Carcinogenicity Study in Rats, “Expertise de toxicology chronique sur le produit GR 3114 (antioxidant)”. Prof. M. Mosinger, Instituts Universitaires de Recherches Scientifiques, Marseille, France, 1978.

[2]Klimisch, H.J., Andreae, M and Tillman, U. A systemic approach for evaluating the quality of experimental toxicological and ecotoxicological data. *Regulatory Toxicology and Pharmacology*. 25:1-5, 1997.

I U C L I D

D a t a S e t

Existing Chemical	Substance ID: 128-37-0
CAS No.	128-37-0
EINECS Name	2,6-di-tert-butyl-p-cresol
EINECS No.	204-881-4
Molecular Weight	220.36
Molecular Fromula	C15H24O

Producer Related Part

Company:	Bayer AG
Creation date:	03-MAR-1994

Substance Related Part

Company:	Bayer AG
Creation date:	03-MAR-1994

Memo:	X AKTUELL EG
Printing date:	29-JAN-2001
Revision date:	04-JUN-1994
Date of last Update:	**29-JAN-2001**
Number of Pages:	**41**
Chapter (profile):	Chapter: 1.1, 1.2, 1.3, 1.4, 1.5, 1.7, 1.9, 1.15, 2.1, 2.2, 2.3, 2.4, 2.5, 2.6.1, 2.12, 3.1.1, 3.1.2, 3.2, 3.3.1, 3.3.2, 3.5, 3.7, 3.8, 4.1, 4.2, 4.3, 4.5.2, 4.6.1, 4.6.2, 4.6.3, 4.9, 5.1.1, 5.1.2, 5.1.3, 5.1.4, 5.4, 5.5, 5.6, 5.8, 5.9, 5.11, 7
Reliability (profile):	Reliability: without reliability, 1, 2, 3, 4
Flags (profile):	Flags: robust summary

1.1 General Substance Information

Substance type: organic
Physical status: solid
Purity: > 99 % w/w
Remark:
- Bayer AG is lead company for the substance.
- Great Lakes Chemicals France S.A. is another manufacturer/ importer who has agreed on the above lead function.
- Derivados Fenolicos S.A. (Derfesa) is owned by Shell Espana S.A. For this submission both are represented by Shell International Chemical Company Ltd.
- Bayer AG, Great Lakes Chemicals France S.A. and Shell International Chemical Company Ltd. are cooperating companies of the CEFIC Sector Group European Butylated Hydroxytoluene Manufacturers Association (EBMA).

Flag: robust summary
10-JUN-1994

1.2 Synonyms

2,6-DI-TERT-BUTYL-4-METHYLPHENOL
Flag: robust summary

2,6-DI-TERT-BUTYL-P-CRESOL
Flag: robust summary

4-HYDROXY-3,5-DI-TERT-BUTYLTOLUENE
Flag: robust summary

BHT
Flag: robust summary

BUTYLATED HYDROXY TOLUENE
Flag: robust summary

BUTYLATED HYDROXYTOLUENE
Flag: robust summary

P-CRESOL, 2,6-DI-TERT-BUTYL-
Flag: robust summary

PHENOL, 2,6-BIS(1,1-DIMETHYLETHYL)-4-METHYL-
Flag: robust summary

1.3 Impurities

-

1.4 Additives

-

1.5 Quantity

Production during the last 12 months: yes
Quantity produced : 5 000 - 10 000 tonnes in 1993
Remark: 1992 5000 - 10000 t/a
1991 1000 - 5000 t/a
1990 1000 - 5000 t/a
Flag: robust summary

Quantity
Remark: no change of production volume 1999
Flag: robust summary
17-NOV-2000

1.7 Use Pattern

Type: type
Category: Wide dispersive use
Flag: robust summary

Type: industrial
Category: Fuel industry
Flag: robust summary

Type: industrial
Category: Polymers industry
Flag: robust summary

Type: industrial
Category: other: foodstuffs and feed industry
Flag: robust summary

Type: use
Category: Food/foodstuff additives
Flag: robust summary

Type: use
Category: Stabilizers
Flag: robust summary

1.9 Source of Exposure

Remark: human exposure by direct and indirect food additive consumption
Flag: robust summary

1.15 Additional Remarks

-

2.1 Melting Point

Value: 70 degree C
Reliability: (2) valid with restrictions
Flag: robust summary
02-NOV-2000 (1) (2) (3)

2.2 Boiling Point

Value: 265 degree C at 1013 hPa
Reliability: (2) valid with restrictions
Flag: robust summary
02-NOV-2000 (1) (4) (2) (3)

2.3 Density

Type: density
Value: 1.03 g/cm3 at 20 degree C
Reliability: (1) valid without restriction
Flag: robust summary
17-NOV-2000 (5)

Type: density
Value: 1.048 at 20 degree C
Reliability: (2) valid with restrictions
Flag: robust summary
18-OCT-2000 (4) (2)

2.4 Vapour Pressure

Value: .01 hPa at 20 degree C
Reliability: (1) valid without restriction
Flag: robust summary
02-NOV-2000 (6)

Value: .03 hPa at 25 degree C
Reliability: (1) valid without restriction
Flag: robust summary
02-NOV-2000 (6)

2.5 Partition Coefficient

log Pow: 5.1
Method: other (measured): no data
Year:
Flag: robust summary
(7)

2.6.1 Water Solubility

Value: 1.1 mg/l at 20 degree C
Reliability: (2) valid with restrictions
Flag: robust summary
17–NOV–2000 (8)

Value: .4 mg/l at 20 degree C
Reliability: (2) valid with restrictions
Flag: robust summary
02–NOV–2000 (9)

2.12 Additional Remarks

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3.1.1 Photodegradation

Type: water
Light source: Sun light
Light spect.: 310 – 400 nm
Conc. of subst.: .6 mg/l
Method: other (measured)
Year: **GLP:** no data
Test substance: other TS: purity of 4-14CH3-BHT > 99%
Result: 25.2% of applied radiolabelled BHT was found after 8 days of exposure (volatiles amounted to ca. 1.4%)
Test condition: test duration: 8 days, 8 hours sunlight per day
Reliability: (2) valid with restrictions
study well documented, meets generally accepted scientific principles
Flag: robust summary
29-JAN-2001 (10)

Type:
INDIRECT PHOTOLYSIS
Sensitizer: OH
Conc. of sens.: 500000 molecule/cm3
Method: other (calculated): acc. to Atkinson
Year: **GLP:**
Test substance:
Remark: Calculated half-life: t1/2 ca. 17 hours (0.5 x 10E6 OH radicals/cm3, under conditions of Western Europe; rate constant 23.3 x 10E-12 cm3/molecule x s, sigma-value for meta position of OH group to H-atoms derived from Hammet)
Reliability: (2) valid with restrictions
accepted calculation method
Flag: robust summary
09-NOV-2000 (11)

3.1.2 Stability in Water

Type: abiotic
Method: other: (measured)
Year: **GLP:** no data
Test substance: other TS: purity of radiolabelled BHT > 99%
Result: 59.6% of radiolabelled BHT was recovered after 8 days in the
Test condition: test duration: 8 days; test medium: distilled water without irradiation
Reliability: (2) valid with restrictions
study well documented, meets generally accepted scientific principles
Flag: robust summary
29-JAN-2001 (10)

3.2 Monitoring Data (Environment)

-

3.3.1 Transport between Environmental Compartments

Type: adsorption
Media: other: water-sediment
Method:
Year: 1978
Method: adsorption to river sediment calculated from measured test substance concentrations in river water and sediment; GC/MS analysis
Result: adsorption factor: 4000
Reliability: (2) valid with restrictions
Flag: robust summary
10-NOV-2000 (12)

3.3.2 Distribution

Media: air – biota – sediment(s) – soil – water
Method: Calculation according Mackay, Level I
Year:
Result:

Air:	81.2 %
Water:	0.9 %
Soil:	9.2 %
Sediment:	8.6 %
suspended Sediment:	<0.1 %
Biota:	<0.1 %

Reliability: (1) valid without restriction
accepted calculation method
Flag: robust summary
29-JAN-2001 (13)

3.5 Biodegradation

Type: aerobic
Inoculum: activated sludge
Concentration: .3 mg/l related to Test substance
Degradation: ca. 10 % after 56 day
Method: other
Year: **GLP:** no data
Test substance: other TS: purity of radiolabelled BHT > 99%
Remark: mineralization/elimination depended on ratio BHT/activated sludge; concentration (solubility) of test substance, and the presence of a dispersing agent (e.g. ethanol)
Result: after 56 days of exposure about 10% of 14C-phenyl-BHT were mineralized and about 99% eliminated altogether; half-life of disappearance: 3.4 days
Test condition: incubation at 25°C in the dark, ethanol as dispersing agent, sludge concentration: 100 mg/l, measurement of CO2 evolution
Reliability: (2) valid with restrictions
study well documented, meets generally accepted scientific principles
Flag: robust summary
09-NOV-2000 (14)

Type: aerobic
Inoculum: activated sludge
Concentration: 50 mg/l related to Test substance
Degradation: 4.5 % after 28 day
Result: other: not readily biodegradable
Method: other: see remarks
Year: **GLP:** no data
Test substance: no data
Remark: The test was conducted in accordance with "Biodegradation test of chemical substance by microorganisms etc." stipulated in the Order Prescribing the Items of the Test Relating to the New Chemical Substance (1974, Order of the Prime Minister, the Minister of Health and Welfare, the Minister of International Trade and Industry No. 1). This guideline corresponds to "301C, Ready Biodegradability: Modified MITI Test I" stipulated in the OECD Guidelines for Testing of Chemicals (May 12, 1981)
Test condition: deviations from guideline:
sludge concentration: 50 mg/l
substance concentration: 50 mg/l
Reliability: (2) valid with restrictions
study conducted similar to guideline
Flag: robust summary
09-NOV-2000 (15)

3.7 Bioaccumulation

Species: Cyprinus carpio (Fish, fresh water)
Exposure period: 56 day
Concentration: .05 mg/l
BCF: 230 – 2500
Elimination:
Method: other: see remarks
Year: **GLP:** no data
Test substance: no data
Remark: The test was conducted in accordance with "Bioaccumulation test of chemical substance in fish and shellfish" stipulated in the Order Prescribing the Items of the Test Relating to the New Chemical Substance (1974, Order of the Prime Minister, the Minister of Health and Welfare, the Minister of International Trade and Industry No. 1). This guideline corresponds to "305C, Bioaccumulation: Degree of Bioconcentration in Fish" stipulated in the OEDC Guidelines for Testing of Chemicals (May 12, 1981)
Reliability: (1) valid without restriction
guideline study
Flag: robust summary
09-NOV-2000 (15)

Species: Cyprinus carpio (Fish, fresh water)
Exposure period: 56 day
Concentration: .005 mg/l
BCF: 330 – 1800
Elimination:
Method: other: see remarks
Year: **GLP:** no data
Test substance: no data
Remark: The test was conducted in accordance with "Bioaccumulation test of chemical substance in fish and shellfish" stipulated in the Order Prescribing the Items of the Test Relating to the New Chemical Substance (1974, Order of the Prime Minister, the Minister of Health and Welfare, the Minister of International Trade and Industry No. 1). This guideline corresponds to "305C, Bioaccumulation: Degree of Bioconcentration in Fish" stipulated in the OEDC Guidelines for Testing of Chemicals (May 12, 1981)
Reliability: (1) valid without restriction
guideline study
Flag: robust summary
09-NOV-2000 (15)

3.8 Additional Remarks

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AQUATIC ORGANISMS

4.1 Acute/Prolonged Toxicity to Fish

Type: semistatic
Species: Brachydanio rerio (Fish, fresh water)
Exposure period: 96 hour(s)
Unit: mg/l **Analytical monitoring:** yes
LC0: > .57
Method: Directive 84/449/EEC, C.1 "Acute toxicity for fish"
Year: 1994 **GLP:** yes
Test substance:
Remark: only 1 test substance concentration was applied (1.0 mg/l; nominal); before starting the test, the test substance was crushed with a pestle. To accelerate the adjustment of the test concentration, 5 mg of the test substance was added to 1 litre of water, the resulting suspension was stirred on a magnetic stirrer for 24 hours, treated in an ultrasonic bath for 1 hour, and finally filtered to remove undissolved particels of the test substance; analyt. monitoring: GC
Result: LC0 related to effective test substance concentration measured after 24 h exposure (water change after 24 h).
Test condition: 21.4-21.9° C; pH 7.6-8.1; dissolved oxygen: 8.4-9.7 mg/l
Reliability: (2) valid with restrictions
Guideline study, but recovery of test substance at end of test < 80 %
Flag: robust summary
29-JAN-2001 (16)

4.2 Acute Toxicity to Aquatic Invertebrates

Species: Daphnia magna (Crustacea)
Exposure period: 48 hour(s)
Unit: mg/l **Analytical monitoring:** yes
EC0: > .31
Method: other: Directive 67/548/EEC, C.2 "Acute Toxicity for Daphnia"
Year: 1994 **GLP:** yes
Test substance: as prescribed by 1.1 - 1.4
Method: only 1 test substance concentration was applied (1.0 mg/l; threshold of water solubility); before starting the test, the test substance was crushed with a pestle. To accelerate the adjustment of the test concentration, the test substance was added to 1 liter of Elendt medium, the resulting suspension was stirred on a magnetic stirrer for 24 hours, treated in an ultrasonic bath for 1 hour, and finally filtered to remove undissolved particels of the test substance; analytical monitoring: GC
Result: EC0 related to mean of the test substance concentration measured at beginning of test and after 48 hours of exposure
Reliability: (2) valid with restrictions
Guideline study, but recovery of test substance at end of test < 80 %
Flag: robust summary
25-JAN-2001 (17)

4.3 Toxicity to Aquatic Plants e.g. Algae

Species: Scenedesmus subspicatus (Algae)
Endpoint: other: biomass and growth rate
Exposure period: 72 hour(s)
Unit: mg/l **Analytical monitoring:** yes
EC50: > .42
Method: other: Directive 67/548/EEC, C.3 "Algal inhibition test"
Year: 1994 **GLP:** yes
Test substance:
Method: only one test substance concentration applied (1 mg/l; nominal); before starting the test, the test substance was crushed with a pestle. To accelerate the adjustment of the test concentration, 5 mg of the test substance was added to 1 litre of water, the resulting suspension was stirred on a magnetic stirrer for 24 hours, treated in an ultrasonic bath for 1 hour, and finally filtered to remove undissolved particles of the test substance; analytical monitoring: GC
Remark: at a measured test concentration of 0.42 mg/l (= arithmetic mean of analytical values at start and end of the test) there was a slightly lower cell density at the end of test as compared to control (304000 and 358000 cells/ml, respectively); on the other hand, the cell density multiplied by a factor of 30 within 72 hours, which is much more than required for fullfilling the quality criteria with respect to the growth in the control (>= factor 16). For this reason, the slight differences of growth between control and test is regarded and not relevant to the result.
Result: EC50 is given as arithmetic mean of the measured test substance concentration at the beginning and end of test after 72 hours of exposure
Reliability: (2) valid with restrictions
Guideline study, but recovery of test substance at end of test < 80 %
Flag: robust summary
29-JAN-2001 (18)

4.5 Chronic Toxicity to Aquatic Organisms

4.5.2 Chronic Toxicity to Aquatic Invertebrates

Species: Daphnia magna (Crustacea)
Endpoint: reproduction rate
Exposure period: 21 day
Unit: mg/l **Analytical monitoring:** yes
NOEC: .14
Method: other: OECD Guide–line 202, part 2 "Daphnia sp., Reproduction Test" draft 1993
Year: 1994 **GLP:** yes
Test substance:
Method: semi–static test with 3 test substance concentration applied (0.1, 0.316 and 1 mg/l; nominal); before starting the test, the test substance was crushed with a pestle. To accelerate the adjustment of the test concentration 1 mg/l (= limit of water solubility), 5 mg of the test substance was added to 1 litre of Elendt medium, the resulting suspension was stirred on a magnetic stirrer for 24 hours, treated in an ultrasonic bath for 1 hour, and finally filtered to remove undissolved particles of the test substance; test medium renewed; analytical monitored by GC after 48 and 72 h of exposure
Remark: EC0 based on mean measured test substance concentrations (at the start and after 48 h and 72 h of exposure at water change)
Test condition: 20.0–21.6° C; pH 7.8–8.4; dissolved oxygen: 9.2–11.7 mg/l; irradiation: 7.5 uE/m3 x s; light/dark–cycle: 16/8 h
Reliability: (2) valid with restrictions
Guideline study, but recovery of test substance at end of test < 80 %
Flag: robust summary
29–JAN–2001 (19)

TERRESTRIAL ORGANISMS

4.6.1 Toxicity to Soil Dwelling Organisms

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4.6.2 Toxicity to Terrestrial Plants

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4.6.3 Toxicity to other Non–Mamm. Terrestrial Species

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4.9 Additional Remarks

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5.1 Acute Toxicity

5.1.1 Acute Oral Toxicity

Type: LD50
Species: rat
Sex: male/female
Number of Animals:
Vehicle: other: an aqueous dispersion at 10% (W/V) of gum Arabic
Value: > 2930 mg/kg bw
Method: OECD Guide-line 401 "Acute Oral Toxicity"
Year: 1988 **GLP:** yes
Test substance: other TS: Rhodianox BHT AP5
Remark: NUMBER OF ANIMALS: 5/dose/sex
MORTALITY: 0/10 (2150 mg/kg); 1/5 (f)/0/5 (2510 mg/kg) death occurred 5th day after application; 0/10 (2930 mg/kg)
CLINICAL SIGNS: no
BODY WEIGHT: no effect
GROSS EXAMINATION: no effect
Reliability: (1) valid without restriction
Flag: robust summary
29-NOV-2000 (20)

Type: LD50
Species: rat
Sex: male/female
Number of Animals:
Vehicle: other: propyleneglycol
Value: > 10000 mg/kg bw
Method: other: 1 dose level; 14 days observation period
Year: 1978 **GLP:** no
Test substance: other TS: Vulkanox KB
Remark: NUMBER OF ANIMALS: 10/dose/sex
MORTALITY: 0/20 (10 g/kg)
CLINICAL SIGNS: no
BODY WEIGHT: no data
GROSS EXAMINATION: no effect
Reliability: (2) valid with restrictions
Flag: robust summary
14-NOV-2000 (21) (22)

5.1.2 Acute Inhalation Toxicity

-

5.1.3 Acute Dermal Toxicity

Type: LD50
Species: rat
Sex: male/female
Number of Animals:
Vehicle: other: an aqueous dispersion at 10% (W/V) of gum Arabic
Value: > 2000 mg/kg bw
Method: OECD Guide-line 402 "Acute dermal Toxicity"
Year: 1988 **GLP:** yes
Test substance: other TS: Rhodianox BHT AP5
Remark: NUMBER OF ANIMALS: 5/dose/sex
MORTALITY: 0/10 (2000 mg/kg)
CLINICAL SIGNS: no
LOCAL EFFECTS: no
BODY WEIGHT: no effect
Reliability: (1) valid without restriction
Flag: robust summary
14-NOV-2000 (23)

5.1.4 Acute Toxicity, other Routes

-

5.4 Repeated Dose Toxicity

Species: rat **Sex:** male
Strain: Fischer 344
Route of admin.: oral feed
Exposure period: 76 weeks
Frequency of treatment: daily
Post. obs. period: none
Doses: 100, 300, 1000, 3000 and 6000 ppm
(ca. 7.5, 23, 75, 225 and 450 mg/kg bw day)
Control Group: yes, concurrent no treatment
NOAEL: 3000 ppm
Method: other: see remark field
Year: 1990 **GLP:** no data
Test substance: other TS: purity: > 99 %
Remark: The study was not designed as definitive chronic bioassay. 21 rats /dose and 36 control rats; the diets were prepared every 4 weeks and stored at 4oC until use (no analytical data available); interim kill at 12, 36 and 48 weeks of 4 randomly selected animals; observations of pathology: To demonstrate a deficiency in iron storage in cells of altered hepatocellular foci, rats were iron-loaded with sc injections of 12.5 mg elemental iron/100 g body weight in the inguinal regions, alternating sides 3 times/week for 2 weeks prior to killing. Complete autopsies livers were performed on all animals. At autospsy, livers were weighed and slices from each lobe were taken and fixed in 10% neutral buffered formalin. Sections were stanined with haematoxylin and eosin and tested for iron to determine the presence of iron storage-deficient lesions.

Tumors and lesions other organs were submitted for histology.

Result: All scheduled rats survived for up to 76 weeks
6000 ppm:
BODY WEIGHT: decreased
LIVER WEIGHT: increased
HISTOPATHOLOGICAL EXAMINATION (liver): no altered foci by 36 weeks; slightly, but not significantly altered foci at 48 and 76 weeks; after 76 weeks slightly increased incidence of hepatic adenomas (33 %)
3000 ppm:
BODY WEIGHT: decreased
LIVER WEIGHT: no effect
HISTOPATHOLOGICAL EXAMINATION (liver): no altered foci by 36 weeks; slightly, but not significantly altered foci at 48 and 76 weeks
1000 ppm:
BODY WEIGHT: no effect
LIVER WEIGHT: no effect
HISTOPATHOLOGICAL EXAMINATION (liver): no altered foci by 36 weeks; slightly, but not significantly altered foci at 48 and 76 weeks
300 ppm:
BODY WEIGHT: no effect
LIVER WEIGHT: no effect
HISTOPATHOLOGICAL EXAMINATION (liver): no altered foci by 36 weeks; slightly, but not significantly altered foci at 48 and 76 weeks
100 ppm:
BODY WEIGHT: no effect
LIVER WEIGHT: no effect
HISTOPATHOLOGICAL EXAMINATION (liver): no altered foci by 36 weeks; slightly, but not significantly altered foci at 48 and 76 weeks

Reliability: (2) valid with restrictions
Flag: robust summary
17-NOV-2000 (24)

Species: rat **Sex:** male/female
Strain: Wistar
Route of admin.: oral feed
Exposure period: male: 14 weeks (P); 141-144 weeks (F1)
female: 20 weeks (P); 141-144 weeks (F1)
Frequency of treatment: daily
Post. obs. period: non
Doses: nominal: 0, 25 100 and 500 mg/kg bw (P); 0, 25, 100 and 250 mg/kg bw (F1)
Control Group: yes, concurrent no treatment
NOAEL: 25 mg/kg bw
Method: other: Two generation carcinogenicity study; the F1 generation being dosed for their entire lifespan (for further details see remark field and also chapter 5.8)
Year: 1986 **GLP:** no data
Test substance: other TS: purity > 99.5 %
Remark: ADMINISTRATION OF BHT: The BHT was mixed into a semi-synthetic powdered diet in concentrations adjusted according to food

consumption. Diet was prepared every second week. the stability of BHT in the diet was examined four times during each of the feeding periods fot the F0 and F1 generations. The actual levels of BHT in the prepared diets were a few percent less than the added amounts.
NUMBER OF ANIMALS (F1): Control: 100/sex; 25 mg/kg: 80/sex; 100 mg/kg: 80/sex; 250 mg/kg: 100/sex
SERUM CHEMISTRY (only high dose F1, 20/sex):
glucose
blood urea nitrogen
free and total cholesterol
triglycerides
phospholipids
BLOOD ANALYSES (only high dose F1):
haematocrit
haemoglobin
red and white blood cell
differential white cell counts
PATHOLOGY (only F1): Specimens from the liver, kidneys, heart, lungs, brain, spleen, pituitary gland, tyroid, thymus (if any), pancreas, adrenals, testes, ovaries, seminal gland, uterus, mesenteric and axillary lymph nodes, salivary gland, gastro-intestinal tract (six levels), urinary bladder, spinal cord, peripheral nerve, skeletal muscle, bone, skin, mammary gland, eye and Harderian gland were fixed in 10 % neutral buffered formalin and embedded in paraffin, and sections were stained with haematoxylin and eosin for histological examination. Other appropriate staining methods were used for selected specimens.
SURVIVAL in Controls: 16 males and 17 females
EFFECTIVE NUMBERS: animals that survived beyond wk 43, the time when the first tumour appeared in the spleen of a male rat in the high-dose group

Result: 500 mg/kg (P):
BODY WEIGHT: decrease (m/f)
250 mg/kg (F1):
BODY WEIGHT: decrease (m: 21%; f:16%)
SURVIVAL: increase (m: 44 f: 39)
SERUM CHEMISTRY: decreased levels of triglyceride (f/m)
BLOOD ANALYSES: no effect (data not tabulated)
PATHOLOGY: increased number of liver adenomas in the males (18 animals with adenoma/99 (= "effective numbers")
100 mg/kg (P):
BODY WEIGHT: no effect described
100 mg/kg (F1)
BODY WEIGHT: decrease (m: 11%; f:10%)
SURVIVAL: increase (m: 34; f: 26)
PATHOLOGY: no signifcant effect
25 mg/kg (P):
BODY WEIGHT: no effect described
25 mg/kg (F1):
BODY WEIGHT: decrease (m: 7%; f:5%)
SURVIVAL: (m: 44; f: 39)
PATHOLOGY: no significant effect

Reliability: (2) valid with restrictions
Flag: robust summary
21-NOV-2000 (25)

Species: rat **Sex:** male
Strain: Wistar
Route of admin.: gavage
Exposure period: 28 days
Frequency of treatment: daily
Post. obs. period: none
Doses: 0, 25, 250 and 500 mg/kg bw day
Control Group: yes, concurrent vehicle
NOAEL: = 25 mg/kg bw
Method: other: see remark field
Year: 1986 **GLP:** yes
Test substance: other TS: purity: 99.9 %; vehicle: arachis oil
Remark: EXPERIMENTAL DESIGN: Twenty rats were randomly to one of four groups and were given a dose of 25, 250 of 500 mg BHT/kg vehicle for 7 days. The rats in the 500 mg/kg group initially received doses of 750 mg BHT/kg for the first 3 days and a dose of 500 mg BHT/kg for the remaining days. After 7 days the rat were killed by cervical dislocation and autopsied.
In the next phase of the experiment, groups of ten rats were treated with 0, 25, 250 or 500 mg BHT/kg daily for 28 days and were then killed and autopsied. Small samples of liver and epididymal adipose tissue were stored at –20oC and later analysed for BHT by HPLC.
EXPERIMENTAL TECHNIQUES USED TO EXAMINE LIVER TOXICITY:
BIOCHEMICAL ASSAYS:
Mircosomal protein
Glucose–6–phosphatase
Epoxide hydrolase
Total cytochrome P–450
Cytochrome b5
Ethoxyresorufin–O–deethylase
BHT oxidase
IMMUNOCYTOCHEMISTRY: sections of liver from rats killed after 28 days were stained immunocytochemically for cytochromes P–448 and P–450 using the three–layer PAP method of Sternburger (Immunocytochemistry, 2nd Ed. Raven Press, N.Y. (1979))
MICROSCOPIC EXAMINATION: samples of the 4 major lobes were fixed in 10% neutral buffered formalin; sections were stained with haematoxylin and eosin, with Van Giesons´s stain for collagen and with Gordon and Sweet´s method for reticulin
Result: 500 mg/kg:
BODY WEIGHT: weight loss reversed when dose was reduced (7 days); marginally lower than that of the control group (28 days)
LIVER WEIGHT: marked increase (7 or 28 days)
BHT CONTENT: very little (liver, 7 or 28 days)); 227.4 mg/kg wet weight (7 days), 168.4 mg/kg wet weight (28 days)
LIVER BIOCHEMISTRY: increase of proteins (7 or 28 days); decrease in glucose 6–phosphatase activity (7 or 28 days); increase in ethoxycoumarin o–deethylase– and epoxide hydrolase activity (7 or 28 days)
HISTOPATHOLOGICAL EXAMINATION:
After 7 days:
Periportal region

hepatocyte necrosis	2/5
fibrosis	3/5
hepatocyte hypertrophy	3/5
hepatocyte hyperplasia	4/5
glycogen accumulation	4/5

After 28 days:
Periportal region

hepatocyte necrosis	6/10
fibrosis	5/10
bile–duct cell proliferation	4/10
hepatocyte hypertrophy	2/10
hepatocyte hyperplasia	3/10
pigment–laden macrophages	3/10
glycogen depletion	7/10
glycogen accumulation	0/10

IMMUNOCYTOCHEMISTRY: moderately –increased staining intensity in the hypertrophied viable hepatocytes adjacent to the areas of damage
250 mg/kg:
BODY WEIGHT: no effect (7 or 28 days)
LIVER WEIGHT: moderate increase (7 or 28 days)
BHT CONTENT: very little (liver, 7 or 28 days); 66.6 mg/kg wet weight (7 days), 119.8 mg/kg wet weight (28 days)
LIVER BIOCHEMISTRY: increase of protein (28 days); decrease in glucose 6–phosphatase activity (28 days); increase in ethoxycoumarin o–deethylase– and epoxide hydrolase activity (7 or 28 days)
HISTOPATHOLOGICAL EXAMINATION: glycogen accumulation (7 days: (4/5) 28 days: (8/10));
IMMUNOCYTOCHEMISTRY: no effects
25 mg/kg:
BODY WEIGHT: no effect (7 or 28 days)
LIVER WEIGHT: slight increase (7 or 28 days)
BHT CONTENT: very little (liver, 7 or 28 days); 11 mg/kg wet weight (7 days), 15.5 mg/kg wet weight (28 days)
LIVER BIOCHEMISTRY: no effects (7 or 28 days)
HISTOPATHOLOGICAL EXAMINATION: no effects
IMMUNOCYTOCHEMISTRY: no effect

Reliability: (1) valid without restriction
Flag: robust summary
20–NOV–2000 (26)

Species: rat **Sex:** male/female
Strain: Wistar
Route of admin.: other: diet
Exposure period: male: 5 weeks (P); 4 weeks (F1), 6, 11, 16 and 22 months (F1)
female: 8 weeks (P)
Frequency of treatment: daily (during the period of mating, food pots were removed when male and females were mated)
Post. obs. period: no
Doses: nominal: 0, 25, 100 and 500 mg/kg bw (P); 0, 25, 100 and 250 mg/kg bw (F1)
Control Group: yes, concurrent no treatment
NOAEL: 25 mg/kg bw
Method: other: Two generation study with emphasis on hepatocellular changes in F1 generation (for further details see remark field and also chapter 5.8)
Year: 1994 **GLP:** yes
Test substance: other TS: purity: 99.96%
Remark: EXPERIMENTAL TECHNIQUES USED TO EXAMINE LIVER TOXICITY:
BIOCHEMICAL ASSAYS:
Glucose 6-phosphatase
Epoxide hydrolase
Glutathione S-transferase
Total cytochrome P450
Ethoxyresorufin O-deethylase
Pentoxyresorufin O-dependentylase
Total glutathione
Total, microsomal and cytosolic protein
IMMUNOCYTOCHEMISTRY: Slides were stained with a three layer biothinylated streptavidin horseradish peroxidase method and the following polyclonal primary antibodies:
anti rat Cytochrome P450 1A subfamily
anti rat Cytochrome P450 2B subfamily
anti murine microsomal Epoxide Hydrolase
MICROSCOPIC EXAMINATION: light and electron microscopy were used; cellular proliferation using the technique of pulse labelling with osmotic pumps containing bromodeoxyuridine was only assessed in the high dose F1-animals beginning with 4 weeks after weaning
MICROSCOPIC EXAMINATION OF THE THYRIOD: The diagnostic criteria for hyperactivity are the presence of some or all of the following:
Reduction of the follicular size
Absence or reduction of colloid
Irregularities in the follicular outline
Hyperaemia
Increase in number of follicular cells
ADMINISTRATION OF BHT: the amount of BHT incorporated initially per unit weight of diet was calculated from the food consumption measured during acclimatisation and from normal growth rate of this strain of rats; throughout pregnancy and lactation no effort was made to adjust dietry BHT content in line with body weight gain during this time
Result: 500 mg/kg (P, females, 20 gestation day):
BODY WEIGHT: no effect

LIVER WEIGHT: increase
HISTOPATHOLOGICAL EXAMINATION (liver): 4/5 animals showed mild centrilobular enlargement and eosinophilia
LIVER BIOCHEMISTRY:
IMMUNOCYTOCHEMISTRY in the liver: no effect
500 mg/kg (foetuses):
LIVER TO BODY RATIO: no effect
BODY WEIGHT: no effect
LIVER WEIGHT: no effect
HISTOPATHOLOGICAL EXAMINATION (liver): no effect
LIVER BIOCHEMISTRY: a trend towards an increase in glucose 6-phosphatase; activity; results for cytochrome P450 and its isoenzymes have not been presented
IMMUNOCYTOCHEMISTRY in the liver: no effect
500 mg/kg (male pups, 21 days post partum):
LIVER TO BODY RATIO: no effect
BODY WEIGHT: decrease
LIVER WEIGHT: decrease
HISTOPATHOLOGICAL EXAMINATION (liver): no effect
LIVER BIOCHEMISTRY: increase in pentoxyresorufin O-dependentylase; increase in total cytochrome P450; increase in glatathione S-transferase- and epoxide hydrolase activity
IMMUNOCYTOCHEMISTRY in the liver: no effect
250 mg/kg (F1, males 4 weeks post weaning):
LIVER TO BODY RATIO: increase
BODY WEIGHT: decrease
LIVER WEIGHT: decrease
HISTOPATHOLOGICAL EXAMINATION (liver): no effect (incl. cell proliferation)
LIVER BIOCHEMISTRY: statistical significant difference in pentoxyresorufin O-dependentylase activity; increase in ethoxyresorufin O-deethylase; increase in glutathione S-transferase- and epoxide hydrolase activity
IMMUNOCYTOCHEMISTRY in the liver: no effect
250 mg/kg (F1, males 6 months post weaning):
LIVER TO BODY RATIO: increased
BODY WEIGHT: below that of controls
LIVER WEIGHT: no effect
HISTOPATHOLOGICAL EXAMINATION (liver): centrilobular enlargement and eosinophilia (4/5); no cell proliferation
LIVER BIOCHEMISTRY:statistical significant difference in pentoxyresorufin O-dependentylase activity; increase in glutathione S-transferase- and epoxide hydrolase activity
IMMUNOCYTOCHEMISTRY in the liver: no effect
250 mg/kg (F1, males 11 months post weaning):
LIVER TO BODY RATIO: increase
BODY WEIGHT: decrease
LIVER WEIGHT: no effect
HISTOPATHOLOGICAL EXAMINATION (liver, incl. histochemical staining): centrilobular enlargement and eosinophilia (10/10), single altered hepatic focus (2/10), periportal induction of GGT (8/10), no cell proliferation; (kidneys): chronic progressive nephropathy; (thyroid): hyperactivity (10/10); (adrenals): no effects
LIVER BIOCHEMISTRY:statistical significant difference in pentoxyresorufin O-dependentylase activity; increase in total cytochrom P450; increase in glutathione S-transferase- and

epoxide hydrolase activity
IMMUNOCYTOCHEMISTRY in the liver: focal phenotypic or proliferative changes (2/19)
250 mg/kg (F1, males 16 months post weaning):
LIVER TO BODY RATIO: increase
BODY WEIGHT: decrease
LIVER WEIGHT: no effect
HISTOPATHOLOGICAL EXAMINATION (liver, incl. histochemical staining): centrilobular enlargement and eosinophilia (12/13), periportal induction of GGT (13/13), no cell proliferation; (kidneys): chronic progressive nephropathy; (thyroid): hyperactivity (13/13); (adrenals): no effects
LIVER BIOCHEMISTRY:statistical significant difference in pentoxyresorufin O-dependentylase activity; increase in total cytochrom P450; increase in glutathione S-transferase- and epoxide hydrolase activity
IMMUNOCYTOCHEMISTRY in the liver: focal phenotypic or proliferative changes (8/13)
TOTAL THYROXINE (T4): no effect
250 mg/kg (F1, males 22 months post weaning):
LIVER TO BODY RATIO: no effect
BODY WEIGHT: below that of controls
LIVER WEIGHT: no effect
HISTOPATHOLOGICAL EXAMINATION (liver, incl. histochemical staining): centrilobular enlargement and eosinophilia (18/19), nodules ((6/19) periportal induction of GGT (17/17), no cell proliferation (only one animal examined); (kidneys): chronic progressive nephropathy; (thyroid): hyperactivity (13/13); (adrenals): no effects
LIVER BIOCHEMISTRY: statistical significant difference in pentoxyresorufin O-dependentylase activity; increase in total cytochrom P450; increase in glutathione S-transferase- and epoxide hydrolase activity
IMMUNOCYTOCHEMISTRY in the liver: focal phenotypic or proliferative changes (14/19)
TOTAL THYROXINE (T4): no effect
100 mg/kg (P, females, 20. gestation day):
BODY WEIGHT: no effect
LIVER WEIGHT: no effect
HISTOPATHOLOGICAL EXAMINATION (liver): no effect
100 mg/kg (foetuses):
LIVER TO BODY RATIO: no effect
BODY WEIGHT: no effect
LIVER WEIGHT: no effect
HISTOPATHOLOGICAL EXAMINATION (liver): no effect
LIVER BIOCHEMISTRY: activity; results for cytochrome P450 and its isoenzymes have not been presented
100 mg/kg (F1, male pups, 21 days post partum):
LIVER TO BODY RATIO: no effect
BODY WEIGHT: no effect
LIVER WEIGHT: no effect
HISTOPATHOLOGICAL EXAMINATION (liver): no effect
LIVER BIOCHEMISTRY: increase in pentoxyresorufin O-dependentylase activity; increase in total cytochrome P450; increase in epoxide hydrolase activity
100 mg/kg (F1, males, 4 weeks post weaning):
LIVER TO BODY RATIO: no effect

BODY WEIGHT: below that of control
LIVER WEIGHT: no effect
HISTOPATHOLOGICAL EXAMINATION (liver): no effect
LIVER BIOCHEMISTRY: statistical significant difference in pentoxyresorufin O-depentylase activity; increase in ethoxyresorufin O-deethylase; increase in glutathione S-transferase- and epoxide hydrolase activity
100 mg/kg (F1, males 6 months post weaning):
LIVER TO BODY RATIO: no effect
BODY WEIGHT: below that of controls
LIVER WEIGHT: no effect
HISTOPATHOLOGICAL EXAMINATION (liver): centrilobular enlargement and eosinophilia (3/5)
LIVER BIOCHEMISTRY: statistical significant difference in pentoxyresorufin O-depentylase activity; increase in glutathione S-transferase- and epoxide hydrolase activity
100 mg/kg (F1, males 11 months post weaning): LIVER TO BODY RATIO: increased
BODY WEIGHT: below that of controls
LIVER WEIGHT: increased
HISTOPATHOLOGICAL EXAMINATION (liver, incl. histochemical staining): centrilobular enlargement and eosinophilia (6/8); single altered hepatic focus (2/10), periportal induction of GGT (3/8); (kidneys): chronic progressive nephropathy; (thyroid): hyperactivity (6/8); (adrenals): no effects
LIVER BIOCHEMISTRY: statistical significant difference in pentoxyresorufin O-depentylase activity; increase in glutathione S-transferase activity
100 mg/kg (F1, males 16 months post weaning):
LIVER TO BODY RATIO: no effect
BODY WEIGHT: below that of controls
LIVER WEIGHT: no effect
HISTOPATHOLOGICAL EXAMINATION (liver, incl. histochemical staining): centrilobular enlargement and eosinophilia (0/9), periportal induction of GGT (8/8); (kidneys): chronic progressive nephropathy; (thyroid): hyperactivity (7/9); (adrenals): no effects
LIVER BIOCHEMISTRY: statistical significant difference in pentoxyresorufin O-depentylase activity; increase in glutathione S-transferase- and epoxide hydrolase activity
TOTAL THYROXINE (T4): no effect
100 mg/kg (F1, males 22 months post weaning):
LIVER TO BODY RATIO: no effect
BODY WEIGHT: below that of controls
LIVER WEIGHT: no effect
HISTOPATHOLOGICAL EXAMINATION (liver, incl. histochemical staining): centrilobular enlargement and eosinophilia (4/11), periportal induction of GGT (7/11); (kidneys): chronic progressive nephropathy; (thyroid): hyperactivity (9/11); (adrenals): no effects
LIVER BIOCHEMISTRY: statistical significant difference in pentoxyresorufin O-depentylase activity; increase in glutathione S-transferase activity
TOTAL THYROXINE (T4): no effect
25 mg/kg (P, females, 20. gestation day):
BODY WEIGHT: no effect
LIVER WEIGHT: no effect

HISTOPATHOLOGICAL EXAMINATION (liver): 1/5 animals showed mild centrilobular enlargement and eosinophilia
25 mg/kg (foetuses):
LIVER TO BODY RATIO: no effect
BODY WEIGHT: no effect
LIVER WEIGHT: no effect
HISTOPATHOLOGICAL EXAMINATION (liver): no effect
LIVER BIOCHEMISTRY: results for cytochrome P450 and its isoenzymes have not been presented
25 mg/kg (F1, male pups, 21 days post partum):
LIVER TO BODY RATIO: no effect
BODY WEIGHT: no effect
LIVER WEIGHT: no effect
HISTOPATHOLOGICAL EXAMINATION (liver): no effect
LIVER BIOCHEMISTRY: increase in epoxide hydrolase activity
25 mg/kg (F1, males, 4 weeks post weaning):
LIVER TO BODY RATIO:no effect
BODY WEIGHT: no effect
LIVER WEIGHT: no effect
HISTOPATHOLOGICAL EXAMINATION (liver): no effect
LIVER BIOCHEMISTRY: no effects
25 mg/kg (F1, males 6 months post weaning):
LIVER TO BODY RATIO: no effect
BODY WEIGHT: no effect
LIVER WEIGHT: no effect
HISTOPATHOLOGICAL EXAMINATION (liver): centrilobular enlargement and eosinophilia (3/5)
LIVER BIOCHEMISTRY: increase in epoxide hydrolase activity
25 mg/kg (F1, males 11 months post weaning):
LIVER TO BODY RATIO: increased
BODY WEIGHT: no effect
LIVER WEIGHT: no effect
HISTOPATHOLOGICAL EXAMINATION (liver, incl. histochemical staining): centrilobular enlargement and eosinophilia (0/8), single altered hepatic focus (1/8), periportal induction of GGT (1/8); (kidneys): chronic progressive nephropathy; (thyroid): no effect; (adrenals): no effects
LIVER BIOCHEMISTRY: no effects
25 mg/kg (F1, males 16 months post weaning):
LIVER TO BODY RATIO: no effect
BODY WEIGHT: no effect
LIVER WEIGHT: no effect
HISTOPATHOLOGICAL EXAMINATION (liver, incl histochemical staining): centrilobular enlargement and eosinophilia (3/9), no periportal induction of GGT; (kidneys): chronic progressive nephropathy; (thyroid): no effect; (adrenals): no effects
LIVER BIOCHEMISTRY: increase in epoxide hydrolase
TOTAL THYROXINE (T4): no effect
25 mg/kg (F1, males 22 months post weaning):
LIVER TO BODY RATIO: no effect
BODY WEIGHT: no effect
LIVER WEIGHT: no effect
HISTOPATHOLOGICAL EXAMINATION (liver, incl. histochemical staining): centrilobular enlargement and eosinophilia (1/13); no periportal induction of GGT; (kidneys): chronic progressive nephropathy; (thyroid): no effect (adrenals): no effects
LIVER BIOCHEMISTRY: no effects

TOTAL THYROXINE (T4): no effect
CONCLUSIONS:
No BHT effect was seen in F0 generation although the lievers from lactating dams were much larger than those from respective controls and showed morphological evidence of considerable metabolic activity. The histological and biochemical changes seen in the F1 generation were similar to those reported by other workers on the hepatic effects of BHT and are consiistent with the effects of an inducer of cytochromes P450. The nodules and glucose 6–phosphatase deficient AHF observed at Time Point 7 of this experiment were probably induced by BHT. No evidence of thyroid increased activity as a result of BHT administration was observed at a dose level of 25 mg/kg body weight/day BHT. Hyperactivity occurred at dose levels of 100 and 250 mg/kg body weight/day BHT. It apped that BHT gave some protection against the development of chronic progressive nephrophathy (CPN), because CPN was observed in all rats (incl. controls) at every time point, but the disease was less serve in rats treated with 250 mg/kg. No adverse effect of BHT was observed in the adrenals.

Reliability: (1) valid without restriction
Flag: robust summary
17–NOV–2000 (27) (28)

5.5 Genetic Toxicity 'in Vitro'

Type: Bacterial gene mutation assay
System of testing: S. typhimurium TA102 and TA2638; E. coli WP2/pKM101 and WP2 uvrA/pKM101
Concentration:
Metabolic activation:
Result: negative
Method:
Year: 1998 **GLP:**
Test substance: other TS: purity: > 99%
Remark: In a large collaborative study ha been performed usinf the four bacterial strains in order to compare the specific spectrum of response to chemicals and to evaluate the usefulness of each strain.
Reliability: (2) valid with restrictions
Flag: robust summary
27–NOV–2000 (29)

Type: Cytogenetic assay
System of testing: CHO cells
Concentration: 0.1; 0.25 and 0.5 ug/ml
Metabolic activation: without
Result:
Method: other: see remark field
Year: 1995 **GLP:** no data
Test substance: other TS: BHT from Sigma (no further information)
Remark: METHOD: CHO cells were cultered for 15-16 h in the presence of the different doses of BHT. Two hours before cell harvesting,, cultures were added with colchicine (0.1 ug/ml final concentration). Air dried slides were prepared following routine protocols. Each treatment was repeated 5 times and a total of 500 metaphases per treatment (100 per repetition) was scored in coded slides. Statistical analysis was performed using X2 test. Untreated cultures and DMSO terated cultures (0.1 ml DMSO per 10 ml culture medium) were used as controls.
CYTOTOXICITY: mitotic index decreased to 71.5, 62.7 and 61.6% in relation to the mitotic index of untreated controls.
Result: Treatment with the three doses induced a significant increase of chromatid and isochromatid breaks with a corresponding increase of abnormal metaphases.
Reliability: (2) valid with restrictions
Flag: robust summary
23-NOV-2000 (30)

Type: Sister chromatid exchange assay
System of testing: CHO cells
Concentration: 0.1, 0.25 and 0.5 ug/ml
Metabolic activation: without
Result: negative
Method: other: see remark field
Year: 1995 **GLP:** no data
Test substance: other TS: BHT from Sigma (no further information)
Remark: METHOD: For SCE analysis, culture medium was added with 10 ug/ml of 5'-bromo-2'-deoxyuridine (BrdU) and the cells were incubated in complete darkness. CHO cells were incubated for 30 h. Two hours before fixation, cells were treated with colchicine (0.1 ug/ml final concentration). For each treatment 5 repetitions were made. Air dried slides were prepared following routine protocols and differential staining of sister chromatids were obtained according to Wolff and Perry (1974). Cytogenetic analysis was performed on coded slides. Statistical analysis was performed using multifactorial ANOVA. Untreated cultures and DMSO terated cultures (0.1 ml DMSO per 10 ml culture medium) were used as controls.
CYTOTOXICITY: >= 0.25 ug/ml; only a few metaphases could be analyzed in cells treated with 0.25 ug/ml (23 in relation to 180 of untreated and vehicle controls) and no cells at second mitosis after 0.5 ug/ml.
Reliability: (2) valid with restrictions
Flag: robust summary
23-NOV-2000 (30)

Type: Sister chromatid exchange assay
System of testing: human lymphocytes (from umbilical cord)
Concentration: 0.1, 0.25 and 0.5 ug/ml
Metabolic activation: without
Result: negative
Method: other: see remark field
Year: 1995 **GLP:** no data
Test substance: other TS: BHT from Sigma (no further information)
Remark: METHOD: For SCE analysis, culture medium was added with 10 ug/ml of 5'-bromo-2'-deoxyuridine (BrdU) and the cells were incubated in complete darkness. Human lymphocytes were incubated for 72 h. Two hours before fixation, cells were treated with colchicine (0.1 ug/ml final concentration). For each treatment 5 repetitions were made. Air dried slides were prepared following routine protocols and differential staining of sister chromatids were obtained according to Wolff and Perry (1974). Cytogenetic analysis was performed on coded slides. Statistical analysis was performed using multifactorial ANOVA. Untreated cultures and DMSO terated cultures (0.1 ml DMSO per 10 ml culture medium) were used as controls.
CYTOTOXICITY: = 0.5%; a decrease of cells in second division with increasing concentration (26 cells scored in relation to 155 and 165 of untreated and vehicle controls).
Reliability: (2) valid with restrictions
Flag: robust summary
22-NOV-2000 (30)

Type: other: Anaphase-telophase test
System of testing: CHO cells
Concentration: 0.1, 0.25 and 0.5 ug/ml
Metabolic activation: without
Result: negative
Method: other: see remark field
Year: 1995 **GLP:** no data
Test substance: other TS: BHT from Sigma (no further information)
Remark: METHOD: CHO cells were cultured as monolayer in 24 x 36 mm cover glasses attached with a small drop of siliconized grease to the bottom of 90-mm Petri dishes. Three cover glasses were placed in each Petri dish. Each cover glass was seeded with 1.5 ml of culture medium containing about 50,000 cells. After 1 h, 8.5 ml of culture medium was added to each Petri dish. Cultures were incubated at 37°C in a humidified atmosphere of 5% CO2. The set of cultures for each experiment was treated simultaneously for 8 h before fixation to avoid the detachment of cells from cover slides. Each treatment was repeated 5 times. Cell harvesting was acomplished by adding an equal volume of fixative (methanol-acetic 3:1) to the culture medium. After 10 min, two changes of fixative were made. Cover glasses were stained with Carbol fuchsin (Carr and Walker, 1961) and atteched with DPX mounting medium to coded slides. Statistical comparisons were made by means of the Sokal and Rohlf G method (Sokal, 1979). Regression analyzes were

performed to evaluate the mitotic index variations. Untreated cultures and DMSO terated cultures (0.1 ml DMSO per 10 ml culture medium) were used as controls.
CYTOTOXICITY: mitotic index decreased to 62.3, 22.2 and 20.2% in relation to the mitotic index of untreated controls.

Reliability: (2) valid with restrictions
Flag: robust summary
22-NOV-2000 (30)

Type: other: DNA synthesis inhibition test
System of testing: HeLa S3 cells
Concentration: 0.4, 0.8, 1.5, 3 and 6 mM
Metabolic activation: without
Result:
Method: other: see remark field
Year: 1996 **GLP:** no data
Test substance: other TS: purity: > 98%
Remark: METHOD: In the DIT a culture of logarithmically growing HeLa S3 cells was transferred into a single cell suspension by gently detaching the cells with EDTA (250 mg/1 PBS). Then the cells were seeded into 96-well microplates at a densitiy of 2 x 10 4 cells/well. The next day, the monolayers of the HeLa cells were exposed for 90 min to the materials to be tested. All concentrations were tested in triplicate; with each set of experiments usually repeated three times. Thereafter, the cells were washed by two rinses with fresh, pre-warmed medium and allowed to recover for 2 h. This was followed by addition of BrdU in a final concentration of 20 uM for 60 min. Subsequently, the cells were fixed with ethanol/acetic acid/water (90:5:5) for 30 min at room temperature. The alcohol was poured off and 4 N HCl was added to the fixed cells for 10 min to denature the DNA. Excess acid was washed away by rinsing the microplate twice with tap water. Then a 1:1500 dilution of a monoclonal anti-BrdU antivody was added to the cells for 30 min. After washing the cells three times with tap water, a 1:500 dilution of perocidase-conjugated F(ab)2-sheep-anti-mouse IgG antibody was added for another 30 min. The cells were washed three times with tap water, and a freshly prepared perocidase sustrate solution was added. The color development was stopped with a stop solution (H2SO4). The extinction of the wells was measured at 495 nm using an ELISA reader. Cell counts were determined by sulforhodamine B (SRB) adsorption to total cell protein, followed by elution of the dye with Tris buffer and colorimetric measurement at 564 nm. In all experiments, the standard genotoxin 4-NQO was used as positive control. BHT was dissolved in DMSO at a stock concentration of 2M. This stock solution was serially diluted in 1:2 steps and transferred onto the microplate with the tester organisms using a laboratory workstation.
CYTOTOXICITY: >= 1.5 mM; cell count decreased to 32 , 23 and 30% in relation to the vehicle control
Result: limited positive because higher degree of cytotoxicity (cell count < 40%) were observed at concentrations >= 1.5 mM
Reliability: (2) valid with restrictions
Flag: robust summary

23-NOV-2000 (31)

Type: other: Umu-test
System of testing: S. typhimurium TA 1535/pSK 1002
Concentration: 0.4, 0.8, 1.5, 3 and 6 mM
Metabolic activation: without
Result: negative
Method: other: see remark field
Year: 1996 **GLP:** no data
Test substance: other TS: purity: > 98%
Remark: METHOD: The umu test was performed by Reifferscheid et al., Mutat. Res. 253, 215-222 (1991). Salmonella from stock were grown in nutrient broth for the overnight culture. Logarithmically growing tester bacteria were exposed to varying concentrations of the test material. All concentrations were tested in triplicate; with each set of experiments usually repeated three times. After 2 h of exposure, the bacterial suspension was diluted 10-fold, followed by a subsequent additional incubation period of 2 h. Thereafter, bacterial growth was measured as turbidity (E600) with a microplate reader. The DNA damage induced expression of umuC was quantified via the determination of ß-galactosidase activity at 420 nm using ONPG o-nitrophenyl-ß-D-galactopyranoside; Sigma) as a substrate. In all experiments, the standard genotoxin 4-NQO (4-nitroquinoline N-oxide) was used as positive control. BHT was dissolved in DMSO at a stock concentration of 2M. This stock solution was serially diluted in 1:2 steps and transferred onto the microplate with the tester organisms using a laboratory workstation.
CYTOTOXICITY: no
Reliability: (2) valid with restrictions
Flag: robust summary

22-NOV-2000 (31)

Type: other: review of the mutagenicity/genotoxicity data up to 1991
System of testing:
Concentration:
Metabolic activation:
Result:
Method:
Year: **GLP:**
Test substance:
Result: A host of studies examining the potential of BHT to cause point mutations have been published. They include in vitro studies on various bacterial species and strains and on various types of mammalian cell lines. Together these studies convincingly show the absence of a potential for BHT to cause point mutations. A great number of studies on many cell types have also been carried out to examine the potential of BHT to cause chromosome aberrations. In vitro studies have been published using plant cells and the WI-38, CHL, CHO and V79 mammalian cell lines. Nearly all studies, especially those

using validated test systems, indicate that BHT lacks clastogenic potential. In vitro studies on bacterial, yeast and various mammalian cells including DON, CHO, CHL cells and primary hepatocytes demonstrate the absence of interactions with or damage to DNA.

Reliability: (2) valid with restrictions
Flag: robust summary
22-NOV-2000 (32)

5.6 Genetic Toxicity 'in Vivo'

Type: other: in vivo-in vitro replicative DNA synthesis test
Species: rat **Sex:** male
Strain: Fischer 344
Route of admin.: other: gavage or s.c. injection (no further information available)
Exposure period: single dose
Doses: 450 mg/kg and 900 mg/kg
Result: positive
Method: other: see remark field
Year: 1994 **GLP:** no data
Test substance: no data
Remark: METHOD: the vehicle used was corn oil; the numbers of animals treated and the number from which primary hepatocyte cultures were produced is not mentioned; production of primary hepatocyte cultures and assessment of RDS induction was performed using published procedures (Uno et al., Toxicol. Lett. 63, 191-199 and 201-209 (1992));
Judgement criteria for RDS incidence: RDS incidence was evaluated by our earlier documented judgement criteria. In the time-course experiment, when the maximum RDS incidence was 2.0% or above, it was considered to indicate a positive response. An incidence less than 1.0% was judged to be negative. an incidence between 1.0 and 2.0% was considered equivocal, and a dose-response experiment was subsequently performed. In this second experiment, when the incidence was 1.0% or above at any of the doses, a final judgement of positive was made, whereas a reponse of less than 1.0% was rated as negative.
Result: In the time course experiment BHT caused dose-related RDS induction; RDS incidence (%) after 450 mg/kg: 0.3 (24 h), 1.2 (39 h), 0.2 (48 h); RDS incidence (%) after 900 mg/kg: 2.5 (24 h), 9.2 (39 h), 0.8 (48 h) the hepatocyte viability did not vary from untreated control value
Reliability: (3) invalid
Flag: robust summary
23-NOV-2000 (33)

Type: other: liver DNA damage
Species: rat **Sex:** female
Strain: Sprague–Dawley
Route of admin.: gavage
Exposure period: first dose 21 h before killing; second dose 4 h before killing
Doses: among others 700 mg/kg bw and 140 mg/kg bw (no further information)
Result:
Method: other: see remark field
Year: 1994 **GLP:** no data
Test substance: no data
Remark: METHOD: the vehicle used for gavage was 2% gum tragacanth in water; the numbers of animals treated and the number from which hepatic DNA was otained is not mentioned; the rat hepatic DNA damage assay (alkaline elution) was performed as described by Kitchin and Brown, Teratogenesis, Carcinogenesis and Mutagenesis 9, 61 (1989). The data was analyzed by analysis of variance, and where statistically significant differences wer found, they were then evaluated with Student´s t–test.
Result: As the highest dose did not show the DNA–damaging effects that one lower dose did, no dose response curve or regression model will fit
the highest tested dose that did not cause rat liver DNA damage to a statistically significant extent: 140 mg/kg
the lowest tested dose that caused rat liver DNA damage: 700 mg/kg
Reliability: (3) invalid
Flag: robust summary
23–NOV–2000 (34)

Type: other: review of the mutagenicity/genotoxicity data up to 1991
Species: **Sex:**
Strain:
Route of admin.:
Exposure period:
Doses:
Result:
Method:
Year: **GLP:**
Test substance:
Result: A host of studies examining the potential of BHT to cause point mutations have been published. They include in vivo studies on Drosophila melanogaster, silk worms and also the mouse specific locus test (involving long–term exposure.) Together these studies convincingly show the absence of a potential for BHT to cause point mutations. A great number of studies on many species have also been carried out to examine the potential of BHT to cause chromosome aberrations. In vivo studies have been carried out on somatic and/or germ cells of Drosophila melanogaster, rats and mice. Nearly all studies, especially those using validated test systems, indicate that BHT lacks clastogenic potential.
Reliability: (2) valid with restrictions
Flag: robust summary
22–NOV–2000 (32)

5.8 Toxicity to Reproduction

Type: Two generation study
Species: mouse **Sex:** male/female
Strain: other: Crj:CD-1
Route of admin.: oral feed
Exposure Period: F0 and F1: during premating, mating, gestation and lactation (ca. 11 weeks)
Frequency of treatment: daily
Premating Exposure Period
male: no exact information given (probable during premating and mating period)
female: no exact information given (probable during premating, mating period, during gestation and lactation)
Duration of test: until postnatal day 21 of the F2 generation
Doses: 0.015, 0.045, 0.135 and 0.405 % in diet (ca. 22.5, 67.5, 202.5 and 607.5 mg/kg bw/day)
Control Group: yes, concurrent no treatment
NOAEL F1 Offspr.: .405 %
NOAEL F2 Offspr.: .405 %
Method: other: see remark field
Year: 1993 **GLP:** no data
Test substance: no data
Remark: METHOD: No. of mice/sex/dose: 10; mating period: 5 days; M/F ratio per cage: 1/1; length of cohabitation: no data; neurobehavioural procedure: The functional and behavioural developmental parameters were measured and scored for the individual pups in the lactation period in F1 and F2 generations, and were analyzed on a whole-litter basis. The measured parameters were as follows: surface righting on postnatal day 4 and 7, negative geotaxis on PND 4 and 7, cliff avoidance on PND 7, swimming behaviour (direction, head angle, and limb movement) on PND 4 and 14, and olfactory orientation on PND 14. Open field activity of mice was measured at 3 weeks of age in the F1 and F2 generations, both male and female. the apparatus used in this study was a square white board, 30 x 30 cm, divided by black lines into 25 equal squares. Ambulation, rearing, 180° turn, defectation, urination, and preening were recorded for 3 min in the apparatus. In the F1 generation, the following parameters were measured on postnatal (PND) 0: litter size, litter weight, and sex ration (m/f); the pubs were weighed on PND 0,4,7,14 and 21 in the lactation period; the pups were removed from their dams at 4 weeks of age, and were selected at random to continue treatment; the F1 animals were mated at 9 weeks of age; in the F2 generation some parameter of the pups were measured identically to the F1 generation from birth to weaning. For the F0 generation only data on mortality are reported administration of BHT: no further information given
Result: F0 generation:
MORTALITY: Two dams died during the second week of the lactation period; one dam in the 0.015% group and one in the 0.045% group.
F1 generation:
0.015%:
MORTALITY: 1 dam died during 2nd week of lactation period

SURVIVAL INDEX (PND 21): 100% (control: 91.8%)
BODY WEIGHT: increased at PND 0,4 and 21
NO. of LITTERS: no effect
NO. of PUPS: no effect
LITTER SIZE: no effect
LITTER WEIGHT: no effect
SEX RATIO: no effect
NEUROBEHAVIOURAL PARAMETERS: increased surface righting at PND 7
0.045%:
SURVIVAL INDEX (PND 21): 90.3% (control: 91.8%)
BODY WEIGHT: no effect
NO. of LITTERS: no effect
NO. of PUPS: no effect
LITTER SIZE: no effect
LITTER WEIGHT: no effect
SEX RATIO: no effect
NEUROBEHAVIOURAL PARAMETERS: reduced ambulation in male mice
0.135%:
SURVIVAL INDEX (PND 21): 100% (control: 91.8%)
BODY WEIGHT: decreased at PND 14
NO. of LITTERS: no effect
NO. of PUPS: no effect
LITTER SIZE: no effect
LITTER WEIGHT: no effect
SEX RATIO: no effect
NEUROBEHAVIOURAL PARAMETERS: no effect
0.405%:
SURVIVAL INDEX (PND 21): 98.3% (control: 91.8%)
BODY WEIGHT: decreased at PND 7, 14 and 21
NO. of LITTERS: no effect
NO. of PUPS: no effect
LITTER SIZE: no effect
LITTER WEIGHT: no effect
SEX RATIO: no effect
NEUROBEHAVIOURAL PARAMETERS: no effect
F2 generation:
0.015%:
SURVIVAL INDEX (PND 21): 100% (control: 100%)
BODY WEIGHT: increased at PND 0,4, 7, 14 and 21
NO. of LITTERS: no effect
NO. of PUPS: no effect
LITTER SIZE: no effect
LITTER WEIGHT: no effect
SEX RATIO: no effect
NEUROBEHAVIOURAL PARAMETERS: reduced 180o turn (m)
0.045%:
SURVIVAL INDEX (PND 21): 99.1% (control: 100%)
BODY WEIGHT: no effect
NO. of LITTERS: no effect
NO. of PUPS: no effect
LITTER SIZE: no effect
LITTER WEIGHT: no effect
SEX RATIO: no effect
NEUROBEHAVIOURAL PARAMETERS: reduced 180o turn (m), reduced ambulation in both sex
0.135%:

SURVIVAL INDEX (PND 21): 99.1% (control: 100%)
BODY WEIGHT: decreased at PND 14
NO. of LITTERS: no effect
NO. of PUPS: no effect
LITTER SIZE: no effect
LITTER WEIGHT: no effect
SEX RATIO: no effect
NEUROBEHAVIOURAL PARAMETERS: increased surface righting at PND 4, reduced 180o turn (m)
0.405%:
SURVIVAL INDEX (PND 21): 99.1% (control: 100%)
BODY WEIGHT: decreased at PND 7, 14 and 21
NO. of LITTERS: no effect
NO. of PUPS: no effect
LITTER SIZE: no effect
LITTER WEIGHT: no effect
SEX RATIO: no effect
NEUROBEHAVIOURAL PARAMETERS: increased negative geotaxis at PND 4, reduced 180o turn (m)
CONCLUSION:
No effect on No. of litters, No. of pups, litter size, litter weight and sex ratio in any dose group of F1 and F2 animals; no effect on neurobehavioural parameters in F1 and F2 generation; the body weight of pups was increased in the 0.015% group at birth and during lactation period for each generation

Reliability: (2) valid with restrictions
Flag: robust summary
21-NOV-2000 (35)

Type: other: two generation carcinogenicity study
Species: rat **Sex:** male/female
Strain: Wistar
Route of admin.: oral feed
Exposure Period: male: 14 weeks (P); 141-144 weeks (F1)
female: 20 weeks (P); 141-144 weeks (F1)
Frequency of treatment: daily
Premating Exposure Period
male: 13 weeks
female: 13 weeks
Duration of test: 144 weeks
Doses: nominal: 0,25,100 and 500 mg/kg bw (P); 0, 25, 100 and 250 mg/kg bw (F1)
Control Group: yes, concurrent no treatment
Method: other: see remark
Year: 1986 **GLP:** no data
Test substance: other TS: purity: > 99.5 %
Remark: METHOD: No. of rats/sex/dose: 60 (control); 40 (25 mg/kg), 40 (100 mg/kg) and 100 (500 mg/kg); mating period was terminated within 1week; M/F ratio per cage: no data; length of cohabitation: no data; The only data reported are: gestation rate, No. of pups/litter and the body weight of pups at birth and at weaning
Result: F0 generation:
No difference was found in food consumption between treated and control rats; body weight gain of males and females was

reduced significantly from week 6 of treatment with 500 mg/kg, persisting throughout the lifespan of the F0 rats. Gestation rate was not affected by treatment (or even slightly increased in the treated groups).
The number of litters of ten or more pups at birth decreased significantly with increasing test substance dose.
F1 generation:
At weaning F1 rats had significantly lower body weights than the controls, the extend of the reduction being dose-related, although food consumption was not reduced in the treated groups. The effect was most pronounced in males.
500 mg/kg: decreased body weight (m/f) at weaning; the fraction of litters with ten or more pups decreased
100 mg/kg: decreased body weight (m/f) at birth and at weaning
25 mg/kg: no effects
The pathology findings (F1) including blood analysis and serum chemistry are presented in chapter 5.4 and 5.7("Repeated Dose Toxicity" and "Carcinogenicity").

Reliability: (2) valid with restrictions
Flag: robust summary
22-NOV-2000 (25)

Type: other: two generation study with emphasis on hepatocellular changes in F1 generation
Species: rat **Sex:** male/female
Strain: Wistar
Route of admin.: other: diet
Exposure Period: male: 5 weeks (P); 4 weeks (F1), 6, 11, 16 and 22 months (F1)
female: 8 weeks (P)
Frequency of treatment: daily (during the period of mating, food pots were removed when male and females were mated)
Premating Exposure Period
male: 3 weeks
female: 3 weeks
Duration of test: 22 months
Doses: nominal: 0,25,100 and 500 mg/kg bw (P); 0, 25, 100 and 250 mg/kg bw (F1)
Control Group: yes, concurrent no treatment
Method: other: see remark
Year: 1994 **GLP:** yes
Test substance: other TS: purity: 99.96%
Remark: NOAEL PARENTAL:
The NOEL for clinical signs during premating and mating phases, for both males and females, was 500 mg/kg.
The NOEL for effects on body weight during premating and mating phases was 500 mg/kg for the females and 100 mg/kg for the males.
The NOEL for maternal clinical signs and for effects on maternal body weight during gestationphase was 500 mg/kg.
The NOEL for maternal clinical signs and for effects on maternal body weight and food consumption during the lactation phase was 500 mg/kg.
NOAEL F1 OFFSPRING:
The NOEL for pup clinical signs were 500 mg/kg; the NOEL for pup body weight during lactation phase were 100 mg/kg

METHOD: premating exposure period for males (7/dose) and females (50/dose): 3 weeks; mating exposure period for males (6/dose) and females (48/dose): 2 weeks; M/F ratio per cage: 1/8; length of cohabitation: 15 hours/day; number of animals allocated for each scheduled autopsy: 20 days gestation: 5 pregnat females/dose, 21 days after parturition: 5 mothers/dose and 20 pups/dose, 4 weeks after weaning: 5 male pups/dose, 6 months after weaning: 5 male pups/dose; 11 months after weaning: 8-10 male pups/dose, 16 months after weaning: 9-13 male pups/dose, 22 months after weaning: 10-19 male pups, administration of BHT: the amount of BHT incorporated initially per unit weight of diet was calculated from the food consumption measured during acclimatisation and from normal growth rate of this strain of rats; throughout pregnancy and lactation no effort was made to adjust dietry BHT content in line with body weight gain during this time

Result: There were no differences in mating success. Pregnancy proceeded normally in all groups. There was no alteration in numbers of resorption sites. No statistically significant change was seen in the number of foetuses/dams. The number of pups per litter did not differ. There was a trend to an increase in the number of pups found dead or dying soon after birth with increase in dose but the acutal number of deaths in affected litters influenced by treatment with BHT. The total litter weight was significantly decreased for dams treated with the high dose of BHT. The weight gain of pups from dams receiving the hightest dose of BHT was consistently less than that of control pups or pups of dams receiving lower doses of BHT. The development was retarded in the high dose group. The pathology findings (P and F1), including liver-biochemistry, organ weights, gross and microscopic evaluations are presented in chapter 5.4 (Repeated Dose Toxicity").

Reliability: (1) valid without restriction

Flag: robust summary

20-NOV-2000 (27) (28)

5.9 Developmental Toxicity/Teratogenicity

Species: rat **Sex:** female
Strain: Sprague-Dawley
Route of admin.: gavage
Exposure period: 7th to 17th day of gestation
Frequency of treatment: daily
Duration of test: until day 20 on gestation
Doses: 100, 200, 300 and 400 mg/kg
Control Group: other: no data
Method: other: no data
Year: 1993 **GLP:** no data
Test substance: other TS: BHT (no further information) in corn oil
Remark: only abstract
Result: Pregnant performance and fetal developments were not affected; no significant differences were detected in maternal body weight gains and food intakes; a dose related increase in relative organ weight of liver at high doses; no significant fetal abnormalities in external and visceral observations; on skeletal examination sternebral retardation in BHT 300 mg/kg treated group were observed without dose dependence
Reliability: (4) not assignable
Flag: robust summary
21-NOV-2000 (36)

Species: rat **Sex:** female
Strain: Wistar
Route of admin.: gavage
Exposure period: days 7 to 17 of pregnancy
Frequency of treatment: daily
Duration of test: until day 20 of gestation
Doses: 0, 93.5, 187 and 375 mg/kg bw
Control Group: other: no data
Method: other: see remark field
Year: 1990 **GLP:** no data
Test substance: no data
Remark: abstract, figures and tables in English
METHOD: Number of animals per dose: 24 (control); 20 (93.5 and 187 mg/kg); 22 (375 mg/kg)
MATERNAL PARAMETERS assessed: clinical signs, body weight, food consumption and mortality;
REPRODUCTIVE PARAMETERS assessed: number of corpora lutea, number of implantation, number of live fetuses and sex ratio
FETAL PARAMETERS assessed: body weight; postnatal survival; external abnormalities; visceral and skeletal abnormality
Result: In the dams at the two higher doses of 187 and 375 mg/kg, toxic signs such as hair fluffing and diarrhoea were observed, and their body weight gain and food consumption were suppressed. Two dams, which showed marked diarrhoea in the highest dose group, died. However, there was no evidence of fetal malformation attributable to treatment with the compound in any of the dose groups treated, although a slight increase in fetal death was found in the highest dose group.
It is concluded that 2,2'-methylenebis (4-methyl-6-tert-butylphenol) has a weak lethal effect on fetal development but

not a teratogenic effect in the rat.
Reliability: (4) not assignable
Flag: robust summary
27-NOV-2000 (37)

Species: mouse **Sex:** female
Strain: other: JCL-ICR
Route of admin.: gavage
Exposure period: 7th to 13th day of gestation
Frequency of treatment: once a day
Duration of test: until the 18th day of gestation
Doses: 70, 240 and 800 mg/kg bw/day
Control Group: other: yes, concurrent vehicle and concurrent untreated
NOAEL Maternalt.: = 800 mg/kg bw
NOAEL Teratogen.: = 800 mg/kg bw
Method: other: see remark field
Year: **GLP:** no data
Test substance: other TS: food additive grade
Remark: BHT was dissoved in olive oil and was administered at a rate of 10 ml/kg/day
Age at study initiation: 8-13 week old
Number of animals per dose and vehicle control: 26
Number of animals in untreated control: 30
Mating: After keeping a pair of male and female mice together overnight, the female was examined in the next morning for the presence of vaginal plug. The mice with plug were considered as pregnant animal. The day where female mouse had virginal plug was designed as gestation day 0.
Body weight were measured everyday with the observation of general condition of the animal. The mice were sacrificed on 18th day of gestation by ether anesthetization. Immediately after sacrifice, abdomen of the dam was opened, then the number of implantation sites, corpus luteum absorbed embryos, dead or alive fetuses were counted. The alive fetuses were examined for their body weights, sex and external malformation. Major organs were weighed and the abnormality was observed grossly. Five dams were chosen at random and their alive fetuses were fixed with Bouin's fixative for observation of internal abnormalities. The remaining alive fetuses were fixed in 95% ethanol, then were stained with alizarin red S for examination of skeletal abnormalities.
MATERNAL PARAMETERS assessed: behavior; body weight; mortality; organ weights (liver, heart, spleen, kidneys, lung, adrenals and ovaries);
REPRODUCTIVE PARAMETERS assessed: gestation rate; number of corpora lutea, number of implantation and sex ratio
FETAL PARAMETERS assessed: body weight; postnatal survival; external abnormalities; skeletal deformity and abnormality
Result: 800 mg/kg:
MATERNAL PARAMETER: increased spleen weight; decreased liver weight (compared to the untreated control animals)
REPRODUCTIVE PARAMETERS: no effects
FETAL PARAMETER: no effects
240 mg/kg:
MATERNAL PARAMETER: no effects
REPRODUCTIVE PARAMETERS: no effects

FETAL PARAMETER: no effects
70 mg/kg:
MATERNAL PARAMETER: no effects
REPRODUCTIVE PARAMETERS: no effects
FETAL PARAMETER: no effects

Reliability: (2) valid with restrictions
Flag: robust summary
21-NOV-2000 (38)

Species: mouse **Sex:** female
Strain: other: JCL-ICR
Route of admin.: gavage
Exposure period: 9th day of gestation
Frequency of treatment: single administration
Duration of test: until the 18th day of gestation
Doses: 1200 and 1800 mg/kg bw
Control Group: yes, concurrent no treatment
NOAEL Maternalt.: < 1200 mg/kg bw
NOAEL Teratogen.: 1800 mg/kg bw
Method: other: see remark field
Year: **GLP:** no data
Test substance: other TS: food additive grade
Remark: BHT was dissoved in olive oil and was administered at a rate of 10 ml/kg/day
Age at study initiation: 8-13 week old
Number of animals per dose: 15
Number of animals untreated control: 19
Mating: After keeping a pair of male and female mice together overnight, the female was examined in the next morning for the presence of vaginal plug. The mice with plug were considered as pregnant animal. The day where female mouse had virginal plug was designed as gestation day 0.
Body weight were measured everyday with the observation of general condition of the animal. The mice were sacrificed on 18th day of gestation by ether anesthetization. Immediately after sacrifice, abdomen of the dam was opened, then the number of implantation sites, corpus luteum absorbed embryos, dead or alive fetuses were counted. The alive fetuses were examined for their body weights, sex and external malformation. Major organs were weighed and the abnormality was observed grossly. Five dams were chosen at random and their alive fetuses were fixed with Bouin's fixative for observation of internal abnormalities. The remaining alive fetuses were fixed in 95% ethanol, then were stained with alizarin red S for examination of skeletal abnormalities.
MATERNAL PARAMETERS assessed: behavior; body weight; mortality; organ weights (liver, heart, spleen, kidneys, lung, adrenals andovaries);
REPRODUCTIVE PARAMETERS assessed: gestation rate; number of corpora lutea, number of implantation and sex ratio
FETAL PARAMETERS assessed: body weight; postnatal survival; external abnormalities; skeletal deformity and abnormality
Result: 1800 mg/kg:
MATERNAL PARAMETER: 5/20 died (11th day 3; 14th day 1 and 15th day 1), increased lung and spleen weights
REPRODUCTIVE PARAMETERS: no effects

FETAL PARAMETER: delay of progression of ossification
1200 mg/kg:
MATERNAL PARAMETER: 2/20 died (11th day 1 and 15th day 1), increased lung weight
REPRODUCTIVE PARAMETERS: no effects
FETAL PARAMETER: delay of progression of ossification

Reliability: (2) valid with restrictions
Flag: robust summary
21-NOV-2000 (38)

5.11 Experience with Human Exposure

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(1) American Conference of Governmental Industrial Hygienists Inc., Cincinnati, Ohio: Documentation of the threshold limit values and biological exposure indices: 5th ed. (1986), p. 227

(2) Merck Index (CD-ROM), Whitehouse Station, NJ, USA: Merck and Co., Inc. (1996), No. 1583: Butylated Hydroxytoluene

(3) Römpps Chemie-Lexikon/Otto-Albrecht Neumüller. 8. Aufl. 1981, S. 935

(4) Auer Technikum/Auergesellschaft, Berlin, Ausg. 12 (1988)

(5) Bayer AG data, test on density (1973)

(6) Bayer AG data, test on vapour pressure (1986)

(7) Shell, unpublished data (1983)

(8) Bayer AG data, test on water solubility (1986)

(9) Verschueren, Karel: Handbook of Environmental Data on Organic Chemicals, 3rd ed. (1996), p. 638-639

(10) Mikami, N. et al., Chemosphere 5, 311-315 (1979)

(11) Atkinson, R., Environ. Toxicol. Chem. 7, 435-442 (1988)

(12) Jungclaus, G.A. et al., Environ. Sci. Technol. 12, 88-96 (1978)

(13) Mackay, Calculation of the environmental distribution of butylhydrxytoluene according to fugacity model level I (2000)

(14) Inui, H. et al., Chemosphere 6, 383-391 (1979)

(15) Biodegradation and Bioaccumulation Data of Existing Chemicals Based on the CSCL Japan, Compiled under the Supervision of Chemical Products Safety Division, Basic Industries Bureau MITI, Ed. by CITI, October 1992. Published by Japan Chemical Industry Ecology-Toxicology & Information Center

(16) Bayer AG, Acute fish toxicity of Stabilisator BHT, test report 466 A/94 (1994)

(17) Bayer AG, Acute toxicity of Stabilisator BHT to Daphnia magna, test report 466 A/94 (1994)

(18) Bayer AG, Acute toxicity of Stabilisator BHT to the alga Scenedesmus subspicatus, test report 466 A/94 (1994)

(19) Bayer AG, Chronic toxicity of Stabilisator BHT to daphnia magna; test report 466 A/94 (1994)

(20) Hazleton France (1988): Rapport No. 801300 to Rhone-Poulenc S.A.

(21) Bomhard, E., J. Am. Coll. Toxicol. 15, S72 (1996)

(22) Spanjers, M.T., Til, H.P. (1978): Determination of the acute oral toxicity of Vulkanox KB in rats. Unpublished report to Bayer AG, January 27, 1978

(23) Hazleton France (1988): Rapport No. 801301 to Rhone-Poulenc S.A.

(24) Williams, G.M. et al. (1990): Food Chem. Toxicol. 28, 799 – 806

(25) Olsen, P. et al. (1986): Food Chem. Toxicol. 24, 1 – 12

(26) Powell, C.J. et al. (1986): Food Chem. Toxicol. 24, 1131 – 1143

(27) McFarlane, M. et al., Food and Chemical Toxicology 35, 753-767 (1997)

(28) Price, S.C.; Robens Institute; Report No. RI93/TOX/0020, 29 July 1994

(29) Watanabe, K. et al., Mutat.Res. 416, 169-181 (1998)

(30) Grillo, C.A. & Dulout, F.N., Mutation Research 345, 73-78 (1995)

(31) Heil, J. et al., Mutation Research 368, 181-194 (1996)

(32) Bomhard, E.M. et al., Mutat. Res. 277, 187-200 (1992)

(33) Uno, Y. et al., Mutation Research 320, 189-205 (1994)

(34) Kitchin, K.T. & Brown J.L., Toxicology 88, 31-49 (1994)

(35) Tanaka, T. et al. (1993): Toxicol. Lett. 66, 295 – 304

(36) Han, S.Y. et al., Teratology 48, 507, B-39 (1993)

(37) Tanaka, S. et al., Eisei Shikejo Hokoku 108, 52-57 (1990)

(38) Tokyo Metropolitan Research Laboratory of Public Health (1978):
In: Shell Oil Co. (1992): NTIS/OTS 0535892

7.1 Risk Assessment

-

I U C L I D

D a t a S e t

Existing Chemical	ID: 2082-79-3
CAS No.	2082-79-3
EINECS Name	octadecyl 3-(3,5-di-tert-butyl-4-hydroxyphenyl)propionate
EINECS No.	218-216-0
Molecular Weight	530.88
Structural Formula	CC(C) (C)c1(c(O)=c(C(C) (C)C)cc(CCC(OCCCCCCCCCCCCCCCCCC)=O)c1)
Molecular Formula	C35H62O3

Producer Related Part
- Company: EUROPEAN COMMISSION - European Chemicals Bureau
- Creation date: 11-FEB-2000

Substance Related Part
- Company: EUROPEAN COMMISSION - European Chemicals Bureau
- Creation date: 11-FEB-2000

Printing date:	28-NOV-2001
Revision date:	11-FEB-2000
Date of last Update:	11-FEB-2000

Number of Pages: 47

Chapter (profile):	Chapter: 1, 2, 3, 4, 5, 7
Reliability (profile):	Reliability: without reliability, 1, 2, 3, 4
Flags (profile):	Flags: without flag, confidential, non confidential, WGK (DE), TA-Luft (DE), Material Safety Dataset, Risk Assessment, Directive 67/548/EEC, SIDS

1.0.1 OECD and Company Information

Name: BASF AG
Street: Karl-Bosch-Str
Town: 67056 Ludwigshafen
Country: Germany

Name: Ciba Additive GmbH
Street: Chemiestraße
Town: 68619 Lampertheim
Country: Germany
Phone: 06254-79237
Telefax: 06254-79511

Name: Ciba Specialty Chemicals Inc.
Town: 4002 Basel
Country: Switzerland

Name: Clariant GmbH
Town: 65926 Frankfurt am Main
Country: Germany

Name: GREAT LAKES CHEMICAL ITALIA
Street: VIA QUARANTA 29
Town: 20141 MILAN
Country: Italy
Phone: 0039(2)525751
Telefax: 0039(2)52575233

Name: Lowi Polymer Stabilizers GmbH
Street: Teplitzer Straße 14-16
Town: 84478 Waldkraiburg
Country: Germany
Phone: ++49 8638 608 0
Telefax: ++49 8638 608 200
Telex: 863884

Name: Raschig GmbH
Town: 67063 Ludwigshafen
Country: Germany

Name: Shell Nederland Chemie B.V.
Street: Vondelingenweg 601
Town: 3196 KK Rotterdam
Country: Netherlands

1.0.2 Location of Production Site
-

1.0.3 Identity of Recipients
-

1.1 General Substance Information

Substance type: organic
Physical status: solid

1.1.0 Details on Template
-

1.1.1 Spectra
-

1.2 Synonyms

3,5-Bis(1,1-dimethylethyl)-4-hydroxyphenyl]propionsäureoctadecylester;
Octadecyl(3,5-di-tert.-butyl-4-hydroxyhydrocinnamat;
Source: Raschig GmbH Ludwigshafen

3,5-Di-tert-butyl-4-hydroxyphenylpropionic acid octadecyl ester
Source: BASF AG Ludwigshafen

ADK Stab AO 50
Source: BASF AG Ludwigshafen
Hoechst AG Frankfurt/Main
Clariant GmbH Frankfurt am Main

Anox PP 18
Source: BASF AG Ludwigshafen
Hoechst AG Frankfurt/Main
Clariant GmbH Frankfurt am Main
Lowi Polymer Stabilizers GmbH Waldkraiburg

Antioxidant 1076
Source: BASF AG Ludwigshafen
Hoechst AG Frankfurt/Main
Clariant GmbH Frankfurt am Main

AO 4
Source: BASF AG Ludwigshafen
Hoechst AG Frankfurt/Main
Clariant GmbH Frankfurt am Main

Benzenepropanoic acid, 3,5-bis(1,1-dimethylethyl)-4-hydroxy-, octadecyl ester (9CI)
Source: BASF AG Ludwigshafen

Benzenepropanoic acid, 3,5-bis(1,1-dimethylethyl)-4-hydroxy-octadecyl ester
Source: Ciba Additive GmbH Lampertheim

E 376
Source: BASF AG Ludwigshafen
Hoechst AG Frankfurt/Main
Clariant GmbH Frankfurt am Main

Hydrocinnamic acid, 3,5-di-tert-butyl-4-hydroxy-, octadecyl ester (7CI, 8CI)
Source: BASF AG Ludwigshafen

I 1076
Source: BASF AG Ludwigshafen
Hoechst AG Frankfurt/Main
Clariant GmbH Frankfurt am Main

IR 1076
Source: BASF AG Ludwigshafen
Hoechst AG Frankfurt/Main
Clariant GmbH Frankfurt am Main

Irganox 1076
Source: Shell Nederland Chemie B.V. Rotterdam
BASF AG Ludwigshafen
Ciba Additive GmbH Lampertheim
Hoechst AG Frankfurt/Main
Clariant GmbH Frankfurt am Main

Irganox 1906
Source: BASF AG Ludwigshafen
Hoechst AG Frankfurt/Main
Clariant GmbH Frankfurt am Main

Irganox 1976
Source: BASF AG Ludwigshafen
Hoechst AG Frankfurt/Main
Clariant GmbH Frankfurt am Main

Irganox I 1076
Source: Hoechst AG Frankfurt/Main
Clariant GmbH Frankfurt am Main

Irganox L 107
Source: BASF AG Ludwigshafen
Hoechst AG Frankfurt/Main
Clariant GmbH Frankfurt am Main

Lowinox PO35
Source: Lowi Polymer Stabilizers GmbH Waldkraiburg

Mark AO 50
Source: BASF AG Ludwigshafen
Hoechst AG Frankfurt/Main
Clariant GmbH Frankfurt am Main

n-Ocetadecyl 3,5-di-tert-buthyl-4-hydroxyhydrocinnamate
Source: Hoechst AG Frankfurt/Main
Clariant GmbH Frankfurt am Main

n-Octadecyl .beta.-(4'-hydroxy-3',5'-di-tert-butylphenyl)propionate
Source: BASF AG Ludwigshafen

n-Octadecyl 3-(3,5-di-tert-butyl-4-hydroxyphenyl)propionate
Source: BASF AG Ludwigshafen

Naugard 76
Source: BASF AG Ludwigshafen
Hoechst AG Frankfurt/Main
Clariant GmbH Frankfurt am Main

nylpropanoate. Irganox 1076. Anox PP18.
Source: GREAT LAKES CHEMICAL ITALIA MILAN

Octadecyl .beta.-(4'-hydroxy-3',5'-di-tert-butylphenyl)propionate
Source: BASF AG Ludwigshafen

Octadecyl .beta.-(4-hydroxy-3,5-di-tert-butylphenyl)propionate
Source: BASF AG Ludwigshafen

Octadecyl 3,5-bis(1,1-dimethylethyl)-4-hydroxyphenylpropanoate
Source: BASF AG Ludwigshafen

Octadecyl 3-(3,5-di-tert-butyl-4-hydroxyphenyl)propionate
Source: BASF AG Ludwigshafen

Octadecyl 3-(4'-hydroxy-3',5'-di-tert-butylphenyl)propionate
Source: BASF AG Ludwigshafen

Octadecyl 3-(4-hydroxy-3,5-di-tert-butylphenyl)propionate
Source: BASF AG Ludwigshafen

Octadecyl-3-(3,5-di-tert-butyl-4-hydroxyphenyl)-propionate. Hydrocinnamic acid, 3,5-di-tert-butyl-4-hydroxy-,octadecyl ester.
3,5-di-tert-butyl-4-hydroxyphenylpropionic acid octadecyl ester. Octadecyl 3,5-bis(1,1-dimethylethyl)-4-hydroxyphe
Source: GREAT LAKES CHEMICAL ITALIA MILAN

Ralox 530
Source: BASF AG Ludwigshafen
Hoechst AG Frankfurt/Main
Clariant GmbH Frankfurt am Main

Stearyl .beta.-(3,5-di-tert-butyl-4-hydroxyphenyl)propionate
Source: BASF AG Ludwigshafen

Stearyl 3,5-di-tert-butyl-4-hydroxyhydrocinnamate
Source: BASF AG Ludwigshafen

Stearyl 3-(3,5-di-tert-butyl-4-hydroxyphenyl)propionate
Source: BASF AG Ludwigshafen

Sumilizer BP 76
Source: BASF AG Ludwigshafen
Hoechst AG Frankfurt/Main
Clariant GmbH Frankfurt am Main

TK 10044
Source: Ciba Specialty Chemicals Inc. Basel

U 276
Source: BASF AG Ludwigshafen
Hoechst AG Frankfurt/Main
Clariant GmbH Frankfurt am Main

Ultranox 276
Source: Hoechst AG Frankfurt/Main
Clariant GmbH Frankfurt am Main

Source: Ciba Specialty Chemicals Inc. Basel

1.3 Impurities
-

1.4 Additives
-

1.5 Quantity

Quantity 10 000 - 50 000 tonnes

1.6.1 Labelling
-

1.6.2 Classification
-

1.7 Use Pattern

Type: type
Category: Non dispersive use

Type: type
Category: Use in closed system

Type: type
Category: Use resulting in inclusion into or onto matrix

Type: industrial
Category: Polymers industry

Type: use
Category: Stabilizers

Type: use
Category: other: Anitoxidans

1.7.1 Technology Production/Use
-

1.8 Occupational Exposure Limit Values

Type of limit: MAK (DE)
Limit value: 1.5 mg/m3
Remark: Allgemeiner Staubgrenzwert, alveolengängiger Anteil
Source: Lowi Polymer Stabilizers GmbH Waldkraiburg

Type of limit: MAK (DE)
Limit value: 4 mg/m3
Remark: Allgemeiner Staubgrenzwert, einatembarer Anteil
Source: Lowi Polymer Stabilizers GmbH Waldkraiburg

Type of limit: MEL (UK)
Limit value: 10 mg/m3
Schedule: 8 hour(s)
Source: Ciba Specialty Chemicals Inc. Basel

Type of limit: other: Internal Exposure Limit (IEL),Grenzwert für Totalstaubexposion, 8h TWA
Limit value: 10 mg/m3
Source: Ciba Additive GmbH Lampertheim

Type of limit:
Limit value:
Remark: No occupational exposure limit values estabilished by OSHA, ACGIH, NIOSH.
Source: GREAT LAKES CHEMICAL ITALIA MILAN
(1)

Type of limit:
Limit value:
Remark: IEL-Wert: 10 mg/m3 8h TWA
Source: BASF AG Ludwigshafen
(2)

Type of limit:
Limit value:
Remark: Allgemeinen Staubgrenzwert beachten.
Source: Raschig GmbH Ludwigshafen

1.9 Source of Exposure

Country: Great Lakes Chemical Italia Pedrengo Plant (Bg).
Remark: produced by transesterification reaction of benzenepropanoic acid,3,5-bis(1,1-dimethylethyl)-4-hydroxy, methyl ester with octadecyl alcohol in presence of alkaline catalyst.
Source: GREAT LAKES CHEMICAL ITALIA MILAN

1.10.1 Recommendations/Precautionary Measures
-

1.10.2 Emergency Measures
-

1.11 Packaging
-

1.12 Possib. of Rendering Subst. Harmless
-

1.13 Statements Concerning Waste
-

1.14.1 Water Pollution

Classified by: other: Selbsteinstufung
Labelled by: other: Selbsteinstufung
Class of danger: 1 (weakly water polluting)
Source: BASF AG Ludwigshafen
(2)

Classified by: other: Wassergefährdungsklasse (WGK)
Labelled by:
Class of danger: 2 (water polluting)
Remark: Selbsteinstufung
Source: Hoechst AG Frankfurt/Main
Clariant GmbH Frankfurt am Main
(3)

1.14.2 Major Accident Hazards
-

1.14.3 Air Pollution

Classified by:
Labelled by:
Number: 3.1.7 (organic substances)
Class of danger: III
Source: BASF AG Ludwigshafen

(2)

1.15 Additional Remarks

Remark: DISPOSAL METHOD: by controlled incineration.
probable routes of human exposure may occur by inhalation or dermal contact during manufacturing
TRANSPORT INFORMATION: Rail/road(RID/ADR): NOT RESTRICTED
Sea(IMO/IMDG) : NOT RESTRICTED
AIR(ICAO/IATA) : NOT RESTRICTED
Source: GREAT LAKES CHEMICAL ITALIA MILAN

1.16 Last Literature Search
-

1.17 Reviews
-

1.18 Listings e.g. Chemical Inventories
-

2.1 Melting Point

Value: = 49 degree C
Decomposition: no
Sublimation: no
Method: other
Year: 1993
GLP: no
Source: GREAT LAKES CHEMICAL ITALIA MILAN
(1)

Value: = 50 - 55 degree C
Decomposition: no
Sublimation: no
Method: other
Year: 1990
GLP: no data
Source: GREAT LAKES CHEMICAL ITALIA MILAN
(4)

Value: = 50 - 55 degree C
Decomposition: no
Sublimation: no
Method: other: CIBA-GEIGY AG, Allgemeine Analytik,FO 3.31
Year: 1989
GLP: no
Source: Ciba Specialty Chemicals Inc. Basel
Ciba Additive GmbH Lampertheim

2.2 Boiling Point

Value:
Remark: not determinate
Source: GREAT LAKES CHEMICAL ITALIA MILAN

2.3 Density

Type: relative density
Value: = 1.02 g/cm3 at 25 degree C
Method: other
Year: 1994
GLP: no data
Source: GREAT LAKES CHEMICAL ITALIA MILAN
(5)

Type: relative density
Value: = 1.02 at 25 degree C
Method: other
Year: 1985
GLP: no
Source: Ciba Specialty Chemicals Inc. Basel
Ciba Additive GmbH Lampertheim

Type: relative density
Value: = 1.07 g/cm3 at 25 degree C
Year: 1993
GLP: no
Source: GREAT LAKES CHEMICAL ITALIA MILAN
(6)

2.3.1 Granulometry
-

2.4 Vapour Pressure

Value: = .00000000267 hPa at 20 degree C
Method: other (measured)
Year: 1990
GLP: no data
Source: GREAT LAKES CHEMICAL ITALIA MILAN
(4)

Value: at 20 degree C
Source: Ciba Specialty Chemicals Inc. Basel

2.5 Partition Coefficient

log Pow: > 6
Method: other (measured)
Year: 1994
GLP: no data
Source: GREAT LAKES CHEMICAL ITALIA MILAN
(7)

log Pow: > 6
Method: other (calculated)
Year: 1988
GLP: no
Source: Ciba Specialty Chemicals Inc. Basel
Ciba Additive GmbH Lampertheim

2.6.1 Water Solubility

Value: < .1 g/l at 20 degree C
pH: = 5.7 at 10 g/l
Method: other
Year: 1990
GLP: no data
Source: GREAT LAKES CHEMICAL ITALIA MILAN
(7)

Value: < .2 mg/l at 20 degree C
Qualitative: of very low solubility
pH: ca. 5.8 - 5.9
Method: Directive 84/449/EEC, A.6 "Water solubility"
Year: 1992
GLP: yes
Source: Ciba Specialty Chemicals Inc. Basel
Ciba Additive GmbH Lampertheim

2.6.2 Surface Tension

-

2.7 Flash Point

Value: = 273 degree C
Type: open cup
Method: Directive 84/449/EEC, A.9 "Flash point"
Year: 1994
GLP: no data
Source: GREAT LAKES CHEMICAL ITALIA MILAN
(8)

Value: 273 degree C
Type:
Method: other
Year:
Remark: DIN 51584
Source: Ciba Specialty Chemicals Inc. Basel

2.8 Auto Flammability

Value: = 340 degree C
Method: other
Year: 1994
GLP: no data
Source: GREAT LAKES CHEMICAL ITALIA MILAN
(4)

2.9 Flammability

Result:
Remark: no data
Source: GREAT LAKES CHEMICAL ITALIA MILAN

Result:
Source: Ciba Additive GmbH Lampertheim

2.10 Explosive Properties

Result:	not explosive
Method:	Directive 84/449/EEC, A.14 "Explosive properties"
Year:	1990
GLP:	yes
Remark:	Dust cloud may explode if ignited in an enclosed area 95 (bar m) 1/sec
Source:	GREAT LAKES CHEMICAL ITALIA MILAN

(9)

2.11 Oxidizing Properties

Result:	no oxidizing properties
Method:	other
Year:	1994
GLP:	no
Source:	GREAT LAKES CHEMICAL ITALIA MILAN

(6)

2.12 Additional Remarks

Remark:	no data
Source:	GREAT LAKES CHEMICAL ITALIA MILAN

3.1.1 Photodegradation

Type:
Method:
Year: GLP:
Test substance:
Remark: no data
Source: GREAT LAKES CHEMICAL ITALIA MILAN

3.1.2 Stability in Water

Type:
Method:
Year: GLP:
Test substance:
Remark: no data
Source: GREAT LAKES CHEMICAL ITALIA MILAN

3.1.3 Stability in Soil

Type: Radiolabel:
Concentration:
Cation exch. capac.
Microbial biomass:
Method:
Year: GLP:
Test substance:
Remark: no data
Source: GREAT LAKES CHEMICAL ITALIA MILAN

3.2 Monitoring Data (Environment)

Type of measurement:
Medium:
Method:
Concentration
Remark: no data
Source: GREAT LAKES CHEMICAL ITALIA MILAN

3.3.1 Transport between Environmental Compartments

Type:
Media:
Air (Level I):
Water (Level I):
Soil (Level I):
Biota (L.II/III):
Soil (L.II/III):
Method:
Year:
Remark: no data
Source: GREAT LAKES CHEMICAL ITALIA MILAN

3.3.2 Distribution

Media:
Method:
Year:
Remark: no data
Source: GREAT LAKES CHEMICAL ITALIA MILAN

3.4 Mode of Degradation in Actual Use

Remark: no data
Source: GREAT LAKES CHEMICAL ITALIA MILAN

3.5 Biodegradation

Type: aerobic
Inoculum: activated sludge
Concentration: 20 mg/l related to Test substance
Degradation: = 32 % after 29 day
Result: other
Testsubstance: 9 day = 0 %
14 day = 8 %
18 day = 16 %
27 day = 29 %
29 day = 32 %
Method: OECD Guide-line 301 B "Ready Biodegradability: Modified Sturm Test (CO_2 evolution)"
Year: 1981 GLP: yes
Test substance: as prescribed by 1.1 - 1.4
Source: Ciba Specialty Chemicals Inc. Basel
Ciba Additive GmbH Lampertheim

Type: aerobic
Inoculum: activated sludge, domestic, adapted
Concentration: 10 mg/l related to Test substance
Degradation: = 6 % after 28 day
Result: other: not readily biodegradable
Method: OECD Guide-line 301 B "Ready Biodegradability: Modified Sturm Test (CO2 evolution)"
Year: 1989 GLP: yes
Test substance: as prescribed by 1.1 - 1.4
Source: GREAT LAKES CHEMICAL ITALIA MILAN

(6)

Type: aerobic
Inoculum: activated sludge
Concentration: 13.3 mg/l related to Test substance
Degradation: = 47 % after 35 day
Result: inherently biodegradable
Testsubstance:
6 day	= 6 %
13 day	= 21 %
20 day	= 35 %
27 day	= 44 %
35 day	= 47 %

Method: other
Year: 1991 GLP: yes
Test substance: as prescribed by 1.1 - 1.4
Source: Ciba Specialty Chemicals Inc. Basel

Type: aerobic
Inoculum: activated sludge
Concentration: 13.3 mg/l related to Test substance
Degradation: = 47 % after 35 day
Result: inherently biodegradable
Testsubstance:
6 day	= 6 %
13 day	= 21 %
20 day	= 35 %
27 day	= 44 %
35 day	= 47 %

Method: other
Year: 1981 GLP: yes
Test substance: as prescribed by 1.1 - 1.4
Source: Ciba Additive GmbH Lampertheim
Test condition: Die Substanz wurde für inherente Bioabbaubarkeit in einem modifizierten Sturm Test/Zahn-Wellens Test untersucht (84/449/EEC, C.5 und OECD 302 B (12/05/81)

Type:
Inoculum:
Method:
Year: 1990 GLP: no data
Test substance: other TS
Remark: Sturm test: partially Biodegradable.
Source: GREAT LAKES CHEMICAL ITALIA MILAN

(4)

3.6 BOD5, COD or BOD5/COD Ratio

B O D 5

Method: Directive 84/449/EEC, C.8 "Biodegradation: Biochemical Oxygen Demand"
Year: 1989 GLP: yes
Concentration: 2 mg/l related to Test substance
BOD5: = 0 mgO2/l

C O D

Method: Directive 84/449/EEC, C.9 "Biodegradation: Chemical Oxygen Demand"
Year: 1989 GLP: yes
COD: = 3200 mg/g substance

R A T I O B O D 5 / C O D

BOD5/COD: = 0

Source: GREAT LAKES CHEMICAL ITALIA MILAN
(1)

B O D 5

Method: Directive 84/449/EEC, C.8 "Biodegradation: Biochemical Oxygen Demand"
Year: 1989 GLP: yes
Concentration: 10 mg/l related to Test substance
BOD5: = .02 mgO2/l

C O D

Method: Directive 84/449/EEC, C.9 "Biodegradation: Chemical Oxygen Demand"
Year: 1989 GLP: yes
COD: = 3200 mg/g substance

R A T I O B O D 5 / C O D

BOD5/COD: = .003

Source: GREAT LAKES CHEMICAL ITALIA MILAN
(1)

Source: Ciba Specialty Chemicals Inc. Basel
Ciba Additive GmbH Lampertheim

3.7 Bioaccumulation

Species:
Exposure period:
Concentration:
BCF:
Elimination:
Method:
Year: GLP:
Test substance:
Remark: no data
Source: GREAT LAKES CHEMICAL ITALIA MILAN

3.8 Additional Remarks

Remark: no data
Source: GREAT LAKES CHEMICAL ITALIA MILAN

AQUATIC ORGANISMS

4.1 Acute/Prolonged Toxicity to Fish

Type: static
Species: Lepomis macrochirus (Fish, fresh water)
Exposure period: 96 hour(s)
Unit: mg/l Analytical monitoring: yes
LC0: = 50
LC50: > 100
LC100: > 100
Method: OECD Guide-line 203 "Fish, Acute Toxicity Test"
Year: 1984 GLP: yes
Test substance: as prescribed by 1.1 - 1.4
Source: Ciba Specialty Chemicals Inc. Basel

Type: static
Species: Lepomis macrochirus (Fish, fresh water)
Exposure period: 96 hour(s)
Unit: mg/l Analytical monitoring: yes
LC0: = 50
LC50: > 100
LC100: > 100
Method: OECD Guide-line 203 "Fish, Acute Toxicity Test"
Year: 1981 GLP: yes
Test substance: as prescribed by 1.1 - 1.4
Source: Ciba Additive GmbH Lampertheim

Type: static
Species: Leuciscus idus (Fish, fresh water)
Exposure period: 96 hour(s)
Unit: mg/l Analytical monitoring:
LC50: > 5000
Method: OECD Guide-line 203 "Fish, Acute Toxicity Test"
Year: 1989 GLP: yes
Test substance: as prescribed by 1.1 - 1.4
Remark: Ten fishes/group, concentration 312,5 ; 625; 1250; 2500; 5000 mg/l
Observation after: 2,24,48,72,96 hour.
Source: GREAT LAKES CHEMICAL ITALIA MILAN

(1)

Type: static
Species: Salmo gairdneri (Fish, estuary, fresh water)
Exposure period: 96 hour(s)
Unit: mg/l Analytical monitoring: yes
LC0: > 100
LC50: > 100
LC100: > 100
Method: OECD Guide-line 203 "Fish, Acute Toxicity Test"
Year: 1984 GLP: yes
Test substance: as prescribed by 1.1 - 1.4
Source: Ciba Specialty Chemicals Inc. Basel

Type: static
Species: Salmo gairdneri (Fish, estuary, fresh water)
Exposure period: 96 hour(s)
Unit: mg/l Analytical monitoring: yes
LC0: > 100
LC50: > 100
LC100: > 100
Method: OECD Guide-line 203 "Fish, Acute Toxicity Test"
Year: 1981 GLP: yes
Test substance: as prescribed by 1.1 - 1.4
Source: Ciba Additive GmbH Lampertheim

Type:
Species: Lepomis macrochirus (Fish, fresh water)
Exposure period: 96 hour(s)
Unit: mg/l Analytical monitoring:
LC50: > 100
Method: other
Year: 1994 GLP: no data
Test substance: no data
Source: GREAT LAKES CHEMICAL ITALIA MILAN

(7)

Type:
Species: Salmo gairdneri (Fish, estuary, fresh water)
Exposure period: 96 hour(s)
Unit: mg/l Analytical monitoring:
LC50: > 100
Method: other
Year: 1990 GLP: no data
Test substance: no data
Source: GREAT LAKES CHEMICAL ITALIA MILAN

(4)

4.2 Acute Toxicity to Aquatic Invertebrates

Type:
Species: Daphnia magna (Crustacea)
Exposure period: 24 hour(s)
Unit: mg/l Analytical monitoring: yes
EC0: > 100
EC50: > 100
EC100: > 100
Method: OECD Guide-line 202, part 1 "Daphnia sp., Acute Immobilisation Test"
Year: 1984 GLP: yes
Test substance: as prescribed by 1.1 - 1.4
Source: Ciba Specialty Chemicals Inc. Basel

Type:
Species: Daphnia magna (Crustacea)
Exposure period: 24 hour(s)
Unit: mg/l Analytical monitoring: yes
EC0: > 100
EC50: > 100
EC100: > 100
Method: OECD Guide-line 202, part 1 "Daphnia sp., Acute Immobilisation Test"
Year: 1981 GLP: yes
Test substance: as prescribed by 1.1 - 1.4
Source: Ciba Additive GmbH Lampertheim

Type:
Species: Daphnia magna (Crustacea)
Exposure period: 24 hour(s)
Unit: mg/l Analytical monitoring:
EC50: > 100
Method: other
Year: 1994 GLP: no data
Test substance: no data
Source: GREAT LAKES CHEMICAL ITALIA MILAN

(7)

4.3 Toxicity to Aquatic Plants e.g. Algae

Species: Scenedesmus subspicatus (Algae)
Endpoint: growth rate
Exposure period: 72 hour(s)
Unit: mg/l Analytical monitoring: yes
NOEC: 30
EC50: > 30
Method: Directive 87/302/EEC, part C, p. 89 "Algal inhibition test"
Year: 1992 GLP: yes
Test substance: as prescribed by 1.1 - 1.4
Source: Ciba Specialty Chemicals Inc. Basel

Species: Scenedesmus subspicatus (Algae)
Endpoint: growth rate
Exposure period: 72 hour(s)
Unit: mg/l Analytical monitoring: yes
NOEC: 30
EC50: > 30
Method: Directive 87/302/EEC, part C, p. 89 "Algal inhibition test"
Year: 1987 GLP: yes
Test substance: as prescribed by 1.1 - 1.4
Source: Ciba Additive GmbH Lampertheim

Species: other algae
Endpoint:
Exposure period: 72 hour(s)
Unit: mg/l Analytical monitoring:
EC50: > 30
Method: other
Year: 1994 GLP: no data
Test substance: no data
Source: GREAT LAKES CHEMICAL ITALIA MILAN

(7)

4.4 Toxicity to Microorganisms e.g. Bacteria

Type: aquatic
Species: Pseudomonas putida (Bacteria)
Exposure period: 18 hour(s)
Unit: Analytical monitoring:
Method:
Year: 1989 GLP: yes
Test substance: as prescribed by 1.1 - 1.4
Remark: No toxic at water saturated concentration.
Source: GREAT LAKES CHEMICAL ITALIA MILAN

(1)

Type: aquatic
Species: other bacteria
Exposure period:
Unit: mg/l Analytical monitoring:
IC20 : > 100
IC80 : > 100
Method: other
Year: 1994 GLP: no data
Test substance: no data
Source: GREAT LAKES CHEMICAL ITALIA MILAN

(4)

Type: soil
Species: activated sludge
Exposure period: 3 hour(s)
Unit: mg/l Analytical monitoring: no
EC50: > 100
EC80 : > 100
Method: OECD Guide-line 209 "Activated Sludge, Respiration Inhibition Test"
Year: 1988 GLP: no data
Test substance: as prescribed by 1.1 - 1.4
Source: Ciba Specialty Chemicals Inc. Basel

Type: soil
Species: activated sludge
Exposure period: 3 hour(s)
Unit: mg/l Analytical monitoring: no
EC50: > 100
EC80 : > 100
Method: OECD Guide-line 209 "Activated Sludge, Respiration Inhibition Test"
Year: 1984 GLP: no data
Test substance: as prescribed by 1.1 - 1.4
Source: Ciba Additive GmbH Lampertheim

4.5 Chronic Toxicity to Aquatic Organisms

4.5.1 Chronic Toxicity to Fish

Species:
Endpoint:
Exposure period:
Unit: Analytical monitoring:
Method:
Year: GLP:
Test substance:
Remark: no data
Source: GREAT LAKES CHEMICAL ITALIA MILAN

4.5.2 Chronic Toxicity to Aquatic Invertebrates

Species:
Endpoint:
Exposure period:
Unit: Analytical monitoring:
Method:
Year: GLP:
Test substance:
Remark: no data
Source: GREAT LAKES CHEMICAL ITALIA MILAN

TERRESTRIAL ORGANISMS

4.6.1 Toxicity to Soil Dwelling Organisms

Type:
Species:
Endpoint:
Exposure period:
Unit:
Method:
Year: GLP:
Test substance:
Remark: no data
Source: GREAT LAKES CHEMICAL ITALIA MILAN

Type:
Species:
Endpoint:
Exposure period:
Unit:
Method:
Year: GLP:
Test substance:
Source: Ciba Additive GmbH Lampertheim

4.6.2 Toxicity to Terrestrial Plants

Species: Lolium perenne (Monocotyledon)
Endpoint: growth
Expos. period: 19 day
Unit: mg/kg soil dw
EC50: = 50
LC50: > 100
Method: OECD Guide-line 208 "Terrestrial Plants, Growth Test"
Year: 1991 GLP: yes
Test substance: as prescribed by 1.1 - 1.4
Source: Ciba Specialty Chemicals Inc. Basel

Species: Brassica rapa (Dicotyledon)
Endpoint: growth
Expos. period: 19 day
Unit: mg/kg soil dw
EC50: = 24
LC50: > 100
Method: OECD Guide-line 208 "Terrestrial Plants, Growth Test"
Year: 1991 GLP: yes
Test substance: as prescribed by 1.1 - 1.4
Source: Ciba Specialty Chemicals Inc. Basel

Species:	Vicia sativa (Dicotyledon)
Endpoint:	growth
Expos. period:	19 day
Unit:	mg/kg soil dw
EC50:	> 100
LC50:	> 100
Method:	OECD Guide-line 208 "Terrestrial Plants, Growth Test"
Year:	1991 GLP: yes
Test substance:	as prescribed by 1.1 - 1.4
Source:	Ciba Specialty Chemicals Inc. Basel

Species:	Lolium perenne (Monocotyledon)
Endpoint:	growth
Expos. period:	19 day
Unit:	mg/kg soil dw
EC50:	= 50
LC50:	> 100
Method:	OECD Guide-line 208 "Terrestrial Plants, Growth Test"
Year:	1984 GLP: yes
Test substance:	as prescribed by 1.1 - 1.4
Source:	Ciba Additive GmbH Lampertheim

Species:	Brassica rapa (Dicotyledon)
Endpoint:	growth
Expos. period:	19 day
Unit:	mg/kg soil dw
EC50:	= 24
LC50:	> 100
Method:	OECD Guide-line 208 "Terrestrial Plants, Growth Test"
Year:	1984 GLP: yes
Test substance:	as prescribed by 1.1 - 1.4
Source:	Ciba Additive GmbH Lampertheim

Species:	Vicia sativa (Dicotyledon)
Endpoint:	growth
Expos. period:	19 day
Unit:	mg/kg soil dw
EC50:	> 100
LC50:	> 100
Method:	OECD Guide-line 208 "Terrestrial Plants, Growth Test"
Year:	1984 GLP: yes
Test substance:	as prescribed by 1.1 - 1.4
Source:	Ciba Additive GmbH Lampertheim

Species:	
Endpoint:	
Expos. period:	
Unit:	
Method:	
Year:	GLP:
Test substance:	
Remark:	no data
Source:	GREAT LAKES CHEMICAL ITALIA MILAN

4.6.3 Toxicity to other Non-Mamm. Terrestrial Species

Species:
Endpoint:
Expos. period:
Unit:
Method:
Year: GLP:
Test substance:
Remark: no data
Source: GREAT LAKES CHEMICAL ITALIA MILAN

4.7 Biological Effects Monitoring

Remark: no data
Source: GREAT LAKES CHEMICAL ITALIA MILAN

4.8 Biotransformation and Kinetics

Type:
Remark: no data
Source: GREAT LAKES CHEMICAL ITALIA MILAN

4.9 Additional Remarks

Remark: no data
Source: GREAT LAKES CHEMICAL ITALIA MILAN

5.1 Acute Toxicity

5.1.1 Acute Oral Toxicity

Type:	LD50	
Species:	rat	
Strain:		
Sex:		
Number of Animals:		
Vehicle:		
Value:	> 10000 mg/kg bw	
Method:	other	
Year:	1990	GLP: no data
Test substance:	no data	
Source:	GREAT LAKES CHEMICAL ITALIA MILAN	

(7)

Type:	LD50	
Species:	rat	
Strain:		
Sex:		
Number of Animals:		
Vehicle:		
Value:	> 5000 mg/kg bw	
Method:	other	
Year:	1981	GLP: no
Test substance:	as prescribed by 1.1 - 1.4	
Source:	Ciba Specialty Chemicals Inc. Basel Ciba Additive GmbH Lampertheim	

(10)

Type:	LD50	
Species:	Chinese hamster	
Strain:		
Sex:		
Number of Animals:		
Vehicle:		
Value:	> 6000 mg/kg bw	
Method:	other	
Year:	1975	GLP: no
Test substance:	as prescribed by 1.1 - 1.4	
Source:	Ciba Specialty Chemicals Inc. Basel	

Type: LD50
Species: Chinese hamster
Strain:
Sex:
Number of Animals:
Vehicle:
Value: > 6000
Method: other
Year: 1975 GLP: no
Test substance: as prescribed by 1.1 - 1.4
Source: Ciba Additive GmbH Lampertheim

5.1.2 Acute Inhalation Toxicity

Type: LC50
Species: rat
Strain:
Sex:
Number of Animals:
Vehicle:
Exposure time: 4 hour(s)
Value: > 1.8 mg/l
Method: other
Year: 1990 GLP: no data
Test substance:
Remark: Dust exposure with approx. 90% of particles < 7 micrometers diameter.
Source: GREAT LAKES CHEMICAL ITALIA MILAN
(11)

Type: LC50
Species: rat
Strain:
Sex:
Number of Animals:
Vehicle:
Exposure time: 4 hour(s)
Value: > 1.8 mg/l
Method: other
Year: 1978 GLP: no
Test substance: as prescribed by 1.1 - 1.4
Source: Ciba Specialty Chemicals Inc. Basel
Ciba Additive GmbH Lampertheim

Type: LCLo
Species: rat
Strain:
Sex:
Number of Animals:
Vehicle:
Exposure time: 4 hour(s)
Value: > 1.3 mg/l
Method: other
Year: 1994 GLP: no data
Test substance:
Source: GREAT LAKES CHEMICAL ITALIA MILAN

(12)

5.1.3 Acute Dermal Toxicity

Type: LD50
Species: rat
Strain:
Sex:
Number of Animals:
Vehicle:
Value: > 2000 mg/kg bw
Method: OECD Guide-line 402 "Acute dermal Toxicity"
Year: 1992 GLP: yes
Test substance: other TS
Remark: Test No. 924057
Source: Ciba Specialty Chemicals Inc. Basel

Type: LD50
Species: rabbit
Strain:
Sex:
Number of Animals:
Vehicle:
Value: > 2000 mg/kg bw
Method: other
Year: 1994 GLP: no data
Test substance:
Source: GREAT LAKES CHEMICAL ITALIA MILAN

(13)

Type: LD50
Species: rabbit
Strain:
Sex:
Number of
Animals:
Vehicle:
Value: > 2000 mg/kg bw
Method: other
Year: 1962 GLP: no
Test substance: as prescribed by 1.1 - 1.4
Source: Ciba Specialty Chemicals Inc. Basel
Ciba Additive GmbH Lampertheim

5.1.4 Acute Toxicity, other Routes

Type: LD50
Species: rat
Strain:
Sex:
Number of
Animals:
Vehicle:
Route of admin.: i.p.
Value: > 1000 mg/kg bw
Method:
Year: 1994 GLP: no data
Test substance: no data
Source: GREAT LAKES CHEMICAL ITALIA MILAN

(14)

Type: LD50
Species: rat
Strain:
Sex:
Number of
Animals:
Vehicle:
Route of admin.: i.p.
Value: > 1000 mg/kg bw
Method: others
Year: 1982 GLP: no
Test substance: as prescribed by 1.1 - 1.4
Source: Ciba Specialty Chemicals Inc. Basel

Type: LD50
Species: rat
Strain:
Sex:
Number of Animals:
Vehicle:
Route of admin.: i.p.
Value: > 1000 mg/kg bw
Method: sonstige
Year: 1982 GLP: no
Test substance: as prescribed by 1.1 - 1.4
Source: Ciba Additive GmbH Lampertheim

5.2 Corrosiveness and Irritation

5.2.1 Skin Irritation

Species: rabbit
Concentration:

Exposure:
Exposure Time:
Number of Animals:
PDII:
Result: slightly irritating
EC classificat.: not irritating
Method: other
Year: 1990 GLP: no data
Test substance: no data
Remark: draize score 0.95/8
Source: GREAT LAKES CHEMICAL ITALIA MILAN
(11)

Species: rabbit
Concentration:

Exposure:
Exposure Time:
Number of Animals:
PDII:
Result: not irritating
EC classificat.: not irritating
Method: other
Year: 1982 GLP: no
Test substance: as prescribed by 1.1 - 1.4
Source: Ciba Specialty Chemicals Inc. Basel

Species: rabbit
Concentration:

Exposure:
Exposure Time:
Number of
Animals:
PDII:
Result: not irritating
EC classificat.: not irritating
Method: other
Year: 1981 GLP: no
Test substance: as prescribed by 1.1 - 1.4
Source: Ciba Additive GmbH Lampertheim

5.2.2 Eye Irritation

Species: rabbit
Concentration:
Dose:
Exposure Time:
Comment:
Number of
Animals:
Result: slightly irritating
EC classificat.: not irritating
Method: other
Year: 1990 GLP: no data
Test substance: no data
Remark: Draize score 4/110
Source: GREAT LAKES CHEMICAL ITALIA MILAN

(4)

Species: rabbit
Concentration:
Dose:
Exposure Time:
Comment:
Number of
Animals:
Result: not irritating
EC classificat.: not irritating
Method: other
Year: 1982 GLP: no
Test substance: as prescribed by 1.1 - 1.4
Source: Ciba Specialty Chemicals Inc. Basel
Ciba Additive GmbH Lampertheim

5.3 Sensitization

Type:	Maurer optimisation test	
Species:	guinea pig	
Number of Animals:		
Vehicle:		
Result:	not sensitizing	
Classification:	not sensitizing	
Method:	other	
Year:	1976	GLP: no
Test substance:	as prescribed by 1.1 - 1.4	
Source:	Ciba Specialty Chemicals Inc. Basel Ciba Additive GmbH Lampertheim	

Type:	Patch-Test	
Species:	human	
Number of Animals:		
Vehicle:		
Result:	not sensitizing	
Classification:	not sensitizing	
Method:		
Year:	1990	GLP: no data
Test substance:	other TS	
Remark:	In 4 separate studies, a total of 3 of 183 subjects exibited reactions indicative of sensitization; concentrations ranged from 25% in petrolatum (25 subjects), 0.5% in dimethyl phtalate (58 subjects), to neat material (100 subjects).	
Source:	GREAT LAKES CHEMICAL ITALIA MILAN	

(7)

Type:		
Species:	guinea pig	
Number of Animals:		
Vehicle:		
Result:	not sensitizing	
Classification:	not sensitizing	
Method:		
Year:	1994	GLP: no data
Test substance:	no data	
Source:	GREAT LAKES CHEMICAL ITALIA MILAN	

(11)

5.4 Repeated Dose Toxicity

Species:	rat		Sex: male/female
Strain:	other: RAI f (SPF)		
Route of admin.:	inhalation		
Exposure period:	21 days		
Frequency of treatment:	6 hours/day during 5 days/week		
Post. obs. period:	no		
Doses:	0, 23, 128, 543 mg/m3		
Control Group:	yes		
NOAEL:	> .543 mg/l		
Method:	other: CIBA-GEIGY AG, Test No. 441678, 09.07.1979		
Year:	1979	GLP: no	
Test substance:	as prescribed by 1.1 - 1.4		
Source:	Ciba Specialty Chemicals Inc. Basel		

Species:	rat		Sex: male/female
Strain:	other: RAI f (SPF)		
Route of admin.:	inhalation		
Exposure period:	21 Tage		
Frequency of treatment:	6 Stunden/Tag während 5 Tage/Woche		
Post. obs. period:	keine		
Doses:	0, 23, 128, 543 mg/m3		
Control Group:	yes		
NOAEL:	> .543 mg/l		
Method:	other: CIBA-GEIGY AG, Test No. 441678, 09.07.1979		
Year:	1979	GLP: no	
Test substance:	as prescribed by 1.1 - 1.4		
Source:	Ciba Additive GmbH Lampertheim		

Species:	rat		Sex: male/female
Strain:	other: CFY		
Route of admin.:	oral feed		
Exposure period:	104 weeks		
Frequency of treatment:	daily		
Post. obs. period:	no		
Doses:	0, 500, 1500, 5000 ppm		
Control Group:	yes		
NOAEL:	= 500 ppm		
Method:	other: CIBA-GEIGY AG (executed with HUNTIGDON, GB), Test No. CGB26/74398,08.07.1974		
Year:	1974	GLP: no	
Test substance:	as prescribed by 1.1 - 1.4		
Source:	Ciba Specialty Chemicals Inc. Basel		

Species:	rat		Sex: male/female
Strain:	other: CFY		
Route of admin.:	oral feed		
Exposure period:	104 Wochen		
Frequency of treatment:	täglich		
Post. obs. period:	keine		
Doses:	0, 500, 1500, 5000 ppm		
Control Group:	yes		
NOAEL:	= 500 ppm		
Method:	other: CIBA-GEIGY AG (durchgeführt bei HUNTIGDON, GB), Test No. CGB26/74398,08.07.1974		
Year:	1974	GLP:	no
Test substance:	as prescribed by 1.1 - 1.4		
Source:	Ciba Additive GmbH Lampertheim		

Species:	rat		Sex: male/female
Strain:			
Route of admin.:	gavage		
Exposure period:	28 days feeding		
Frequency of treatment:	daily		
Post. obs. period:			
Doses:	0,1,10,100,1000 mg/kg/d		
Control Group:	yes		
NOAEL:	= 100 - 1000 mg/kg bw		
Method:	Directive 84/449/EEC, B.7 "Sub-acute toxicity (oral)"		
Year:	1991	GLP:	yes
Test substance:	as prescribed by 1.1 - 1.4		
Remark:	Administration of 0.5% of product in methyl cellulose. 10 animal:(5 males, 5 females)/group. 4 groups+ 1 control group.		
Result:	100 mg/kg/d for male; 1000 mg/kg/d for female. Mortality: no deaths during study. Clinical signs: no clinical change in any of the treated animals. Body weight: did not affect body weight growth and food consumption up to and comprising 100 mg/kg/d for males and 1000 mg/kg/d for females. Post mortem exams: no changes attributable to treatment were seen. Hematoloy and blood: no modifications at any dosage in either sex.		
Source:	GREAT LAKES CHEMICAL ITALIA MILAN		

(1)

Species:	rat	Sex:	male/female
Strain:	Sprague-Dawley		
Route of admin.:	gavage		
Exposure period:	28 days		
Frequency of treatment:	daily		
Post. obs. period:	no		
Doses:	5, 30, 100, 300 mg/kg/day		
Control Group:	yes		
NOAEL:	= 30 mg/kg bw		
Method:	other		
Year:	1991	GLP:	yes
Test substance:	as prescribed by 1.1 - 1.4		
Remark:	This study was specially designed to determine liver effects in young Sprague-Dawley rats over 4 weeks at a concentration equal to the NOEL.		
Source:	Ciba Specialty Chemicals Inc. Basel		

(15)

Species:	rat	Sex:	male/female
Strain:	Sprague-Dawley		
Route of admin.:	gavage		
Exposure period:	28 Tage		
Frequency of treatment:	täglich		
Post. obs. period:	keine		
Doses:	5, 30, 100, 300 mg/kg/Tag		
Control Group:	yes		
NOAEL:	= 30 mg/kg bw		
Method:	other		
Year:	1991	GLP:	yes
Test substance:	as prescribed by 1.1 - 1.4		
Remark:	Diese Studie ist eine Spezialstudie, durchgeführt an jungen Sprague-Dawley Ratten während 4 Wochen um den NOEL von CASRN 2082-79-3 in der Leber zu bestimmen.		
Source:	Ciba Additive GmbH Lampertheim		

(16)

Species: dog Sex: male/female
Strain: Beagle
Route of admin.: oral feed
Exposure period: 3 months
Frequency of treatment: daily
Post. obs. period: 1 month
Doses: 1000, 3000, 10000 ppm
Control Group: yes
NOAEL: ca. 31.5 - 34.5 mg/kg
Method: other: CIBA-GEIGY AG, Test No. 790857, 14.09.1981
Year: 1981 GLP: yes
Test substance: as prescribed by 1.1 - 1.4
Source: Ciba Specialty Chemicals Inc. Basel

Species: dog Sex: male/female
Strain: Beagle
Route of admin.: oral feed
Exposure period: 3 Monate
Frequency of treatment: täglich
Post. obs. period: 1 Monat
Doses: 1000, 3000, 10000 ppm
Control Group: yes
NOAEL: ca. 31.5 - 34.5 mg/kg
Method: other: CIBA-GEIGY AG, Test No. 790857, 14.09.1981
Year: 1981 GLP: yes
Test substance: as prescribed by 1.1 - 1.4
Source: Ciba Additive GmbH Lampertheim

5.5 Genetic Toxicity 'in Vitro'

Type: Ames test
System of testing: S.typhimurium TA 98,100,1535,1537
Concentration: 10-250 microgram/Platte
Cytotoxic Conc.:
Metabolic activation: with
Result: negative
Method: other
Year: 1977 GLP: no
Test substance: as prescribed by 1.1 - 1.4
Source: Ciba Specialty Chemicals Inc. Basel
Ciba Additive GmbH Lampertheim

Type: Ames test
System of testing: Salmonella tiphymurium
Concentration:
Cytotoxic Conc.:
Metabolic activation: with and without
Result: negative
Method:
Year: 1990 GLP: no data
Test substance: no data
Source: GREAT LAKES CHEMICAL ITALIA MILAN
(11)

Type: Ames test
System of testing: Salmonella TA98 TA100
Concentration: 100 micrograms/plate
Cytotoxic Conc.:
Metabolic activation:
Result: negative
Method:
Year: 1981 GLP: no data
Test substance: no data
Remark: Mutagenicity of photoreaction products.
Source: GREAT LAKES CHEMICAL ITALIA MILAN
(17)

Type:
System of testing: mouse
Concentration:
Cytotoxic Conc.:
Metabolic activation:
Result: negative
Method:
Year: 1990 GLP: no data
Test substance: no data
Source: GREAT LAKES CHEMICAL ITALIA MILAN
(4)

Type:
System of testing:
Concentration:
Cytotoxic Conc.:
Metabolic activation:
Result:
Method:
Year: GLP:
Test substance:
Source: Ciba Additive GmbH Lampertheim

5.6 Genetic Toxicity 'in Vivo'

Type: Dominant lethal assay
Species: mouse Sex: male
Strain: NMRI
Route of admin.: gavage
Exposure period: unique
Doses: 1000 und 3000 mg/kg
Result:
Method: other: Ciba-Geigy, Test-No. 327540
Year: 1975 GLP: no
Test substance: as prescribed by 1.1 - 1.4
Result: No dominant lethal effects noted. Not mutagen.
Source: Ciba Specialty Chemicals Inc. Basel

Type: Dominant lethal assay
Species: mouse Sex: male
Strain: NMRI
Route of admin.: gavage
Exposure period: einmalige Verabreichung
Doses: 1000 und 3000 mg/kg
Result:
Method: other: Ciba-Geigy, Test-No. 327540
Year: 1975 GLP: no
Test substance: as prescribed by 1.1 - 1.4
Result: Kein Hinweis eines dominanten lethalen Effektes wurde festgestellt. Nicht mutagen.
Source: Ciba Additive GmbH Lampertheim

Type: Somatic mutation assay
Species: Chinese hamster Sex: male/female
Strain:
Route of admin.: gavage
Exposure period: 2 days
Doses: 500, 1000, 2000 mg/kg
Result:
Method: other: CIBA-GEIGY AG, Test No. 764028, 27.08.1981
Year: 1981 GLP: no
Test substance: as prescribed by 1.1 - 1.4
Result: No core anomaly was determined. Not mutagen.
Source: Ciba Specialty Chemicals Inc. Basel

Type: Somatic mutation assay
Species: Chinese hamster Sex: male/female
Strain:
Route of admin.: gavage
Exposure period: 2 days
Doses: 500, 1000, 2000 mg/kg
Result:
Method: other: CIBA-GEIGY AG, Test No. 764028, 27.08.1981
Year: 1981 GLP: no
Test substance: as prescribed by 1.1 - 1.4
Result: No chromosomal aberrations noted. Not mutagen.
Source: Ciba Specialty Chemicals Inc. Basel

Type: Somatic mutation assay
Species: Chinese hamster Sex: male/female
Strain:
Route of admin.: gavage
Exposure period: 2 Tage
Doses: 500, 1000, 2000 mg/kg
Result:
Method: other: CIBA-GEIGY AG, Test No. 764028, 27.08.1981
Year: 1981 GLP: no
Test substance: as prescribed by 1.1 - 1.4
Result: Keine Kernanomalie wurde festgestellt. Nicht mutagen.
Source: Ciba Additive GmbH Lampertheim

Type: Somatic mutation assay
Species: Chinese hamster Sex: male/female
Strain:
Route of admin.: gavage
Exposure period: 2 Tage
Doses: 500, 1000, 2000 mg/kg
Result:
Method: other: CIBA-GEIGY AG, Test No. 764028, 27.08.1981
Year: 1981 GLP: no
Test substance: as prescribed by 1.1 - 1.4
Result: Keine Chromosomenabberation wurde nach Auswertung der Knochenmarkzellen festgestellt. Nicht mutagen.
Source: Ciba Additive GmbH Lampertheim

Type:
Species: Sex:
Strain:
Route of admin.:
Exposure period:
Doses:
Result:
Method:
Year: GLP:
Test substance:
Remark: no data
Source: GREAT LAKES CHEMICAL ITALIA MILAN

5.7 Carcinogenicity

Species: mouse Sex: male/female
Strain: other: MAGf (SPF)
Route of admin.: oral feed
Exposure period: 24 months
Frequency of treatment: daily
Post. obs. period: no
Doses: 0.6, 5.4, 58 mg/kg b.w.
Result:
Control Group: yes
Method: other: CIBA-GEIGY AG, Test No. 784333, 11.01.1982
Year: 1982 GLP: no
Test substance: as prescribed by 1.1 - 1.4
Result: No tumourigenic potential noted.
Source: Ciba Specialty Chemicals Inc. Basel

Species: mouse Sex: male/female
Strain: other: MAGf (SPF)
Route of admin.: oral feed
Exposure period: 24 Monate
Frequency of treatment: täglich
Post. obs. period: keine
Doses: 0.6, 5.4, 58 mg/kg Körpergewicht
Result:
Control Group: yes
Method: other: CIBA-GEIGY AG, Test No. 784333, 11.01.1982
Year: 1982 GLP: no
Test substance: as prescribed by 1.1 - 1.4
Result: Kein Hinweis für ein tumorigenes Potential in der Maus.
Source: Ciba Additive GmbH Lampertheim

Species: Sex:
Strain:
Route of admin.:
Exposure period:
Frequency of
treatment:
Post. obs.
period:
Doses:
Result:
Control Group:
Method:
Year: GLP:
Test substance:
Remark: no data
Source: GREAT LAKES CHEMICAL ITALIA MILAN

5.8 Toxicity to Reproduction

Type: One generation study
Species: rat Sex: female
Strain:
Route of admin.: gavage
Exposure Period: on 6 through 15 day of gestation
Frequency of
treatment: daily
Duration of test:
Doses: 0,150,500,1000 mg/kg/day
Control Group:
NOAEL Parental: = 150 mg/kg bw
Method:
Year: 1992 GLP: yes
Test substance: as prescribed by 1.1 - 1.4
Remark: 25 females, administration: oral by gavage, on 6 through 15 days of gestation.
Result: body weight: no effects up to and comprising 500 mg/kg/d.
Fetal weight: decreased at 500 and 1000 mg/kg/d.
Unossified phalangeal nuclei were increased at 1000 mg/kg/d
Source: GREAT LAKES CHEMICAL ITALIA MILAN

(18)

Type: Two generation study
Species: rat Sex: male/female
Strain: other: COBS(R)CD(R)
Route of admin.: oral feed
Exposure Period: 10 months
Frequency of treatment: daily
Premating Exposure Period
male: 10 weeks
female: 10 weeks
Duration of test: 10 months
Doses: 0, 500, 1500, 5000 ppm
Control Group: yes
NOAEL Parental: = 1500 ppm
NOAEL F1 Offspr.: < 500 ppm
NOAEL F2 Offspr.: < 500 ppm
Method: OECD Guide-line 416 "Two-generation Reproduction Toxicity Study"
Year: 1986 GLP: yes
Test substance: as prescribed by 1.1 - 1.4
Source: Ciba Specialty Chemicals Inc. Basel

Type: Two generation study
Species: rat Sex: male/female
Strain: other: COBS(R)CD(R)
Route of admin.: oral feed
Exposure Period: 10 Monate
Frequency of treatment: täglich
Premating Exposure Period
male: 10 Wochen
female: 10 Wochen
Duration of test: 10 Monate
Doses: 0, 500, 1500, 5000 ppm
Control Group: yes
NOAEL Parental: = 1500 ppm
NOAEL F1 Offspr.: < 500 ppm
NOAEL F2 Offspr.: < 500 ppm
Method: OECD Guide-line 416 "Two-generation Reproduction Toxicity Study"
Year: 1986 GLP: yes
Test substance: as prescribed by 1.1 - 1.4
Source: Ciba Additive GmbH Lampertheim

5.9 Developmental Toxicity/Teratogenicity

Species:	rat	Sex: female
Strain:	Sprague-Dawley	
Route of admin.:	gavage	
Exposure period:	10 days	
Frequency of treatment:	daily	
Duration of test:	10 days	
Doses:	0, 150, 500, 1000 mg/kg	
Control Group:	yes	
NOAEL Maternalt.:	= 150 mg/kg bw	
NOAEL Teratogen.:	> 1000 mg/kg bw	
Method:	other: CIBA-GEIGY AG, Test No. 227513, 19.06.1975	
Year:	1975	GLP: no
Test substance:	as prescribed by 1.1 - 1.4	
Source:	Ciba Specialty Chemicals Inc. Basel	

Species:	rat	Sex: female
Strain:	Sprague-Dawley	
Route of admin.:	gavage	
Exposure period:	10 Tage	
Frequency of treatment:	täglich	
Duration of test:	10 Tage	
Doses:	0, 150, 500, 1000 mg/kg	
Control Group:	yes	
NOAEL Maternalt.:	= 150 mg/kg bw	
NOAEL Teratogen.:	> 1000 mg/kg bw	
Method:	other: CIBA-GEIGY AG, Test No. 227513, 19.06.1975	
Year:	1975	GLP: no
Test substance:	as prescribed by 1.1 - 1.4	
Source:	Ciba Additive GmbH Lampertheim	

Species:	mouse	Sex: female
Strain:	NMRI	
Route of admin.:	gavage	
Exposure period:	10 days	
Frequency of treatment:	daily	
Duration of test:	10 days	
Doses:	0, 150, 500, 1000 mg/kg	
Control Group:	yes	
NOAEL Maternalt.:	= 500 mg/kg bw	
NOAEL Teratogen.:	> 1000 mg/kg bw	
Method:	other: CIBA-GEIGY AG, Test No. 327533, 28.08.1975	
Year:	1975	GLP: no
Test substance:	as prescribed by 1.1 - 1.4	
Source:	Ciba Specialty Chemicals Inc. Basel	

Species: mouse Sex: female
Strain: NMRI
Route of admin.: gavage
Exposure period: 10 Tage
Frequency of treatment: täglich
Duration of test: 10 Tage
Doses: 0, 150, 500, 1000 mg/kg
Control Group: yes
NOAEL Maternalt.: = 500 mg/kg bw
NOAEL Teratogen.: > 1000 mg/kg bw
Method: other: CIBA-GEIGY AG, Test No. 327533, 28.08.1975
Year: 1975 GLP: no
Test substance: as prescribed by 1.1 - 1.4
Source: Ciba Additive GmbH Lampertheim

Species: Sex:
Strain:
Route of admin.:
Exposure period:
Frequency of treatment:
Duration of test:
Doses:
Control Group:
Method:
Year: GLP:
Test substance:
Remark: no data
Source: GREAT LAKES CHEMICAL ITALIA MILAN

5.10 Other Relevant Information

Type: Biochemical or cellular interactions
Remark: Male and female rats were exposed to 0, 30, 100, 300, and 1000 mg/kg bw of the test substance for 14 days by gavage. Target organ was the liver (weight increase), including induction of cytochrom P450, MF-oxidases and UDP-glucuronyl transferase. Electron-microscopical investigations showed a marked proliferation of the smooth endoplasmic reticulum (SER). These effects are reversible after cessation of treatment. The substance is characterised as strong inducer of xenobiotic metabolic liver enzymes.
Source: Ciba Specialty Chemicals Inc. Basel

Type: Biochemical or cellular interactions
Remark: Die Prüfsubstanz wurde männlichen und weiblichen Ratten während 14 Tage mittels Schlundsonde verabreicht: 0, 30, 100, 300 und 1000 mg/kg Körpergewicht. Zielorgan war die Leber (Organgewichsvergrösserung) sowie die Induktion von cytochrom P450, MFOxidasen sowie UDP-Glucuronyltransferase. Elektonenmikroskopische Untersuchungen zeigten eine markante Proliferation des glatten Endoplasmatischen Reticulus (SER). Diese Effekte sind nach Absetzen der Behandlung reversibel.

Die Prüfsubstanz wird als ein starker Induktor der Leberfremdstoff-metabolisierenden Enzyme charakterisiert.
Source: Ciba Additive GmbH Lampertheim

Type: Toxicokinetics
Remark: After single oral application 14C-labelled test substance is excreted readily (73% after 48 hours).
Source: Ciba Specialty Chemicals Inc. Basel

Type: Toxicokinetics
Remark: C14 markierte Prüfsubstanz, nach einmaliger Verabreichung durch Schlundsonde, wird nach 48 Stunden zu 73% ausgeschieden.
Source: Ciba Additive GmbH Lampertheim

Type:
Remark: no data
Source: GREAT LAKES CHEMICAL ITALIA MILAN

5.11 Experience with Human Exposure

Remark: No specific hazard known to human exposed to the substance during preparation.
Source: GREAT LAKES CHEMICAL ITALIA MILAN

(1) Internal reference.

(2) Ciba Additive GmbH, Sicherheitsdatenblatt Irganox 1076 (03/1994)

(3) Clariant GmbH (1995), EG-Sicherheitsdatenblatt (19.05.95)

(4) MSDS Ciba

(5) MDL information

(6) Internal Reference.

(7) MSDS Ciba.

(8) MSDS Ciba 1994

(9) Internal reference,

(10) Test durchgeführt in der Exp. Toxikologie CIBA-GEIGY AG; Test No. 811493

(11) Ciba MSDS.

(12) Ciba MSDS. MDL information systems.

(13) MDL 30/06/92, revision 30/06/94 information system

(14) MDL information system 30/06/94. Ciba MSDS.

(15) Study executed in the job of CIBA-GEIGY AG with HAZLETON FRANCE, Projekt No. (CG:89 4554), HAZLETON F:380/563), 23.10.1991

(16) Studie durchgeführt im Auftrag von CIBA-GEIGY AG bei HAZLETON FRANCE, Projekt No. (CG:89 4554), HAZLETON F: 380/563), 23.10.1991

(17) OSAKA-OEKSDJ 1981 vol. 12 pp. 95-98

(18) EPA/OTS DOC# 88-920001872

7.1 End Point Summary

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7.2 Hazard Summary

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7.3 Risk Assessment

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I U C L I D

D a t a S e t

Existing Chemical	ID: 6683-19-8
CAS No.	6683-19-8
EINECS Name	pentaerythritol tetrakis(3-(3,5-di-tert-butyl-4-hydroxyphenyl)propionate)
EINECS No.	229-722-6
Molecular Weight	1177.81
Structural Formula	CC(C) (C)c4(c(O)=c(C(C) (C)C)cc(CCC(OCC(COC(=O)CCc1(=cc(C(C) (C)C)=c(O)c(C(C) (C)C)=c1)) (COC(=O)CCc2(=cc(C(C) (C)C)=c(O)c(C(C) (C)C)=c2))COC(=O)CCc3(=cc(C(C) (C)C)=c(O)c(C(C) (C)C)=c3))=O)c4)
Molecular Formula	C73H108O12

Producer Related Part

Company:	EUROPEAN COMMISSION - European Chemicals Bureau
Creation date:	11-FEB-2000

Substance Related Part

Company:	EUROPEAN COMMISSION - European Chemicals Bureau
Creation date:	11-FEB-2000

Printing date:	28-NOV-2001
Revision date:	11-FEB-2000
Date of last Update:	11-FEB-2000

Number of Pages: 37

Chapter (profile):	Chapter: 1, 2, 3, 4, 5, 7
Reliability (profile):	Reliability: without reliability, 1, 2, 3, 4
Flags (profile):	Flags: without flag, confidential, non confidential, WGK (DE), TA-Luft (DE), Material Safety Dataset, Risk Assessment, Directive 67/548/EEC, SIDS

1.0.1 OECD and Company Information

Name: BASF AG
Street: Karl-Bosch-Str
Town: 67056 Ludwigshafen
Country: Germany

Name: Ciba Additive GmbH
Street: Chemiestraße
Town: 68619 Lampertheim
Country: Germany
Phone: 06254-79237
Telefax: 06254-79511

Name: Clariant GmbH
Town: 65926 Frankfurt am Main
Country: Germany

Name: GREAT LAKES CHEMICAL ITALIA
Street: VIA QUARANTA 29
Town: 20141 MILAN
Country: Italy
Phone: 0039(2)525751
Telefax: 0039(2)52575233

Name: Lowi Polymer Stabilizers GmbH
Street: Teplitzer Straße 14-16
Town: 84478 Waldkraiburg
Country: Germany
Phone: ++49 8638 608 0
Telefax: ++49 8638 608 200
Telex: 863884

Name: Raschig GmbH
Town: 67063 Ludwigshafen
Country: Germany

Name: Shell Nederland Chemie B.V.
Street: Vondelingenweg 601
Town: 3196 KK Rotterdam
Country: Netherlands

1.0.2 Location of Production Site
-

1.0.3 Identity of Recipients
-

1.1 General Substance Information

Substance type: organic
Physical status: solid

1.1.0 Details on Template

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1.1.1 Spectra

-

1.2 Synonyms

A0 60
Source: BASF AG Ludwigshafen
Hoechst AG Frankfurt/Main
Clariant GmbH Frankfurt am Main

ADK Stab AO 60
Source: BASF AG Ludwigshafen
Hoechst AG Frankfurt/Main
Clariant GmbH Frankfurt am Main

Anox 20
Source: BASF AG Ludwigshafen
Hoechst AG Frankfurt/Main
Clariant GmbH Frankfurt am Main
Lowi Polymer Stabilizers GmbH Waldkraiburg

Anox 20AM
Source: BASF AG Ludwigshafen
Hoechst AG Frankfurt/Main
Clariant GmbH Frankfurt am Main

AO 1
Source: BASF AG Ludwigshafen
Hoechst AG Frankfurt/Main
Clariant GmbH Frankfurt am Main

AO 3
Source: BASF AG Ludwigshafen
Hoechst AG Frankfurt/Main
Clariant GmbH Frankfurt am Main

AO 60
Source: BASF AG Ludwigshafen
Hoechst AG Frankfurt/Main
Clariant GmbH Frankfurt am Main

Benzenepropanoic acid, 3,5-bis(1,1-dimethylethyl)-4-hydroxy-, 2,2-bis[[3-[3,5-bis(1,1-dimethylethyl)-4-hydroxyphenyl]-1-oxopropoxy]methyl]-1,3-propanediyl ester (9CI)
Source: BASF AG Ludwigshafen

BP 101
Source: BASF AG Ludwigshafen
Hoechst AG Frankfurt/Main
Clariant GmbH Frankfurt am Main

Fenozan 22
Source: BASF AG Ludwigshafen
Hoechst AG Frankfurt/Main
Clariant GmbH Frankfurt am Main

Fenozan 23
Source: BASF AG Ludwigshafen
Hoechst AG Frankfurt/Main
Clariant GmbH Frankfurt am Main

Hostanox O 10
Source: Hoechst AG Frankfurt/Main
Clariant GmbH Frankfurt am Main

Hydrocinnamic acid, 3,5-di-tert-butyl-4-hydroxy-, neopentanetetrayl ester (8CI)
Source: BASF AG Ludwigshafen

Hydrocinnamic acid, 3,5-di-tert-butyl-4-hydroxy-, tetraester with pentaerythritol (7CI)
Source: BASF AG Ludwigshafen

Irfganox 1040
Source: Hoechst AG Frankfurt/Main
Clariant GmbH Frankfurt am Main

Irganox 1010
Source: Shell Nederland Chemie B.V. Rotterdam
BASF AG Ludwigshafen
Hoechst AG Frankfurt/Main
Clariant GmbH Frankfurt am Main

Irganox 1010, TK 10042, Irganox L 101
Source: Ciba Additive GmbH Lampertheim

Irganox 1010FF
Source: BASF AG Ludwigshafen
Hoechst AG Frankfurt/Main
Clariant GmbH Frankfurt am Main

Irganox 1010FP
Source: BASF AG Ludwigshafen
Hoechst AG Frankfurt/Main
Clariant GmbH Frankfurt am Main

Irganox 1040
Source: BASF AG Ludwigshafen

Lowinox PP35
Source: Lowi Polymer Stabilizers GmbH Waldkraiburg

Mark AO 60
Source: BASF AG Ludwigshafen
Hoechst AG Frankfurt/Main
Clariant GmbH Frankfurt am Main

Naugard 10
Source: BASF AG Ludwigshafen
Hoechst AG Frankfurt/Main
Clariant GmbH Frankfurt am Main

Neopentanetetrayl 3,5-di-tert-butyl-4-hydroxyhydrocinnamate
Source: BASF AG Ludwigshafen
Hoechst AG Frankfurt/Main
Clariant GmbH Frankfurt am Main

Pentaerythritol tetrakis(3,5-di-tert-butyl-4-hydroxyhydrocinnamate)
Source: BASF AG Ludwigshafen

Pentaerythritol tetrakis(4-hydroxy-3,5-di-tert-butyl)hydrocinnamate
Source: BASF AG Ludwigshafen

Pentaerythritol tetrakis[(3,5-di-tert-butyl-4- hydroxyphenyl)propionate]
Source: BASF AG Ludwigshafen

Pentaerythritol tetrakis[.beta.-(3,5-di-tert-butyl-4- hydroxyphenyl)propionate]
Source: BASF AG Ludwigshafen

Pentaerythritol tetrakis[3-(3,5-di-tert-butyl-4- hydroxyphenyl)propanoate]
Source: BASF AG Ludwigshafen

Pentaerythritol tetrakis[3-(3,5-di-tert-butyl-4- hydroxyphenyl)propionate]
Source: BASF AG Ludwigshafen

Pentaerythritol tetrakis[3-(4-hydroxy-3,5-di-tert- butylphenyl)propionate]
Source: BASF AG Ludwigshafen

Pentaerythritol, tetrakis(3,5-di-tert-butyl-4-hydroxyhydrocinnamate) (8CI)
Source: BASF AG Ludwigshafen

Pentaerythritol,tetrakis[3-(3,5-di-tert-butyl-4-hydroxyphenyl)propionate].
Pentaerythritol,tetrakis(3,5-di-tert-butyl-4-hydroxyhydrocinnamate).
Tetrakis[methylene(3,5-di-tert-butyl-4-hydroxyhydrocinnamate)]methane.
Neopentanetetrayl 3,5-di-
Source: GREAT LAKES CHEMICAL ITALIA MILAN

Pentaerythrityl tetrakis(3,5-di-tert-butyl-4-hydroxy- phenyl)propionate
Source: BASF AG Ludwigshafen

Pentaerythrityl tetrakis(4-hydroxy-3,5-di-tert- butylphenylpropionate)
Source: BASF AG Ludwigshafen

Pentaerythrityl tetrakis[.beta.-(4-hydroxy-3,5-di-tert- butylphenyl)propionate]
Source: BASF AG Ludwigshafen

Pentaerythrityl tetrakis[3-(3,5-di-tert-butyl-4- hydroxyphenyl)propionate]
Source: BASF AG Ludwigshafen

Pentaerytrityl tetrakis(3,5-di-tert-butyl-4-hydroxyphenyl)propionate
Source: BASF AG Ludwigshafen

Phenosane 23
Source: BASF AG Ludwigshafen
Hoechst AG Frankfurt/Main
Clariant GmbH Frankfurt am Main

RA 1010
Source: BASF AG Ludwigshafen
Hoechst AG Frankfurt/Main
Clariant GmbH Frankfurt am Main

Ralox 630
Source: BASF AG Ludwigshafen
Hoechst AG Frankfurt/Main
Clariant GmbH Frankfurt am Main

Sumilizer BP 101
Source: BASF AG Ludwigshafen
Hoechst AG Frankfurt/Main
Clariant GmbH Frankfurt am Main

tert-butyl-4-hydroxyhydrocinnamate. Irganox 1010. Anox 20
Source: GREAT LAKES CHEMICAL ITALIA MILAN

Tetraalkofen BPE
Source: BASF AG Ludwigshafen
Hoechst AG Frankfurt/Main
Clariant GmbH Frankfurt am Main

Tetrakis(3,5-di-tert-butyl-4-hydroxyhydrocinnamoyloxymethyl)methane
Source: BASF AG Ludwigshafen

Tetrakis[3-(3,5-di-tert-butyl-4-hydroxyphenyl)propionyloxymethyl]met hane
Source: BASF AG Ludwigshafen

Tetrakis[3-(4-hydroxy-3,5-di-tert-butylphenyl)propionyloxymethyl]met hane
Source: BASF AG Ludwigshafen

Tetrakis[methylen(3,5-di-tert.-butyl-4-hydroxyhydrocinnamat)]methan;
Source: Raschig GmbH Ludwigshafen

Tetrakis[methylene(3,5-di-tert-butyl-4-hydroxyhydrocinnamate)]methan e
Source: BASF AG Ludwigshafen

Tetrakis[[[.beta.-(3,5-di-tert-butyl-4-hydroxyphenyl)propionyl]oxy]methyl]methane
Source: BASF AG Ludwigshafen

1.3 Impurities
-

1.4 Additives
-

1.5 Quantity

Quantity	10 000	- 50 000	tonnes

1.6.1 Labelling
-

1.6.2 Classification
-

1.7 Use Pattern

Type: type
Category: Non dispersive use

Type: type
Category: Use in closed system

Type: type
Category: Use resulting in inclusion into or onto matrix

Type: industrial
Category: Polymers industry

Type: use
Category: Stabilizers

Type: use
Category: other: Antioxidans

1.7.1 Technology Production/Use
-

1.8 Occupational Exposure Limit Values

Type of limit: MAK (DE)
Limit value: 1.5 mg/m3
Remark: Allgemeiner Staubgrenzwert, alveolengängiger Anteil
Source: Lowi Polymer Stabilizers GmbH Waldkraiburg

Type of limit: MAK (DE)
Limit value: 4 mg/m3
Remark: Allgemeiner Staubgrenzwert, einatembarer Anteil
Source: Lowi Polymer Stabilizers GmbH Waldkraiburg

Type of limit: other
Limit value: 10 mg/m3
Remark: Der von Ciba Additive festgelegte 8-Stunden Mittelwert (TWA) für Gesamtstaub bei beruflicher Exposition beträgt 10 mg/m3.
Source: Ciba Additive GmbH Lampertheim

Type of limit:
Limit value:
Remark: no occupational exposure limit values established by OSHA ACGIH,NIOSH
Source: GREAT LAKES CHEMICAL ITALIA MILAN

Type of limit:
Limit value:
Remark: Allgemeinen Staubgrenzwert beachten.
Source: Raschig GmbH Ludwigshafen

1.9 Source of Exposure

Country: Italy: GREAT LAKES CHEMICAL RAVENNA PLANT (Ra).
Remark: Anox 20 is produced by transesterification reaction phase from pentaerythritol and methyl 3,5-di-tert-bu tyl-4-hydroxy-hydrocinnamate in presence of soluble base catalyst.
Probable routes of humane exposure, may occur by inhalation or dermal contact during manufatturing
Source: GREAT LAKES CHEMICAL ITALIA MILAN

Source: Ciba Additive GmbH Lampertheim

1.10.1 Recommendations/Precautionary Measures
-

1.10.2 Emergency Measures
-

1.11 Packaging
-

1.12 Possib. of Rendering Subst. Harmless
-

1.13 Statements Concerning Waste
-

1.14.1 Water Pollution

Classified by: other: Selbsteinstufung Ciba-Additive GmbH
Labelled by:
Class of danger: 1 (weakly water polluting)
Source: BASF AG Ludwigshafen
(1)

Classified by: other: Wassergefährdungsklasse (WGK)
Labelled by:
Class of danger: 1 (weakly water polluting)
Remark: Selbsteinstufung
Source: Hoechst AG Frankfurt/Main
Clariant GmbH Frankfurt am Main
(2) (3)

1.14.2 Major Accident Hazards
-

1.14.3 Air Pollution

Classified by: TA-Luft (DE)
Labelled by:
Number: 3.1.7 (organic substances)
Class of danger: III
Source: BASF AG Ludwigshafen
(1)

Classified by: TA-Luft (DE)
Labelled by:
Number:
Class of danger: III
Source: Hoechst AG Frankfurt/Main
Clariant GmbH Frankfurt am Main
(3)

1.15 Additional Remarks

Remark: DISPOSAL METHOD: by controlled incineration.
TRANSPORT INFORMATION: Rail/road(RID/ADR): NOT RESTRICTED
Sea(IMO/IMDG) : NOT RESTRICTED
AIR(ICAO-IATA) : NOT RESTRICTED
Source: GREAT LAKES CHEMICAL ITALIA MILAN

1.16 Last Literature Search
-

1.17 Reviews
-

1.18 Listings e.g. Chemical Inventories
-

2.1 Melting Point

Value: = 110 - 125 degree C
Decomposition: no
Sublimation: no
Method: other
Year: 1994
GLP: no
Source: GREAT LAKES CHEMICAL ITALIA MILAN
(4)

Value: 110 - 125 degree C
Decomposition: no
Sublimation: no
Method: other
Year: 1992
GLP: no
Source: Ciba Additive GmbH Lampertheim

2.2 Boiling Point

Value:
Remark: not applicable
Source: GREAT LAKES CHEMICAL ITALIA MILAN

Value:
GLP: no
Remark: Not applicable
Source: Ciba Additive GmbH Lampertheim

2.3 Density

Type: relative density
Value: = 1.15 g/cm3 at 25 degree C
Method: other
Year: 1994
GLP: no data
Source: GREAT LAKES CHEMICAL ITALIA MILAN
(5)

Type: relative density
Value: 1.15 g/cm3 at 25 degree C
Method: other
Year: 1985
GLP: no data
Source: Ciba Additive GmbH Lampertheim

2.3.1 Granulometry
-

2.4 Vapour Pressure

Value: = .0000000000013 hPa at 20 degree C
Method: other (measured)
Year: 1990
GLP: no data
Source: GREAT LAKES CHEMICAL ITALIA MILAN
(5)

Value: ca. .000000013 hPa at 20 degree C
Method: other (measured)
Year: 1985
GLP: no data
Source: Ciba Additive GmbH Lampertheim

2.5 Partition Coefficient

log Pow: = 23 at 25 degree C
Method: other (measured)
Year: 1994
GLP: no data
Source: GREAT LAKES CHEMICAL ITALIA MILAN
(5)

log Pow: ca. 23 at 25 degree C
Method: Directive 84/449/EEC, A.8 "Partition coefficient"
Year: 1985
GLP: yes
Source: Ciba Additive GmbH Lampertheim

2.6.1 Water Solubility

Value: < .0001 g/l at 20 degree C
Method: Directive 84/449/EEC, A.6 "Water solubility"
Year: 1989
GLP: no
Source: Ciba Additive GmbH Lampertheim

Value: = .3 g/l at 20 degree C
Method: other
GLP: no data
Source: GREAT LAKES CHEMICAL ITALIA MILAN
(6)

Value: < 1 mg/l at 20 degree C
pH: = 6 at 10 g/l
Year: 1990
GLP: no data
Source: GREAT LAKES CHEMICAL ITALIA MILAN
(5)

2.6.2 Surface Tension
-

2.7 Flash Point

Value: = 297 degree C
Type: open cup
Method: Directive 84/449/EEC, A.9 "Flash point"
Year: 1994
GLP: no data
Source: GREAT LAKES CHEMICAL ITALIA MILAN
(7)

Value: 297 degree C
Type: other
Method: other
Year: 1985
GLP: no data
Source: Ciba Additive GmbH Lampertheim

2.8 Auto Flammability

Value: > 350 degree C
Method: other
Year: 1990
GLP: no
Source: Ciba Additive GmbH Lampertheim

Value: = 410 degree C
Method: other
Year: 1994
GLP: no data
Source: GREAT LAKES CHEMICAL ITALIA MILAN
(5)

2.9 Flammability

Result: other
Method: other
Year: 1990
GLP: no
Source: Ciba Additive GmbH Lampertheim
Test condition: Nicht entzuendlich unter 410 Grad Celsius.

Result:
Remark: not available
Source: GREAT LAKES CHEMICAL ITALIA MILAN

2.10 Explosive Properties

Result: not explosive
Method: Directive 84/449/EEC, A.14 "Explosive properties"
Year: 1990
GLP: yes
Remark: not explosive by shock and friction.
Source: GREAT LAKES CHEMICAL ITALIA MILAN
(4)

Result: not explosive
Method: other
Year: 1993
GLP: no
Source: Ciba Additive GmbH Lampertheim
Test condition: Das Produkt ist gegenüber Hitze, mechan. Schläge und Reiben nicht explosiv.

Result:
Method: other: VDI, ISO/DIS NFPA.
Year: 1989
GLP: no
Remark: Dust cloud may explode if ignited in an enclosed area 74 (bar m) 1/sec
Source: GREAT LAKES CHEMICAL ITALIA MILAN
(4)

2.11 Oxidizing Properties

Result: no oxidizing properties
Method: other
Year: 1994
GLP: no
Source: GREAT LAKES CHEMICAL ITALIA MILAN
(4)

Result: no oxidizing properties
Method: other
Year: 1993
GLP: no
Remark: Begruendung aufgrund der Struktur.
Source: Ciba Additive GmbH Lampertheim

2.12 Additional Remarks

Remark: it can react with strong oxidizing material.
Source: GREAT LAKES CHEMICAL ITALIA MILAN

Source: Ciba Additive GmbH Lampertheim
Test substance: Oberflaechenspannung: 72.8 mN/m (Methode: EEC-TG A.5)

3.1.1 Photodegradation

Type:
Method:
Year: GLP:
Test substance:
Remark: no data
Source: GREAT LAKES CHEMICAL ITALIA MILAN

3.1.2 Stability in Water

Type:
Method:
Year: GLP:
Test substance:
Remark: no data
Source: GREAT LAKES CHEMICAL ITALIA MILAN

Type:
Method:
Year: GLP:
Test substance:
Result: Wegen geringer Wasserloeslichkeit konnten keine Teste durchgefuehrt werden. (Hydrolyse in Funktion des pH)
Source: Ciba Additive GmbH Lampertheim

3.1.3 Stability in Soil

Type: Radiolabel:
Concentration:
Cation exch. capac.
Microbial biomass:
Method:
Year: GLP:
Test substance:
Remark: no data
Source: GREAT LAKES CHEMICAL ITALIA MILAN

Type: Radiolabel:
Concentration:
Cation exch. capac.
Microbial biomass:
Method:
Year: GLP:
Test substance:
Remark: Keine terrestrische Oekotox-Daten.
Source: Ciba Additive GmbH Lampertheim

3.2 Monitoring Data (Environment)

Type of measurement:
Medium:
Method:
Concentration
Remark: no data
Source: GREAT LAKES CHEMICAL ITALIA MILAN

3.3.1 Transport between Environmental Compartments

Type:
Media:
Air (Level I):
Water (Level I):
Soil (Level I):
Biota (L.II/III):
Soil (L.II/III):
Method:
Year:
Remark: no data
Source: GREAT LAKES CHEMICAL ITALIA MILAN

Type:
Media:
Air (Level I):
Water (Level I):
Soil (Level I):
Biota (L.II/III):
Soil (L.II/III):
Method:
Year:
Remark: Keine Daten.
Source: Ciba Additive GmbH Lampertheim

3.3.2 Distribution

Media:
Method:
Year:
Remark: no data
Source: GREAT LAKES CHEMICAL ITALIA MILAN

Media:
Method:
Year:
Remark: Keine Daten.
Source: Ciba Additive GmbH Lampertheim

3.4 Mode of Degradation in Actual Use

Remark: no data
Source: GREAT LAKES CHEMICAL ITALIA MILAN

3.5 Biodegradation

Type:
Inoculum:
Method:
Year: GLP:
Test substance:
Remark: In a Sturm test the product isn't biodegradable OECD 303A (coupled units test) 45%.
Source: GREAT LAKES CHEMICAL ITALIA MILAN

Type:
Inoculum:
Method:
Year: GLP:
Test substance:
Remark: Die Substanz ist nicht leicht abbaubar.
Source: Ciba Additive GmbH Lampertheim

3.6 BOD5, COD or BOD5/COD Ratio

C O D

Method: Directive 84/449/EEC, C.9 "Biodegradation: Chemical Oxygen Demand"
Year: 1992 GLP: yes
COD: 1790 mg/g substance

Source: Ciba Additive GmbH Lampertheim

Concentration: g/l related to

Remark: no data
Source: GREAT LAKES CHEMICAL ITALIA MILAN

3.7 Bioaccumulation

Species:
Exposure period:
Concentration:
BCF:
Elimination:
Method:
Year: GLP:
Test substance:
Remark: no data
Source: GREAT LAKES CHEMICAL ITALIA MILAN

Species:
Exposure period:
Concentration:
BCF:
Elimination:
Method:
Year: GLP:
Test substance:
Remark: Keine Daten.
Source: Ciba Additive GmbH Lampertheim

3.8 Additional Remarks

Remark: no data
Source: GREAT LAKES CHEMICAL ITALIA MILAN

AQUATIC ORGANISMS

4.1 Acute/Prolonged Toxicity to Fish

Type:	static	
Species:	Brachydanio rerio (Fish, fresh water)	
Exposure period:	96 hour(s)	
Unit:	mg/l	Analytical monitoring: yes
LC50:	> 100	
Method:	OECD Guide-line 203 "Fish, Acute Toxicity Test"	
Year:	1985	GLP: yes
Test substance:	as prescribed by 1.1 - 1.4	
Source:	Ciba Additive GmbH Lampertheim	

Type:		
Species:	Brachydanio rerio (Fish, fresh water)	
Exposure period:	96 hour(s)	
Unit:	mg/l	Analytical monitoring: no data
LC50:	> 100	
Method:	other	
Year:	1994	GLP: no data
Test substance:	no data	
Source:	GREAT LAKES CHEMICAL ITALIA MILAN	

(5)

4.2 Acute Toxicity to Aquatic Invertebrates

Type:		
Species:	Daphnia magna (Crustacea)	
Exposure period:	24 hour(s)	
Unit:	mg/l	Analytical monitoring: yes
EC50:	> 86	
Method:	OECD Guide-line 202, part 1 "Daphnia sp., Acute Immobilisation Test"	
Year:	1985	GLP: yes
Test substance:	as prescribed by 1.1 - 1.4	
Source:	Ciba Additive GmbH Lampertheim	

Type:		
Species:	Daphnia magna (Crustacea)	
Exposure period:	24 hour(s)	
Unit:	mg/l	Analytical monitoring: no data
EC50:	> 86	
Method:	other	
Year:	1990	GLP: no data
Test substance:	no data	
Source:	GREAT LAKES CHEMICAL ITALIA MILAN	

(5)

4.3 Toxicity to Aquatic Plants e.g. Algae

Species: Scenedesmus subspicatus (Algae)
Endpoint: growth rate
Exposure period: 72 hour(s)
Unit: mg/l Analytical monitoring: yes
EC50: > 100
Method: Directive 87/302/EEC, part C, p. 89 "Algal inhibition test"
Year: 1992 GLP: yes
Test substance: as prescribed by 1.1 - 1.4
Source: Ciba Additive GmbH Lampertheim

Species: other algae
Endpoint:
Exposure period: 72 hour(s)
Unit: mg/l Analytical monitoring:
EC50: > 100
Method: other
Year: 1994 GLP: no data
Test substance: no data
Source: GREAT LAKES CHEMICAL ITALIA MILAN

(5)

4.4 Toxicity to Microorganisms e.g. Bacteria

Type: aquatic
Species: activated sludge of a predominantly domestic sewage
Exposure period: 3 hour(s)
Unit: mg/l Analytical monitoring: no data
IC50 : > 100
Method: OECD Guide-line 209 "Activated Sludge, Respiration Inhibition Test"
Year: 1988 GLP: no data
Test substance: as prescribed by 1.1 - 1.4
Source: Ciba Additive GmbH Lampertheim

Type:
Species: Escherichia coli (Bacteria)
Exposure period: 3 hour(s)
Unit: mg/l Analytical monitoring:
EC50: > 100
Method: other
Year: 1994 GLP: no data
Test substance: no data
Source: GREAT LAKES CHEMICAL ITALIA MILAN

(5)

4.5 Chronic Toxicity to Aquatic Organisms

4.5.1 Chronic Toxicity to Fish

Species:
Endpoint:
Exposure period:
Unit: Analytical monitoring:
Method:
Year: GLP:
Test substance:
Remark: no data
Source: GREAT LAKES CHEMICAL ITALIA MILAN

Species:
Endpoint:
Exposure period:
Unit: Analytical monitoring:
Method:
Year: GLP:
Test substance:
Remark: Keine Pruefungen.
Source: Ciba Additive GmbH Lampertheim

4.5.2 Chronic Toxicity to Aquatic Invertebrates

Species:
Endpoint:
Exposure period:
Unit: Analytical monitoring:
Method:
Year: GLP:
Test substance:
Remark: Keine Pruefungen.
Source: Ciba Additive GmbH Lampertheim

TERRESTRIAL ORGANISMS

4.6.1 Toxicity to Soil Dwelling Organisms

Type:
Species:
Endpoint:
Exposure period:
Unit:
Method:
Year: GLP:
Test substance:
Remark: no data
Source: GREAT LAKES CHEMICAL ITALIA MILAN

Type:
Species:
Endpoint:
Exposure period:
Unit:
Method:
Year: GLP:
Test substance:
Remark: Keine Pruefungen.
Source: Ciba Additive GmbH Lampertheim

4.6.2 Toxicity to Terrestrial Plants

Species:
Endpoint:
Expos. period:
Unit:
Method:
Year: GLP:
Test substance:
Remark: no data
Source: GREAT LAKES CHEMICAL ITALIA MILAN

Species:
Endpoint:
Expos. period:
Unit:
Method:
Year: GLP:
Test substance:
Remark: Keine Pruefungen.
Source: Ciba Additive GmbH Lampertheim

4.6.3 Toxicity to other Non-Mamm. Terrestrial Species

Species:
Endpoint:
Expos. period:
Unit:
Method:
Year: GLP:
Test substance:
Remark: no data
Source: GREAT LAKES CHEMICAL ITALIA MILAN

Species:
Endpoint:
Expos. period:
Unit:
Method:
Year: GLP:
Test substance:
Remark: Keine Informationen.
Source: Ciba Additive GmbH Lampertheim

4.7 Biological Effects Monitoring

Remark: no data
Source: GREAT LAKES CHEMICAL ITALIA MILAN

Remark: Keine Information.
Source: Ciba Additive GmbH Lampertheim

4.8 Biotransformation and Kinetics

Type:
Remark: no data
Source: GREAT LAKES CHEMICAL ITALIA MILAN

Type:
Remark: Keine Informationen.
Source: Ciba Additive GmbH Lampertheim

4.9 Additional Remarks

Remark: no data
Source: GREAT LAKES CHEMICAL ITALIA MILAN

5.1 Acute Toxicity

5.1.1 Acute Oral Toxicity

Type:	LD50	
Species:	rat	
Strain:		
Sex:		
Number of Animals:		
Vehicle:		
Value:	> 5000 mg/kg bw	
Method:	other	
Year:	1990	GLP: no data
Test substance:	no data	
Source:	GREAT LAKES CHEMICAL ITALIA MILAN	

(5)

Type:	LD50	
Species:	rat	
Strain:		
Sex:		
Number of Animals:		
Vehicle:		
Value:	> 5000 mg/kg bw	
Method:	other	
Year:	1974	GLP: no data
Test substance:	as prescribed by 1.1 - 1.4	
Source:	Ciba Additive GmbH Lampertheim	

Type:	LD50	
Species:	mammal	
Strain:		
Sex:		
Number of Animals:		
Vehicle:		
Value:	= 10000 mg/kg bw	
Method:	other	
Year:		GLP: no data
Test substance:	no data	
Source:	GREAT LAKES CHEMICAL ITALIA MILAN	

(8)

5.1.2 Acute Inhalation Toxicity

Type:	LC0	
Species:	rat	
Strain:		
Sex:		
Number of Animals:		
Vehicle:		
Exposure time:	4 hour(s)	
Value:	> .11 mg/l	
Method:		
Year:	1990	GLP: no data
Test substance:	no data	
Remark:	No deaths were observed. Rats were exposed to fumes emitted where product was heated to 316 degrees Celsius.	
Source:	GREAT LAKES CHEMICAL ITALIA MILAN	

(5)

Type:	LC50	
Species:	rat	
Strain:		
Sex:		
Number of Animals:		
Vehicle:		
Exposure time:	1 hour(s)	
Value:	> 46 mg/l	
Method:	other	
Year:	1990	GLP: no data
Test substance:	no data	
Source:	GREAT LAKES CHEMICAL ITALIA MILAN	

(9)

Type:	LC50	
Species:	rat	
Strain:		
Sex:		
Number of Animals:		
Vehicle:		
Exposure time:	4 hour(s)	
Value:	> 1.95 mg/l	
Method:	other	
Year:	1983	GLP: no
Test substance:	as prescribed by 1.1 - 1.4	
Source:	Ciba Additive GmbH Lampertheim	

5.1.3 Acute Dermal Toxicity

Type:	LD50	
Species:	rabbit	
Strain:		
Sex:		
Number of Animals:		
Vehicle:		
Value:	> 3160 mg/kg bw	
Method:	other	
Year:	1990	GLP: no data
Test substance:	no data	
Source:	GREAT LAKES CHEMICAL ITALIA MILAN	

(5)

Type:	LD50	
Species:	rabbit	
Strain:		
Sex:		
Number of Animals:		
Vehicle:		
Value:	> 3160 mg/kg bw	
Method:	other	
Year:	1964	GLP: no data
Test substance:	as prescribed by 1.1 - 1.4	
Source:	Ciba Additive GmbH Lampertheim	

5.1.4 Acute Toxicity, other Routes

Type:		
Species:		
Strain:		
Sex:		
Number of Animals:		
Vehicle:		
Route of admin.:		
Value:		
Method:		
Year:		GLP:
Test substance:		
Remark:	no data	
Source:	GREAT LAKES CHEMICAL ITALIA MILAN	

5.2 Corrosiveness and Irritation

5.2.1 Skin Irritation

Species:	rabbit	
Concentration:		
Exposure:		
Exposure Time:		
Number of Animals:		
PDII:		
Result:	not irritating	
EC classificat.:	not irritating	
Method:	other	
Year:	1990	GLP: no data
Test substance:	no data	
Source:	GREAT LAKES CHEMICAL ITALIA MILAN	

(5)

Species:	rabbit	
Concentration:		
Exposure:		
Exposure Time:		
Number of Animals:		
PDII:		
Result:	not irritating	
EC classificat.:	not irritating	
Method:	other	
Year:	1964	GLP: no
Test substance:	as prescribed by 1.1 - 1.4	
Source:	Ciba Additive GmbH Lampertheim	

5.2.2 Eye Irritation

Species:	rabbit	
Concentration:		
Dose:		
Exposure Time:		
Comment:		
Number of Animals:		
Result:	slightly irritating	
EC classificat.:	not irritating	
Method:		
Year:	1990	GLP: no data
Test substance:	no data	
Remark:	draize score 0/110	
Source:	GREAT LAKES CHEMICAL ITALIA MILAN	

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Species: rabbit
Concentration:
Dose:
Exposure Time:
Comment:
Number of Animals:
Result: not irritating
EC classificat.: not irritating
Method: other
Year: 1964 GLP: no
Test substance: as prescribed by 1.1 - 1.4
Source: Ciba Additive GmbH Lampertheim

5.3 Sensitization

Type: Maurer optimisation test
Species: guinea pig
Number of Animals:
Vehicle:
Result: not sensitizing
Classification: not sensitizing
Method: other
Year: 1977 GLP: no
Test substance: as prescribed by 1.1 - 1.4
Source: Ciba Additive GmbH Lampertheim

Type: Patch-Test
Species: human
Number of Animals:
Vehicle:
Result: not sensitizing
Classification: not sensitizing
Method: other
Year: 1990 GLP: no data
Test substance: no data
Remark: 0.5% w/v solution in dimethyl-phtalate
Source: GREAT LAKES CHEMICAL ITALIA MILAN

(9)

Type:
Species: guinea pig
Number of Animals:
Vehicle:
Result: not sensitizing
Classification: not sensitizing
Method: other
Year: 1990 GLP: no data
Test substance: no data
Source: GREAT LAKES CHEMICAL ITALIA MILAN

(5)

5.4 Repeated Dose Toxicity

Species: rat Sex: male/female
Strain: Sprague-Dawley
Route of admin.: oral feed
Exposure period: 3 Monate
Frequency of treatment:
Post. obs. period: Keine
Doses: 0, 2000, 10000 und 50000 ppm
Control Group: yes
NOAEL: 2500 mg/kg bw
Method: other
Year: 1966 GLP: no
Test substance: as prescribed by 1.1 - 1.4
Source: Ciba Additive GmbH Lampertheim

Species: dog Sex: male/female
Strain: Beagle
Route of admin.: oral feed
Exposure period: 3 Monate
Frequency of treatment:
Post. obs. period:
Doses: 0, 1000 und 10000 ppm
Control Group: yes
NOAEL: 322.4 mg/kg bw
Method: other
Year: 1981 GLP: yes
Test substance: as prescribed by 1.1 - 1.4
Source: Ciba Additive GmbH Lampertheim

Species: Sex:
Strain:
Route of admin.:
Exposure period:
Frequency of treatment:
Post. obs. period:
Doses:
Control Group:
Method:
Year: GLP:
Test substance:
Remark: no data
Source: GREAT LAKES CHEMICAL ITALIA MILAN

5.5 Genetic Toxicity 'in Vitro'

Type: Ames test
System of testing: Salmonella Typhimurium TA98, TA100, TA1535,TA1537, TA1538
Concentration: 1-5000 micrograms/plate
Cytotoxic Conc.:
Metabolic activation: with and without
Result: negative
Method: other
Year: 1991 GLP: yes
Test substance: as prescribed by 1.1 - 1.4
Source: GREAT LAKES CHEMICAL ITALIA MILAN

(11)

Type: Ames test
System of testing: Salmonella thyphi.
Concentration: 10-250 mikrogramm/0,1 ml
Cytotoxic Conc.:
Metabolic activation: with and without
Result: negative
Method: other
Year: 1977 GLP: no
Test substance: as prescribed by 1.1 - 1.4
Source: Ciba Additive GmbH Lampertheim

Type: Ames test
System of testing:
Concentration:
Cytotoxic Conc.:
Metabolic activation:
Result: negative
Method:
Year: 1990 GLP: no data
Test substance: no data
Source: GREAT LAKES CHEMICAL ITALIA MILAN

(5)

5.6 Genetic Toxicity 'in Vivo'

Type: Dominant lethal assay
Species: mouse Sex: male/female
Strain: other
Route of admin.: gavage
Exposure period: 6 Wochen
Doses: 0, 1000 und 3000 mg/kg
Result:
Method: other
Year: 1975 GLP: no
Test substance: as prescribed by 1.1 - 1.4
Result: Kein Hinweis fuer dominant lethalen Effekt.
Source: Ciba Additive GmbH Lampertheim

Type: Mammalian germ cell cytogenetic assay
Species: hamster Sex: male/female
Strain: other
Route of admin.: gavage
Exposure period: 2 Tage
Doses: 500, 1000 und 2000 mg/kg
Result:
Method: other
Year: 1978 GLP: no
Test substance: as prescribed by 1.1 - 1.4
Result: Keine Chromosomenaberation im Knochenmark.
Source: Ciba Additive GmbH Lampertheim

Type: Micronucleus assay
Species: rat Sex: male/female
Strain:
Route of admin.: oral unspecified
Exposure period: 0,18,42,66 hour
Doses: 5000 mg/kg
Result:
Method: Directive 84/449/EEC, B.11 "Other effects - Mutagenicity (in vivo mammalian bone-marrow cytogenic test, chromosomal analysis)"
Year: 1991 GLP: yes
Test substance: as prescribed by 1.1 - 1.4
Result: negative
Source: GREAT LAKES CHEMICAL ITALIA MILAN

(12)

Type: Micronucleus assay
Species: hamster Sex: male/female
Strain: other
Route of admin.: gavage
Exposure period: 48 Stunden
Doses: 500, 1000 und 2000 mg/Kg
Result:
Method: other
Year: 1978 GLP: no
Test substance: as prescribed by 1.1 - 1.4
Result: Kein Hinweis fuer mutagenen Effekt basierend auf Kernanomalie im Knochenmark.
Source: Ciba Additive GmbH Lampertheim

5.7 Carcinogenicity

Species: rat Sex: male/female
Strain: Sprague-Dawley
Route of admin.: oral feed
Exposure period: 104 Wochen
Frequency of treatment:
Post. obs. period:
Doses: 0, 1000, 3000 und 10000 ppm
Result:
Control Group: yes
Method: other
Year: 1974 GLP: no
Test substance: as prescribed by 1.1 - 1.4
Result: Kein Hinweis fuer ein tumorigenes Potential in der Ratte.
Source: Ciba Additive GmbH Lampertheim

Species: mouse Sex: male/female
Strain: other
Route of admin.: oral feed
Exposure period: 24 Monate
Frequency of treatment:
Post. obs. period:
Doses: 0, 100, 300 und 1000 ppm
Result:
Control Group: yes
Method: other
Year: 1981 GLP: yes
Test substance: as prescribed by 1.1 - 1.4
Result: Kein Hinweis fuer ein tumorigenes Potential in der Maus.
Source: Ciba Additive GmbH Lampertheim

Species: Sex:
Strain:
Route of admin.:
Exposure period:
Frequency of treatment:
Post. obs. period:
Doses:
Result:
Control Group:
Method:
Year: GLP:
Test substance:
Remark: no data
Source: GREAT LAKES CHEMICAL ITALIA MILAN

5.8 Toxicity to Reproduction

Type: Two generation study
Species: rat Sex: male/female
Strain: other
Route of admin.: oral feed
Exposure Period: 2-Generationen, 10 Monate
Frequency of treatment:
Premating Exposure Period
male: 10 Wochen
female: 10 Wochen
Duration of test: 10 Monate
Doses: 0, 1000, 3000 und 10000 ppm
Control Group: yes
NOAEL Parental: 10000 ppm
NOAEL F1 Offspr.: 10000 ppm
NOAEL F2 Offspr.: 10000 ppm
Method: other
Year: 1984 GLP: yes

Test substance: as prescribed by 1.1 - 1.4
Result: Kein Effekt auf Reproduktionskapazitaet, Fertilitaet und Ueberlebensfaehigkeit der Jungratten.
Source: Ciba Additive GmbH Lampertheim

Type:
Species: mouse Sex: female
Strain:
Route of admin.: gavage
Exposure Period: on days 6 through 15 of gestation.
Frequency of treatment:
Duration of test:
Doses: 0,150,500,1000 mg/kg/d
Control Group:
Method:
Year: 1992 GLP: no data
Test substance: no data
Result: No teratogenic effects on mice. Fetuses from the 1000 mg/kg/d group displayed a slight increase in the number of incompletely ossified sternebrae.
Source: GREAT LAKES CHEMICAL ITALIA MILAN

(13)

5.9 Developmental Toxicity/Teratogenicity

Species: rat Sex: female
Strain: Sprague-Dawley
Route of admin.: gavage
Exposure period: 10 Tage (Tag 6-15 der Schwangerschaft)
Frequency of treatment:
Duration of test: 10 Tage
Doses: 150, 500 und 1000 mg/Kg
Control Group: yes
NOAEL Maternalt.: 1000 mg/kg bw
NOAEL Teratogen.: 1000 mg/kg bw
Method: other
Year: 1975 GLP: no
Test substance: as prescribed by 1.1 - 1.4
Result: Kein Hinweis auf ein teratogener Effekt.
Source: Ciba Additive GmbH Lampertheim

Species: mouse Sex: female
Strain: other
Route of admin.: gavage
Exposure period: 10 Tage (6-15 Tag der Schwangerschaft)
Frequency of treatment:
Duration of test: 10 Tage
Doses: 150, 500 und 1000 mg/Kg
Control Group: yes
NOAEL Maternalt.: 1000 mg/kg bw
NOAEL Teratogen.: 1000 mg/kg bw
Method: other
Year: 1975 GLP: no
Test substance: as prescribed by 1.1 - 1.4
Result: Kein Hinweis fuer teratogenen Effekt.
Source: Ciba Additive GmbH Lampertheim

Species: Sex:
Strain:
Route of admin.:
Exposure period:
Frequency of treatment:
Duration of test:
Doses:
Control Group:
Method:
Year: GLP:
Test substance:
Remark: no data
Source: GREAT LAKES CHEMICAL ITALIA MILAN

5.10 Other Relevant Information

Type: adsorption
Source: Ciba Additive GmbH Lampertheim
Test substance: Radioaktiv markiertes C14 IRGANOX 1010 wurde via Schlundsonde einer maennlichen und weiblichen Ratte verabreicht.
2 - 3 % der markierten Verbindung wurde nach der Einmalverabreichung durch das gastro-intestinale System resorbiert.

Type:
Remark: no data
Source: GREAT LAKES CHEMICAL ITALIA MILAN

5.11 Experience with Human Exposure

Remark: No specific hazard known to human exposed to the substance during preparation.
Source: GREAT LAKES CHEMICAL ITALIA MILAN

Remark: Keine Daten.
Source: Ciba Additive GmbH Lampertheim

(1) Ciba-Additive GmbH, Sicherheitsdatenblatt Irganox 1010 (03/1994)

(2) Clariant GmbH (1994), EG-Sicherheitsdatenblatt (18.08.94)

(3) Clariant GmbH (1997): EG-Sicherheitsdatenblatt Hostanox 10 Granulat (Stand: 26.04.96)

(4) Internal reference.

(5) MSDS Ciba.

(6) Bennox MSDS

(7) MDL information systems.

(8) GISAAA Gigiena i Sanitariya 42(7),74,7. For English translation, see HYSAAV.

(9) MSDS Ciba-Geigy.¿

(10) MSDS Ciba-Geigy.

(11) RBM report 910077 1991

(12) RBM report 910078

(13) Doc# 88-920001887

7.1 End Point Summary

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7.2 Hazard Summary

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7.3 Risk Assessment

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