SCREENING-LEVEL HAZARD CHARACTERIZATION OF HIGH PRODUCTION VOLUME CHEMICALS

SPONSORED CHEMICAL

Thiodiethylene Bis(3,5-Di-tert-Butyl-4-Hydroxyhydrocinnamate
(IRGANOX 1035; CAS No. 41484-35-9)
[9th CI Name: Benzenepropanoic acid, 3,5-bis(1,1-dimethylethyl)-4-hydroxy-, thiodi-2,1-ethanediyl ester]

SUPPPORTING CHEMICAL

1,2-Bis(3,5-di-tert-butyl-4-hydroxyhydrocinnamoyl)hydrazine
(IRGANOX MD 1024; CAS No. 32687-78-8)
[9th CI Name: Benzenepropanoic acid, 3,5-bis(1,1-dimethylethyl)-4-hydroxy-,-[3-[3,5-bis(1,1-dimethylethyl)-4-hydroxyphenyl]-1-oxopropyl]hydrazide]

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INTERIM

Prepared by

High Production Volume Chemicals Branch
Risk Assessment Division
Office of Pollution Prevention and Toxics
Environmental Protection Agency
1200 Pennsylvania Avenue, NW
Washington, DC 20460-0001

SCREENING-LEVEL HAZARD CHARACTERIZATION OF HIGH PRODUCTION VOLUME CHEMICALS

The High Production Volume (HPV) Challenge Program[1] is a voluntary initiative aimed at developing and making publicly available screening-level health and environmental effects information on chemicals manufactured in or imported into the United States in quantities greater than one million pounds per year. In the Challenge Program, producers and importers of HPV chemicals voluntarily sponsor chemicals; sponsorship entails the identification and initial assessment of the adequacy of existing toxicity data/information, conducting new testing if adequate data do not exist, and making both new and existing data and information available to the public. Each complete data submission contains data on 18 internationally agreed to "SIDS" (Screening Information Data Set[1,2]) endpoints that are screening-level indicators of potential hazards (toxicity) for humans or the environment.

The Environmental Protection Agency's Office of Pollution Prevention and Toxics (OPPT) is evaluating the data submitted in the HPV Challenge Program on approximately 1400 sponsored chemicals. OPPT is using a hazard-based screening process to prioritize review of the submissions. The hazard-based screening process consists of two tiers described below briefly and in more detail on the Hazard Characterization website[3].

Tier 1 is a computerized sorting process whereby key elements of a submitted data set are compared to established criteria to "bin" chemicals/categories for OPPT review. This is an automated process performed on the data as submitted by the sponsor. It does not include evaluation of the quality or completeness of the data.

In Tier 2, a screening-level hazard characterization is developed by EPA that consists of an objective evaluation of the quality and completeness of the data set provided in the Challenge Program submissions. The evaluation is performed according to established EPA guidance[2,4] and is based primarily on hazard data provided by sponsors. EPA may also include additional or updated hazard information of which EPA, sponsors or other parties have become aware. The hazard characterization may also identify data gaps that will become the basis for a subsequent data needs assessment where deemed necessary. Under the HPV Challenge Program, chemicals that have similar chemical structures, properties and biological activities may be grouped together and their data shared across the resulting category. This approach often significantly reduces the need for conducting tests for all endpoints for all category members. As part of Tier 2, evaluation of chemical category rationale and composition and data extrapolation(s) among category members is performed in accord with established EPA[2] and OECD[5] guidance.

The screening-level hazard characterizations that emerge from Tier 2 are important contributors to OPPT's existing chemicals review process. These hazard characterizations are technical documents intended to support subsequent decisions and actions by OPPT. Accordingly, the documents are not written with the goal of informing the general public. However, they do provide a vehicle for public access to a concise assessment of the raw technical data on HPV chemicals and provide information previously not readily available to the public. The public, including sponsors, may offer comments on the hazard characterization documents.

The screening-level hazard characterizations, as the name indicates, do not evaluate the potential risks of a chemical or a chemical category, but will serve as a starting point for such reviews. In 2007, EPA received data on uses of and exposures to high-volume TSCA existing chemicals, submitted in accordance with the requirements of the Inventory Update Reporting (IUR) rule. For the chemicals in the HPV Challenge Program, EPA will review the IUR data to evaluate exposure potential. The resulting exposure information will then be combined with the screening-level hazard characterizations to develop screening-level risk characterizations[4,6]. The screening-level risk characterizations will inform EPA on the need for further work on individual chemicals or categories. Efforts are currently underway to consider how best to utilize these screening-level risk characterizations as part of a risk-based decision-making process on HPV chemicals which applies the results of the successful U.S. High Production Volume Challenge Program and the IUR to support judgments concerning the need, if any, for further action.

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[1] U.S. EPA. High Production Volume (HPV) Challenge Program; http://www.epa.gov/chemrtk/index.htm.
[2] U.S. EPA. HPV Challenge Program – Information Sources; http://www.epa.gov/chemrtk/pubs/general/guidocs.htm.
[3] U.S. EPA. HPV Chemicals Hazard Characterization website (http://www.epa.gov/hpvis/abouthc.html).
[4] U.S. EPA. Risk Assessment Guidelines; http://cfpub.epa.gov/ncea/raf/rafguid.cfm.
[5] OECD. Guidance on the Development and Use of Chemical Categories; http://www.oecd.org/dataoecd/60/47/1947509.pdf.
[6] U.S. EPA. Risk Characterization Program; http://www.epa.gov/osa/spc/2riskchr.htm.

SCREENING-LEVEL HAZARD CHARACTERIZATION
IRGANOX 1035 (CAS No. 41484-35-9)

Introduction

The sponsor, Ciba Specialty Chemicals Corporation, submitted a Test Plan and Robust Summaries to EPA for Thiodiethylene bis(3,5-di-tert-butyl-4-hydroxyhydrocinnamate (IRGANOX 1035, CAS No. 41484-35-9) on August 8, 2003. EPA posted the submission on the ChemRTK HPV Challenge website on August 28, 2003 (http://www.epa.gov/chemrtk/pubs/summaries/thiotbhy/c14690tc.htm). EPA comments on the original submission were posted to the website on January 22, 2004. Public comments were also received and posted to the website. The sponsor submitted updated/revised documents on July 11, 2007 which were posted to the ChemRTK website on August 29, 2007.

This screening level hazard characterization is based primarily on the review of the test plan and robust summaries of studies submitted by the sponsor(s) under the HPV Challenge Program. In preparing the hazard characterization, EPA considered its own comments and public comments on the original submission as well as the sponsor's responses to comments and revisions made to the submission. A summary table of SIDS endpoint data with the structure(s) of the sponsored chemical(s) is included in the appendix. The screening-level hazard characterization for environmental and human health effects is based largely on SIDS endpoints and is described according to established EPA or OECD effect level definitions and hazard assessment practices.

Justification for Supporting Chemicals

In response to EPA comments on the original submission that recommended conducting a combined reproductive/developmental toxicity screening test, the sponsor proposed that developmental toxicity data from related chemicals submitted under the HPV Challenge program could be used to assess the developmental toxicity of IRGANOX 1035. The proposed supporting chemicals and EPA's evaluation of their adequacy for use in fulfilling the developmental endpoint are as follows:

(1) 2,6-Di-tert-butyl-4-(octadecanoxycarbonylethyl) phenol (CAS No. 2082-79-3; submitted as supporting the original Hindered Phenols Category, http://www.epa.gov/chemrtk/pubs/summaries/hndrdphn/c13382tc.htm). Although 2,6-di-tert-butyl-4-(octadecanoxycarbonylethyl) phenol (CAS No. 2082-79-3) is structurally similar to IRGANOX 1035, its physical-chemical properties do not support its use as a supporting chemical for toxicity endpoints.

(2) Tetrakis-(methylene-(3,5-di-tertbutyl-4-hydrocinnamate) methane (CAS No. 6683-19-8; submitted as supporting the original Hindered Phenols Category, http://www.epa.gov/chemrtk/pubs/summaries/hndrdphn/c13382tc.htm). EPA does not consider tetrakis-(methylene-(3,5-di-tertbutyl-4-hydrocinnamate) methane (CAS No. 6683-19-8) an appropriate supporting chemical for IRGANOX 1035 based on its more complex structure.

(3) 1,2-Bis(3,5-di-tert-butyl-4-hydroxyhydrocinnamoyl)hydrazine (IRGANOX MD 1024, CAS No. 32687-78-8, http://www.epa.gov/chemrtk/pubs/summaries/irganox/c14894tc.htm). EPA considers 1,2-bis(3,5-di-tert-butyl-4-hydroxyhydrocinnamoyl)hydrazine (CAS No. 32687-78-8) a reasonable supporting chemical to address the reproductive toxicity endpoint for IRGANOX 1035, based on its structural similarities and similar physical-chemical properties.

Summary-Conclusion

The estimated log K_{ow} for IRGANOX 1035 is high. However, the low water solubility (~ 0.005 mg/L, measured; 4.5×10^{-7}, estimated) and estimated BCF (3.2) suggest the potential of this chemical to bioaccumulate is expected to be low. IRGANOX 1035 is not readily biodegradable, indicating that it has the potential to persist in the environment.

The evaluation of available aquatic toxicity data for fish, aquatic invertebrates and aquatic plants and physical-chemical properties indicates no acute effects were observed at saturation (water solubility limit) for fish and that there were acute effects at or below saturation for aquatic invertebrates and plants. The aquatic toxicity data submitted were difficult to interpret because they were generated in the presence of solvent(s), the concentration of chemical in the test water was not measured and effects concentrations reported were above the chemical's water solubility limit. The measured water solubility for IRGANOX 1035 indicates it is soluble or miscible in water at concentrations that could cause chronic effects. Therefore, EPA continues to recommend chronic aquatic toxicity testing for IRGANOX 1035.

The acute oral, dermal and vapor inhalation toxicity of IRGANOX 1035 is low. Repeated oral exposures to IRGANOX 1035 resulted in a dose-dependent increase in liver weight in rats. The evaluation of reproductive organs from repeated oral exposures suggest testicular effects (increase in testes weight) at high doses. However, no histopathological correlation was apparent. Data from a developmental toxicity study with the supporting chemical, IRGANOX MD 1024, indicate no maternal toxicity or treatment-related effects on fetal development at the highest dose tested. IRGANOX 1035 did not induce gene mutations in bacteria *in vitro* bacterial test or chromosomal aberrations in an *in vivo* test.

The potential health hazard of thiodiethylene bis(3,5-di-tert-butyl-4-hydroxyhydrocinnamate) is high based on the repeated-dose toxicity.

Chronic fish or aquatic invertebrate toxicity remains a data gap under the HPV Challenge Program. Subsequent consideration of fate and exposure information will inform a determination of the need to obtain the chronic aquatic toxicity data.

1. Physical-Chemical Properties and Environmental Fate

A summary of physical-chemical properties and environmental fate data submitted is provided in the Appendix. For the purpose of the screening-level hazard characterization, the review and summary of these data was limited to the octanol-water partition coefficient and biodegradation endpoints as indictors of bioaccumulation and persistence, respectively.

Octanol-Water Partition Coefficient

Log K_{ow}: > 10.36 (estimated)

The model used to estimate the K_{ow} submitted (KOWWIN v.1.66) has been demonstrated to be accurate in predicting log K_{ow} between -4 and 10. Given the estimate for IRGANOX 1035 is outside this range, the absolute value may not be accurate. Nonetheless, it is reasonable to conclude that this prediction is indicative that the log K_{ow} for this chemical is high (> 4).

Biodegradation

In a ready biodegradation test using non-acclimated activated domestic sludge as inoculum, 2% of IRGANOX 1035 had degraded after 28 days
IRGANOX 1035 is not readily biodegradable.

Conclusion: The estimated log K_{ow} for IRGANOX 1035 is high. However, the low water solubility (~ 0.005 mg/L, measured; 4.5×10^{-7}, estimated) and estimated BCF (3.2) suggest the potential of this chemical to bioaccumulate is expected to be low. IRGANOX 1035 is not readily biodegradable, indicating that it has the potential to persist in the environment.

2. Environmental Effects – Aquatic Toxicity

Acute Toxicity to Fish

(1) Rainbow trout (*Salmo gairdneri*) were exposed to IRGANOX 1035, at nominal concentrations of 0 and 100 mg/L (measured concentration = 57 mg/L) under static conditions for 96 hours. DMF and MARLOPON AT50 solvents were used. There were no mortalities and the sponsor reported a 96-h LC_{50} of > 57 mg/L. The substance was tested above its water solubility limit and in the presence of solvent. Therefore, EPA considers the no effect concentration to be the water solubility limit (saturation), which for IRGANOX MD 1024 would be 0.005 mg/L (measured).
No effects at saturation

(2) Zebrafish (*Danio rerio*) were exposed to IRGANOX 1035, at nominal concentrations of 0 and 100 mg/L (measured concentration = 61 mg/L) under static conditions for 96 hours. DMF and MARLOPON AT50 solvents were used. There were no mortalities and the sponsor reported a 96-h LC_{50} of > 61 mg/L. The substance was tested above its water solubility limit and in the presence of solvent. Therefore, EPA considers the no effect concentration to be the water solubility limit (saturation), which for IRGANOX MD 1024 would be 0.005 mg/L (measured).
No effects at saturation

Acute Toxicity to Aquatic Invertebrates

(1) *Daphnia magna* Straus 1820 were exposed to IRGANOX 1035, dissolved in DMF and MARLOPON AT50, at nominal concentrations of 0, 0.32, 0.58, 1.00, 1.80, 3.2, 5.80 and 10 mg/L (0, 0, 0.34, 0.52, 0.91, 1.80, 3.5 and 5.87 mg/L, measured) IRGANOX 1035 under static conditions for 24 hours. Mortality increased with increasing concentration of IRGANOX 1035 added to the test solution. A 24-h EC_{50} of 4.7 mg/L was reported. The results of this test are difficult to interpret because the substance was tested above its water solubility limit and in the presence of solvent, but indicate there were effects at or below the water solubility limit (saturation).
LC_{50} at or below water solubility limit

(2) *Daphnia magna* Straus 1820 were exposed to IRGANOX 1035 as water accommodated fractions (WAF) under static conditions for 48 hours. The loading rate was 100 mg/L and no analytical measurements were made on the WAF. No effects were seen. Therefore, the sponsor concluded that there are no effects at the maximum loading rate of 100 mg/L. EPA does not consider the loading rate as the no effect concentration when the concentration exceeds the water solubility of the substance. Assuming the exposure concentration is the water solubility limit (saturation), the no effect concentration would be approximately 0.005 mg/L.
No effects at saturation

Toxicity to Aquatic Plants

Freshwater green algae *(Scenedesmus subspicatus)* were exposed to 0, 1.23, 3.7, 11, 33 and 100 mg/L (nominal) of IRGANOX 1035 under static conditions for 72 hours. Lecithin vehicle was used at concentrations exceeding the lowest nominal IRGANOX 1035 concentration. Undissolved test substance was observed in the exposure flasks. The robust summary reports an EC_{50} of > 41 mg/L and a NOEC of 11 mg/L, both of which indicate there were effects observed. The results of this test are difficult to interpret because the substance was tested above its water solubility limit and in the presence of solvent, but indicate there were effects at or below the water solubility limit (saturation).
EC_{50} at or below water solubility limit

Chronic Toxicity to Aquatic Organisms

In comments on the original test plan, EPA recognized the inadequacies in the acute toxicity tests submitted and recommended that if the water solubility of IRGANOX 1035 was determined to be > 0.001 mg/L, that either a fish early life stage test or a chronic invertebrate test be conducted. The type of test recommended would depend on which type of organism is determined to be more sensitive to IRGANOX 1035. The results of the water solubility test indicate the water solubility of IRGANOX 1035 is 0.005 mg/L. Therefore, EPA continues to recommend chronic aquatic toxicity testing for IRGANOX 1035.

Conclusion: The evaluation of available aquatic toxicity data for fish, aquatic invertebrates and aquatic plants and physical-chemical properties indicates no acute effects were observed at saturation (water solubility limit) for fish and that there were acute effects at or below saturation for aquatic invertebrates and plants. The aquatic toxicity data submitted were difficult to interpret because they were generated in the presence of solvent(s), the concentration of chemical in the test water was not measured and effects concentrations reported were above the chemical's water solubility limit. The measured water solubility for IRGANOX 1035 indicates it is soluble or miscible in water at concentrations that could cause chronic effects. Therefore, EPA continues to recommend chronic aquatic toxicity testing for IRGANOX 1035.

3. Human Health Effects

Acute Oral Toxicity

IRGANOX 1035 (Thiodiethylene bis(3,5-di-tert-butyl-4-hydroxyhydrocinnamate; CAS No. 41484-35-9)
The acute oral LD_{50} value in Tif:RAIf rats is > 5000 mg/kg-bw, indicating low acute toxicity via the oral route of exposure.
LD_{50} > 5000 mg/kg-bw

Acute Dermal Toxicity

IRGANOX 1035 (Thiodiethylene bis(3,5-di-tert-butyl-4-hydroxyhydrocinnamate; CAS No. 41484-35-9)
New Zealand White rabbits were administered IRGANOX 1035 dermally at 100, 1000 or 3000 mg/kg-bw to their shaved backs, under occlusive conditions for 24 hours and were observed for 14 days post exposure.
LD_{50} > 3000 mg/kg-bw

Acute Inhalation Toxicity

IRGANOX 1035 (Thiodiethylene bis(3,5-di-tert-butyl-4-hydroxyhydrocinnamate; CAS No. 41484-35-9)
Charles River rats (5/sex) were exposed to IRGANOX 1035 vapor at 6300 mg/m^3 for four hours and were observed for 14 days post exposure. There were no mortalities and no adverse reactions during exposure or the 14-day observation period. There was no effect on body weight gain and necropsy did not reveal any gross pathologic alterations.
LD_{50} > 6.3 mg/L

Repeated-Dose Toxicity

IRGANOX 1035 (Thiodiethylene bis(3,5-di-tert-butyl-4-hydroxyhydrocinnamate; CAS No. 41484-35-9)
(1) Tif: RAIf (SPF) rats (20/sex/dose) were administered IRGANOX 1035 via the diet at 0, 60, 200, 600 and 2000 ppm (approximately 0, 4.4, 12.5, 39 and 138 mg/kg-bw/day in males and 0, 4.5, 13, 40, and 140 mg/kg bw/day in females) for 90 days. No treatment-related effects, including mortality and clinical symptoms, were noted at any dose. However, both absolute and relative liver weight showed a dose-dependant increase and relative liver weights were significantly ($p < 0.01$) increased at concentrations of 60, 200, 600 and 2000 ppm for males and 600 and 2000 ppm for females.
LOAEL ~ 4.4 mg/kg-bw/day (based on increased relative liver weight in males)
NOAEL = Not established

Reproductive Toxicity

A reproductive toxicity test was not submitted. Evaluation of reproductive organs from the 90-day repeated-dose toxicity study and availability of a developmental toxicity study address the reproductive toxicity endpoint for the purposes of the HPV Challenge Program.

IRGANOX 1035 (Thiodiethylene bis(3,5-di-tert-butyl-4-hydroxyhydrocinnamate; CAS No. 41484-35-9)
In the 90-day repeated-dose toxicity study described previously, a statistically significant ($p = 0.05$) increase in absolute testes weights correlated with an increase in body weights; however, testes weight relative to brain weight were also statistically significantly increased ($p = 0.05$). Gross necropsy and histopathological examination of the testes, epididymes, uterus and ovary showed that the reproductive organs were comparable among all treatment groups.

IRGANOX MD 1024 (1,2-Bis(3,5-di-tert-butyl-4-hydroxyhydrocinnamoyl)hydrazine; CAS No. 32687-78-8, supporting chemical)
In a repeated-dose toxicity study, Tif: RAIf (SPF) rats (20/sex/dose) were administered IRGANOX MD 1024 via the diet at 0, 400, 2000 and 10,000 ppm (approximately 0, 25, 123 and 624 mg/kg bw/day for males and 0, 27, 127 and 667mg/kg bw/day for females, respectively) for 90 days. A statistically significant ($p < 0.05$) decrease in testes weights at 10,000 ppm was observed and correlated with a decrease in male body weights. Gross necropsy and histopathological examination of the testes, prostate, uterus, ovaries and fallopian tubes were unremarkable.

Developmental Toxicity

IRGANOX MD 1024 (1,2-Bis(3,5-di-tert-butyl-4-hydroxyhydrocinnamoyl)hydrazine; CAS No. 32687-78-8, supporting chemical)
Pregnant female Sprague-Dawley rats were administered IRGANOX 1\MD 1024 by oral intubation at 0, 500, 1500 and 3000 mg/kg bw/day on days 6 – 15 of gestation. No statistically significant effects were observed on dams or development of fetuses at any dose.
NOAEL (maternal and developmental toxicity) = 3000 mg/kg-bw/day (based on no effects at highest dose tested)

Genetic Toxicity – Gene Mutation

In vitro
IRGANOX 1035 (Thiodiethylene bis(3,5-di-tert-butyl-4-hydroxyhydrocinnamate; CAS No. 41484-35-9)
In a bacterial reverse mutation assay, *Salmonella typhimurium* strains TA98, TA100, TA1535 and TA1537 were exposed to IRGANOX 1035 at concentrations up to 5120 µg/plate in the presence and absence of metabolic activation. A precipitate was observed at concentrations > 320 µg/plate. No increases in mutation frequency were observed at any concentration with or without metabolic activation.
IRGANOX 1035 was not mutagenic in this assay.

Genetic Toxicity – Chromosomal Aberrations

In vivo
IRGANOX 1035 (Thiodiethylene bis(3,5-di-tert-butyl-4-hydroxyhydrocinnamate; CAS No. 41484-35-9)
Chinese hamsters (6 males and 4 females) were exposed to 825, 1750 and 3500 mg/kg-bw/day for 2 days. The negative and positive controls responded appropriately. No clastogenic effects were observed in the bone marrow cells at any concentration tested.
IRGANOX 1035 did not induce chromosomal aberrations in this assay.

Conclusion: The acute oral, dermal and vapor inhalation toxicity of IRGANOX 1035 is low. Repeated oral exposures to IRGANOX 1035 resulted in a dose-dependent increase in liver weight in rats. The evaluation of reproductive organs from repeated oral exposures suggest testicular effects (increase in testes weight) at high doses. However, no histopathological correlation was apparent. Data from a developmental toxicity study with the supporting chemical, IRGANOX MD 1024, indicate no maternal toxicity or treatment-related effects on fetal

development at the highest dose tested. IRGANOX 1035 did not induce gene mutations in bacteria *in vitro* bacterial test or chromosomal aberrations in an *in vivo* test.

The potential health hazard of thiodiethylene bis(3,5-di-tert-butyl-4-hydroxyhydrocinnamate) is high based on the repeated-dose toxicity.

4. Hazard Characterization

The estimated log K_{ow} for IRGANOX 1035 is high. However, the low water solubility (~ 0.005 mg/L, measured; 4.5×10^{-7}, estimated) and estimated BCF (3.2) suggest the potential of this chemical to bioaccumulate is expected to be low. IRGANOX 1035 is not readily biodegradable, indicating that it has the potential to persist in the environment.

The evaluation of available aquatic toxicity data for fish, aquatic invertebrates and aquatic plants and physical-chemical properties indicates no acute effects were observed at saturation (water solubility limit) for fish and that there were acute effects at or below saturation for aquatic invertebrates and plants. The aquatic toxicity data submitted were difficult to interpret because they were generated in the presence of solvent(s), the concentration of chemical in the test water was not measured and effects concentrations reported were above the chemical's water solubility limit. The measured water solubility for IRGANOX 1035 indicates it is soluble or miscible in water at concentrations that could cause chronic effects. Therefore, EPA continues to recommend chronic aquatic toxicity testing for IRGANOX 1035.

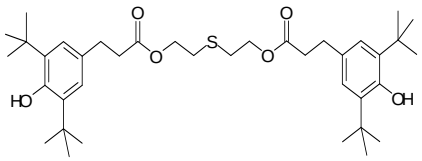
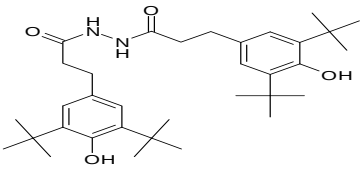
The acute oral, dermal and vapor inhalation toxicity of IRGANOX 1035 is low. Repeated oral exposures to IRGANOX 1035 resulted in a dose-dependent increase in liver weight in rats. The evaluation of reproductive organs from repeated oral exposures suggest testicular effects (increase in testes weight) at high doses. However, no histopathological correlation was apparent. Data from a developmental toxicity study with the supporting chemical, IRGANOX MD 1024, indicate no maternal toxicity or treatment-related effects on fetal development at the highest dose tested. IRGANOX 1035 did not induce gene mutations in bacteria *in vitro* bacterial test or chromosomal aberrations in an *in vivo* test.

The potential health hazard of thiodiethylene bis(3,5-di-tert-butyl-4-hydroxyhydrocinnamate) is high based on the repeated-dose toxicity.

5. Data Gaps

Chronic fish or aquatic invertebrate toxicity remains a data gap under the HPV Challenge Program. Subsequent consideration of fate and exposure information will inform a determination of the need to obtain the chronic aquatic toxicity data.

APPENDIX

Summary Table of the Screening Information Data Set as Submitted under the U.S. HPV Challenge Program		
Endpoints	**SPONSORED CHEMICAL IRGANOX 1035 (Thiodiethylene bis(3,5-di-tert-butyl-4-hydroxyhydrocinnamate)) (41484-35-9)**	**SUPPORTING CHEMICAL IRGANOX MD 1024 (1,2-bis(3,5-di-tert-butyl-4-hydroxy-hydrocinnamoyl)hydrazine) (32687-78-8)**
		
Summary of Physical-Chemical Properties and Environmental Fate Data		
Melting Point (°C)	63 – 68 (estimated)	227 – 232
Boiling Point (°C)	664.9	741.68
Vapor Pressure (hPa at 25°C)	7.5×10^{-18}	1.04×10^{-20}
Log K_{ow}	> 10.36 (estimated)	7.79 (estimated
Water Solubility (mg/L at 25°C)	0.005 (measured)	< 1 at 20°C (measured)
Direct Photodegradation	2.6 hours (experimental)	—*
Indirect (OH^-) Photodegradation Half-life ($t_{1/2}$)	2.103 h	2.3 h
Stability in Water (Hydrolysis) ($t_{1/2}$)	No Data. Low water solubility makes testing impractical or impossible. Expected to be resistant to hydrolysis due to lack of hydrolysable functional groups.	> 1 yr (estimated)
Fugacity (Level III Model)		
Air (%)	0.0005	0.027
Water (%)	1.04	1.23
Soil (%)	44.4	35.6
Sediment (%)	54.6	63.2
Biodegradation at 28 days (%)	2 Not readily biodegradable	1 Not readily biodegradable
Summary of Environmental Effects – Aquatic Toxicity Data		
Fish 96-h LC_{50} (mg/L)	No effects at saturation	—*
Aquatic Invertebrates 48-h EC_{50} (mg/L)	Effects at or below saturation	—*
Aquatic Plants 72-h EC_{50} (mg/L) (growth) (biomass)	Effects at or below saturation	—*
Chronic Aquatic Toxicity	Data Gap	—*

Summary Table of the Screening Information Data Set as Submitted under the U.S. HPV Challenge Program		
Endpoints	**SPONSORED CHEMICAL IRGANOX 1035 (Thiodiethylene bis(3,5-di-tert-butyl-4-hydroxyhydrocinnamate)) (41484-35-9)**	**SUPPORTING CHEMICAL IRGANOX MD 1024 (1,2-bis(3,5-di-tert-butyl-4-hydroxy-hydrocinnamoyl)hydrazine) (32687-78-8)**
Summary of Human Health Data		
Acute Oral Toxicity LD_{50} (mg/kg-bw)	> 5000	> 5000 – > 7000
Acute Inhalation Toxicity LC_{50} (mg/L)	> 6.3 mg/L	—*
Acute Dermal Toxicity LD_{50} (mg/kg-bw)	> 3000	—*
Repeated-Dose Toxicity NOAEL/LOAEL Oral (mg/kg-bw/day)	LOAEL ~ 4.4 NOAEL = Not established	—*
Reproductive Toxicity NOAEL/LOAEL (mg/kg-bw/day)	No effects were seen in evaluation of reproductive organs from 90-day repeated-dose toxicity study in rats.	No effects were seen in evaluation of reproductive organs from 90-day repeated-dose toxicity study in rats.
Developmental Toxicity NOAEL/LOAEL (mg/kg-bw/day) Maternal/Developmental Toxicity	No Data NOAEL =3000 LOAEL > 3000 (RA)	NOAEL =3000 LOAEL > 3000
Genetic Toxicity – Gene Mutation *In vitro*	Negative	Negative
Genetic Toxicity – Chromosomal Aberrations *In vivo*	Negative	Negative

— indicates endpoint was not addressed for this chemical; * indicates endpoint not required for this chemical