GreenScreen® Assessment for Bumetrizole *(CAS No. 3896-11-5)*

Method Version: GreenScreen® Version 1.2[1]

Assessment Type[2]: UNACCREDITED

GreenScreen® Assessment Prepared By:	**GreenScreen® Assessment Quality Control Performed By:**
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Organization: BotkinChemie	Organization: Washington State Dept. of Ecology
Date: December 2015	Date: November 29, 2016
Assessor Type: Authorized GreenScreen® Practitioner	

[1] Use GreenScreen® Assessment Procedure (Guidance) V1.2
[2] GreenScreen reports are either "UNACCREDITED" (by unaccredited person), "AUTHORIZED" (by Authorized GreenScreen Practitioner), "CERTIFIED" (by Licensed GreenScreen Profiler or equivalent) or "CERTIFIED WITH VERIFICATION" (Certified or Authorized assessment that has passed GreenScreen Verification Program)

Confirm application of the *Disclosure and Assessment Rules and Best Practice*[3]:
This GreenScreen® assessment is based on a review of the theoretically pure substance. No information about impurities in commercial bumetrizole products was available.

This assessment relies heavily on an information dossier submitted to the European Chemicals Agency as part of the REACH registration process (ECHA 2015a). The contributions of the registrants, BASF SE and Huntsman Textile Effects (Germany) GmbH, in conducting the tests and assembling the information in the dossier are gratefully acknowledged.

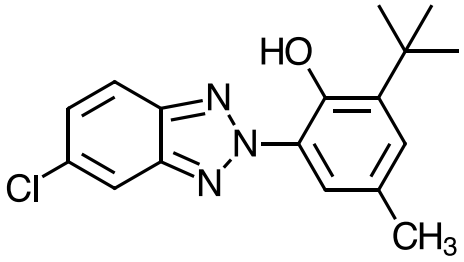
In the ECHA legal notice, the Agency points out that the correctness of the information in the dossiers is not guaranteed, that the information has not been reviewed or verified by the Agency or any other authority, and that it is subject to change without prior notice. Furthermore, study summaries derived from its information dossiers (including those contained in this assessment) may only be used for the purpose of registrations where the potential registrant is in legitimate possession of the full study report and/or has permission to refer to the full study report.

Chemical Name (CAS #):
Bumetrizole (CAS No. 3896-11-5)

Also Called:
- Phenol, 2−(5−chloro−2H−benzotriazol−2−yl)−6−(1,1−dimethylethyl)−4−methyl−
- 2−(2'−Hydroxy−3'−*tert*−butyl−5'−methylphenyl)−5−chlorobenzotriazole
- TINUVIN® 326 (TINUVIN® is a registered trademark of the BASF Group)
- TINOGARD® AS (TINOGARD® is a registered trademark of the BASF Group)
- UV 326

Suitable analogs or moieties of chemicals used in this assessment (CAS #'s):
Data for structural analogs, including UV-327 (CAS No. 3864-99-1), drometrizole (CAS No. 2440-22-4), and CG20-568 (CAS No. 84268-36-0) were used to help fill data gaps for bumetrizole in this assessment. Note that other phenolic benzotriazoles were considered to fill the data gap for acute inhalation toxicity, but the only reliable study that could be found was for drometrizole.

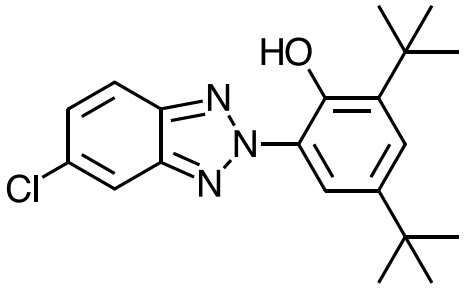
Chemical Structure(s):
Bumetrizole (CAS No. 3896-11-5)



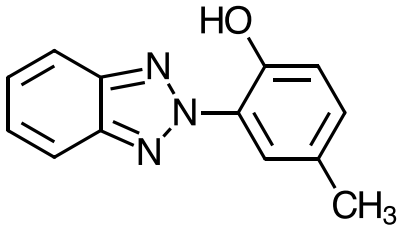
[3] See GreenScreen Guidance V1.2

Structural analogs:

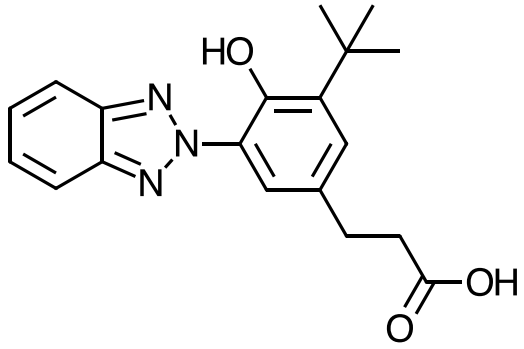
UV-327 (CAS No. 3864-99-1)
96.31% similarity (ChemIDplus 2015)



Drometrizole (CAS No. 2440-22-4)
76.3% similarity (ChemIDplus 2015)



CG20-568 (CAS No. 84268-36-0)
81.6% similarity (ChemIDplus 2015)



Notes related to production specific attributes[4]:
This assessment relies heavily on information dossiers submitted to the European Chemicals Agency as part of the REACH registration process (ECHA 2015a). Recognizing that product impurity profiles, physical form (including particle size distribution), and overall quality can vary from manufacturer to manufacturer, this assessment should be regarded as being most applicable to products produced by the registrants.

For Inorganic Chemicals and relevant particulate organics (*if not relevant, list NA*)
Define Properties:

1. Particle size (ECHA 2015a)
   The particle size distribution of a commercial sample of bumetrizole was investigated using the laser diffraction method according to ISO 13320-1, which was found to contain 18.3% respirable particles smaller than 10 microns in diameter.
2. Structure (e.g., amorphous vs. crystalline) Not applicable (N/A)
3. Mobility (e.g., water solubility, volatility)
   Water Solubility: 4 ± 2 μg/L at 20°C (OECD Guideline 105, ECHA 2015a)
   < 1 mg/L at 20°C (EU Method A.6, ECHA 2015a)
   Vapor pressure: 7.5×10^{-7} Pa (20°C), 0.07 Pa (100°C) (TGA method, ECHA 2015a)

[4] Note any composition or hazard attributes of the chemical product relevant to how it is manufactured. For example, certain synthetic pathways or processes result in typical contaminants, by-products or transformation products. Explain any differences between the manufactured chemical product and the GreenScreen assessment of the generic chemical by CAS #.

4. Bioavailability Not applicable (N/A)

Identify Applications/Functional Uses:
(e.g., Cleaning product, TV casing)

1. Light stabilizer for plastics, lubricants, foams, fibers, and adhesives
2. UV filter for protection of ingredients in personal care products

GreenScreen Benchmark Score and Hazard Summary Table:[5,6,7,8]

Bumetrizole was assigned a Benchmark Score of 2 (USE BUT SEARCH FOR SAFER SUBSTITUTES). The benchmark score is driven by the chemical's VERY HIGH / HIGH environmental fate scores (P and B respectively), MODERATE chronic aquatic toxicity (CA) score, and MODERATE Group I and II Human Toxicity (E and N-single) scores. This corresponds to the following GreenScreen® benchmark classifications:

- 2a: Moderate P + Moderate B + Moderate T (Ecotoxicity or Group I, II, or II* Human)
- 2b: High P + High B
- 2c: High P + Moderate T (Ecotoxicity or Group I, II, or II* Human)
- 2d: High B + Moderate T (Ecotoxicity or Group I, II, or II* Human)
- 2e: Moderate T (Group I Human)

The only data gap is for the Group II* Human hazard respiratory sensitization (SnR*). This meets the data gap requirements for Benchmark 2, which require 4 of 7 of the Group II/II* endpoints, with permissible gaps including respiratory or skin sensitization, skin or eye irritation, and one other hazard endpoint.

For the Group II* Human Hazard respiratory sensitization (SnR*), in a worst-case scenario a hazard score of HIGH would be assigned. In this case, the Benchmark score of 1 (Avoid – Chemical of High Concern) would be assigned through triggering Benchmark 1 classifications 1a (PBT) and 1c (vPT).

Green Screen Hazard Ratings: Bumetrizole																			
Group I Human					**Group II and II* Human**									**Ecotox**		**Fate**		**Physical**	
C	**M**	**R**	**D**	**E**	**AT**	**ST**		**N**		**SnS***	**SnR***	**IrS**	**IrE**	**AA**	**CA**	**P**	**B**	**Rx**	**F**
						single	rep.*	single	rep.*										
L	**L**	**L**	**L**	*M*	*L*	**L**	*L*	*M*	*L*	**L**	DG	**L**	**L**	*L*	**M**	*vH*	*H*	**L**	**L**

Note: Hazard levels (Very High (vH), High (H), Moderate (M), Low (L), Very Low (vL)) in *italics* reflect estimated values, authoritative B lists, screening lists, weak analogues, and lower confidence. Hazard levels in **BOLD** font are used with good quality data, authoritative A lists, or strong analogues. Group II Human Health endpoints differ from Group II* Human Health endpoints in that they have four hazard scores (*i.e.*, vH, H, M and L) instead of three (*i.e.*, H, M and L), and are based on single exposures instead of repeated exposures.

[5] See Appendix A for a glossary of hazard endpoint acronyms
[6] See Appendix B for alternative GreenScreen Hazard Summary Table (Classification presented by exposure route)
[7] For inorganic chemicals only, see GreenScreen Guidance V1.2 Section 14.4. (Exceptions for Persistence)
[8] For Systemic Toxicity and Neurotoxicity, repeated exposure data are preferred. Lack of single exposure data is not a Data Gap when repeated exposure data are available. In that case, lack of single exposure data may be represented as NA instead of DG. See GreenScreen Guidance V1.2 Section 9.3.

Environmental Transformation Products and Ratings[9]:
Identify feasible and relevant environmental transformation products (i.e., dissociation products, transformation products, valence states) and/or moieties of concern[10]

The exact biodegradation pathway of bumetrizole has not been elucidated. A metabolite was observed in one of the bioaccumulation studies with bumetrizole (ECHA 2015a), but could not be identified.

Since no experimental data were available, the biodegradation pathways of bumetrizole were investigated using the EAWAG Biocatalysis/Biodegradation Database (EAWAG 2015, Appendix C). Three main pathways were identified:

1. Oxidation of the methyl group on the phenolic ring to a carboxylic acid,
2. Hydroxylation of the 3- and 4-positions of the benzotriazole moiety followed by oxidative cleavage, and
3. Dechlorination.

After several steps, these processes yield a complex mixture of products. None of the eight degradation products proposed after the first two steps (plus the carboxylic acid formed by oxidation of the methyl group) could be identified in the ChemIDplus database (ChemIDplus 2015).

The abiotic degradation of bumetrizole by oxidation and/or photo-oxidation likewise appears to give a complex mixture of products, and is discussed in the section of this assessment dealing with Persistence. The only feasible and possibly relevant transformation product that has been identified is 5-chlorobenzotriazole (also known as 6-chloro-1H-benzotriazole). This chemical is not listed in the Pharos database. However, the structural analog benzotriazole has been listed and is assigned a GreenScreen® List Translator Score of LT-UNK. Therefore adjustment of the GreenScreen® Benchmark Score based on this transformation product is not applicable. Note that the relevance of 5-chlorobenzotriazole as a degradation product is questionable considering that abiotic degradation is considered less relevant as a degradation pathway for phenolic benzotriazoles as compared to biodegradation (ECHA 2015c).

Functional Use	Life Cycle Stage	Transformation Pathway	Environmental Transformation Products	CAS #	Feasible and Relevant?	GreenScreen List Translator Score or GreenScreen Benchmark Score
All	End of life	Oxidation or photo-oxidation	5-chloro-benzotriazole	94-97-3	yes/ possibly	LT-UNK (structural analog benzotriazole)

[9] See GreenScreen Guidance V1.2 Section 13
[10] A moiety is a discrete chemical entity that is a constituent part or component of a substance. A moiety of concern is often the parent substance itself for organic compounds. For inorganic compounds, the moiety of concern is typically a dissociated component of the substance or a transformation product.

Introduction

Phenolic benzotriazoles are extensively used in plastics, coatings, and other materials as light stabilizers. These products function by competitive absorption of the damaging UV radiation in sunlight. Compared to the substrates they protect, phenolic benzotriazoles are characterized by a much stronger UV absorbance, outstanding photostability (owing to the rapid deactivation of excited states via radiation-less processes), and high chemical stability. In this way they are able to provide long-term protection for many different types of plastics and coatings against the effects of sunlight.

Products of this chemical family have been developed with properties tailored to meet the needs of many specific applications. For example, solid products have been developed for plastic applications where this form is preferred, liquid products for coatings (where the liquid form is advantageous), high molecular weight products with low volatility for use in engineering plastics processed at high temperatures, and products with solubility/compatibility in non-polar as well as polar plastic and coating substrates.

Recently some chemicals of this family have faced regulatory scrutiny due to their persistence, bioaccumulative tendencies, and toxicity. Four chemicals of this class (UV-320, UV-327, UV-328, and UV-350) have been identified as potential substances of very high concern and have been added to the REACH Candidate List for Authorisation.

The persistence and bioaccumulation properties of phenolic benzotriazoles may represent unintended consequences of the design of products having useful performance properties. For example, the need for long-term protection of plastics and coatings has driven the development of products that are chemically stable and able to function as light stabilizers over multi-year timeframes. Unfortunately, these highly stable products are also resistant to biodegradation processes and as a result tend to be persistent in the environment. Similarly, a design approach successfully used to reduce volatility and/or improve compatibility with plastic and coating substrates has been to substitute the phenolic moiety with alkyl groups (especially those with branching). This can increase the tendency to bioaccumulate by increasing the lipophilicity (and therefore the octanol-water partition coefficient).

There is currently much activity in the plastics and coatings industries towards replacing phenolic benzotriazoles that have been identified as SVHC. Alternatives include UV absorbers from different chemical families (including hydroxybenzophenones, oxalanilides, hydroxyphenyltriazines, cyanoacrylates, and others), as well as alternative phenolic benzotriazoles having better profiles in terms of persistence, bioaccumulation, and toxicity.

Bumetrizole (aka UV-326) is an alternative phenolic benzotriazole UV absorber that is being promoted and evaluated as a replacement for other phenolic benzotriazoles in plastic applications. Thus it was of interest to undertake a GreenScreen® assessment in order to provide information to guide informed decision-making in formulation work aimed at replacing chemicals of concern with safer alternatives. Bumetrizole was assessed against GreenScreen® version 1.2 (CPA 2012) by James H. Botkin dba BotkinChemie as part of the GreenScreen® 2015 Practitioner Program.

Hazard Classification Summary Section:

For all hazard endpoints:

- **Search all GreenScreen specified lists. Report relevant results either in each hazard endpoint section or attach to the end of the report.**
- **Always indicate if suitable analogs or models were used.**
- **Attach modeling results (See Appendix C).**
- **Include all references either in each hazard endpoint section or at the end of the report.**

Group I Human Health Effects (Group I Human)

Carcinogenicity (C) Score (H, M or L): L

Bumetrizole was assigned a score of LOW with high confidence (**L**) for carcinogenicity based on negative study data in rats and in mice. This finding is further supported in that bumetrizole was found not to be mutagenic in multiple *in vitro* and *in vivo* tests (see the Mutagenicity/ Genotoxicity section). The high level of confidence is justified on the basis that the score is based on high quality animal data.

- Authoritative and Screening Lists (Pharos 2015a)
  - Bumetrizole is not present on any authoritative or screening lists for carcinogenicity.
- ECHA 2015a
  - In a two-year feeding study reported in 1978 according to a protocol comparable to OECD Guideline 453 (Combined Chronic Toxicity / Carcinogenicity Studies), groups of male and female Tif: MAGf (SPF) mice (50 animals per sex per dose) were fed diets containing 0, 1000, 3000, or 10,000 ppm of bumetrizole for 104 weeks. The total number of rats bearing neoplasms was similar in treated and control groups. The NOAEL for carcinogenicity was greater than 10,000 ppm, corresponding to greater than 382.6 mg/kg/day for males and greater than 501.9 mg/kg/day for females. This study was assigned a reliability score of 2 (reliable with restrictions) by the secondary source.
  - In a two-year feeding study reported in 1981 according to a protocol comparable to OECD Guideline 451 (Carcinogenicity Studies), groups of male and female Sprague-Dawley rats (50 animals per sex per dose) were fed diets containing 0, 5, 50, or 500 ppm of bumetrizole for 104 weeks. The top dose level did not produce inflammatory, degenerative, proliferative, or neoplastic lesions on examination at the end of the dosing period. Therefore the NOAEL can be assigned as greater than the top dose. The NOAEL for carcinogenicity was greater than 500 ppm, corresponding to greater than 61.72 mg/kg/day for males and greater than 58.94 mg/kg/day for females. This study was assigned a reliability score of 2 (reliable with restrictions) by the secondary source.

Mutagenicity/Genotoxicity (M) Score (H, M or L): L

Bumetrizole was assigned a score of LOW with high confidence (**L**) for mutagenicity/ genotoxicity based on multiple negative *in vitro* and *in vivo* study data, including data on mammalian cell lines (both germ cells and somatic cells). The available data suggest that the substance has a low propensity for causing mutagenic responses, and it can be concluded based on the weight of evidence that bumetrizole is not classified as mutagenic/genotoxic according to GHS criteria. The high level of confidence is justified on the basis of using multiple

high quality study data (*in vitro* and *in vivo*, including mammalian cell lines) in assigning the LOW score.

- Authoritative and Screening Lists (Pharos 2015a)
    - Bumetrizole is not present on any authoritative or screening lists for mutagenicity/ genotoxicity.

- *In vitro* –
    - ECHA 2015a
        - A GLP compliant in *vitro* study was conducted in 2006 according to OECD Guideline 473 (In vitro Mammalian Chromosome Aberration Test) utilizing CHL/IU cells with and without metabolic activation (rat liver induced with phenobarbital and 5,6-benzoflavone). Bumetrizole was considered negative for inducing chromosomal aberrations with and without metabolic activation. This study was assigned a reliability score of 1 (reliable without restriction) by the secondary source.
        - A GLP compliant *in vitro* study was conducted in 2006 according to OECD Guideline 471 (Bacterial Reverse Mutation Assay, or "Ames Test") utilizing four different strains of *Salmonella typhimurium* (TA 1535, TA 1537, TA 98 and TA 100) and one strain of *Escherichia coli* (WP2 uvr A) with and without metabolic activation (rat liver induced with phenobarbital and 5,6-benzoflavone). Bumetrizole did not cause a positive increase in the mean number of revertants per plate with any of the tester strains in the presence or absence of metabolic activation. This study was assigned a reliability score of 1 (reliable without restriction) by the secondary source.
        - An in vitro study was conducted in 1978 according to a test protocol similar to OECD Guideline 471 (Bacterial Reverse Mutation Assay, or "Ames Test") utilizing four different strains of *Salmonella typhimurium* (TA 1535, TA 1537, TA 98 and TA 100) with and without metabolic activation (rat liver S9 induced with Aroclor 1254). Bumetrizole did not cause a positive increase in the mean number of revertants per plate with any of the tester strains in the presence or absence of metabolic activation. This study was assigned a reliability score of 2 (reliable with restrictions) by the secondary source.

- *In vivo* –
    - ECHA 2015a
        - A chromosome aberration test was conducted in 1978 according to a protocol similar to OECD Guideline 474 (Mammalian Erythrocyte Micronucleus Test). Groups of Chinese hamsters (6 per sex per dose) were given daily doses by oral gavage of either 0, 500, 1000, or 2000 mg/kg bumetrizole on two consecutive days. After a 24-hour post-exposure period, bone marrow was harvested and examined on slides, with 1000 cells from each animal being scored for anomalies. In all dosage groups the percentage of cells displaying anomalies of nuclei did not differ significantly from the negative control. The results were interpreted as negative for chromosome aberrations. The study was assigned a reliability score of 2 (reliable with restrictions) by the secondary source.
        - A rodent dominant lethal test was conducted in 1977 according to a protocol similar to OECD Guideline 478 (only two treated dose levels were applied). Groups of male NMRI mice were given single doses by oral gavage of either 0, 1000, or 3000 mg/kg bumetrizole. Each group consisted of 20 males, each of which was placed in a cage with 2 untreated females immediately after

treatment. At the end of 1 week, the females were removed from the cages and replaced by another group of 2 females. The procedure was continued for 6 consecutive weeks. The females sacrificed on Day 14 of gestation and the number of live embryos and embryonic resorptions/deaths were determined. The results were negative as no significant differences in mating ratio, numbers of implantations or embryonic deaths between the mating groups were observed. This study was assigned a reliability score of 2 (reliable with restrictions) by the secondary source.

- A chromosome aberration test was conducted in 1979 according to a protocol similar to OECD Guideline 475 (Mammalian Bone Marrow Chromosome Aberration Test). Groups of Chinese hamsters (4 per sex per dose) were given daily doses by oral gavage of 0, 500, 1000, or 2000 mg/kg bumetrizole on two consecutive days. The animals were injected intraperitoneally with colcemide (10 mg/kg bw) two hours after the second dose, and sacrificed four hours later. Chromosome preparations were made from the femoral bone marrow of two males and two females from each group and 100 metaphases from each animal analysed for chromatid-type and chromosome-type aberrations. In the negative control group as well as in the groups treated with the various doses of the test substance neither chromosome-type nor chromatid-type aberrations were detected. The results were interpreted as negative for chromosome aberrations. The study was assigned a reliability score of 2 (reliable with restrictions) by the secondary source.

Reproductive Toxicity (R) Score (H, M, or L): L
Bumetrizole was assigned a score of LOW with high confidence (**L**) for reproductive toxicity based on a lack of reproductive effects in an OECD Guideline 422 study in rats at doses up to 1000 mg/kg/day. The LOW score is also supported by the negative rodent dominant lethal test results (referenced above in the Mutagenicity/Genotoxicity section), where no significant differences in mating ratio, numbers of implantations or embryonic deaths between the treated and control mating groups were observed. The high level of confidence is justified on the basis of using high quality animal data in assigning the score.

- Authoritative and Screening Lists (Pharos 2015a)
  - Bumetrizole is not present on any authoritative or screening lists for reproductive toxicity.
- ECHA 2015a
  - A GLP-compliant Combined Oral Repeated Dose and Reproductive/Developmental Toxicity Screening study was conducted in 2007 in Crj: CD(SD) rats according to OECD Guideline 422. Bumetrizole was administered in a vehicle of methylcellulose by oral gavage at dose levels of 0 (vehicle control), 62.5, 250 or 1000 mg/kg/day to 12 rats/sex/group. Rats were dosed 7 days/week for 2 weeks prior to mating, during the 2-week mating period, and throughout gestation and lactation until sacrifice, for a total of 42 days of dosing for males and 44-56 days for females. No significant effects were observed in reproductive parameters (including copulation required days, copulation index, fertility index, gestation index, pregnancy period, number of corpora lutea, number of implantations, or implantation index) up to the highest dose tested. A NOAEL (reproductive) of 1000 mg/kg/day was established. This study was assigned a reliability score of 1 (reliable without restriction) by the secondary source.

Developmental Toxicity incl. Developmental Neurotoxicity (D) Score (H, M or L): L
Bumetrizole was assigned a score of LOW with high confidence (**L**) for developmental toxicity based on a lack of developmental effects in two different studies in rats and mice (a recent OECD Guideline 422 study in rats and older studies under protocols similar to OECD Guideline 414). Effects on skeletal maturation were observed in the study in mice at the highest dose (3000 mg/kg/day), but not in the studies in rats. This finding was not considered sufficient to constitute "limited or marginal evidence" for developmental toxicity given that effects were only observed at the highest dose tested and were not observed in studies in other species. The high level of confidence is assigned based on the use of high quality animal data in assigning the score.

- Authoritative and Screening Lists (Pharos 2015a)
    - Bumetrizole is not present on any authoritative or screening lists for developmental toxicity.
- ECHA 2015a
    - In the above referenced OECD Guideline 422 study with bumetrizole, the offspring were sacrificed at 4 days of age. No significant effects were observed in developmental parameters (including viability, clinical signs, body weight, gross pathology, total number of pups born, number of dead pups, number of live pups on day 0, sex ratio on day 0, delivery index, rate of pups delivery, or live birth index) at any dose tested. A NOAEL (developmental) of 1000 mg/kg/day for the offspring (F1) was established. This study was assigned a reliability score of 1 (reliable without restriction) by the secondary source.
    - A developmental toxicity study in rats was conducted in 1977 under a protocol similar to OECD Guideline 414 (Prenatal Developmental Toxicity Study). The test compound (TK 10048) was administered orally by gavage (carboxymethylcellulose carrier) to pregnant Sprague-Dawley rats (25 per dose) from day 6 to day 15 of gestation at doses of 0, 300, 1000, and 3000 mg/kg/day. Dams were observed during the pregnancy and then sacrificed on day 21 of the pregnancy and an autopsy performed to examine the dam and the fetuses. No effects were noted on the dams or fetuses at any dose. NOAEL of 3000 mg/kg/day for maternal toxicity, teratogenicity, and developmental toxicity were established. Deviations from the current guideline (treatment of dams was limited to gestation periods day 6-15 of gestation only as opposed to a day before scheduled kill, certain maternal parameters not checked) were considered to be acceptable by the secondary source and the study was assigned a reliability score of 2 (reliable with restrictions).
    - A developmental toxicity study in mice was conducted in 1977 under a protocol similar to OECD Guideline 414 (Prenatal Developmental Toxicity Study). The test compound (TK 10048) was administered orally by gavage (carboxymethylcellulose carrier) to pregnant NMRI mice (30 per dose) from day 6 to day 15 of gestation at doses of 0, 300, 1000, and 3000 mg/kg/day. Dams were observed during the pregnancy and then sacrificed on day 18 of the pregnancy and an autopsy performed to examine the dam and the fetuses. The only adverse effect notes on the fetuses was a slight but statistically significant increase in number of still incompletely ossified sternabrae in high dose group (3000 mg/kg bw/day). No effects were noted on the fetuses at lower doses (300 and 1000 mg/kg/day) or on the dams at any dose. NOAEL of 3000 mg/kg/day for maternal toxicity and teratogenicity were established, and a NOAEL of 1000 mg/kg/day for developmental toxicity was established. Deviations from the current guideline (treatment of dams was limited to gestation periods day 6-15 of gestation only as opposed to a day

before scheduled kill, certain maternal parameters not checked) were considered to be acceptable by the secondary source and the study was assigned a reliability score of 2 (reliable with restrictions). While developmental effects were observed at 3000 mg/kg/day, this is not considered sufficient for classification as GHS Category 2 or to constitute "limited or marginal evidence" for developmental toxicity.

Endocrine Activity (E) Score (H, M or L): *M*

Bumetrizole was assigned a score of MODERATE with low confidence (*M*) for endocrine activity based on aryl hydrocarbon receptor (AhR) activity observed in *in vitro* and *in vivo* tests.

The endocrine activity of phenolic benzotriazoles is an active area of current research. Bumetrizole tested negative for estrogenic activity in multiple *in vitro* assays, including studies conducted in mammalian and human cell lines. The chemical also tested negative for androgenic and thyroid hormone activity in *in vitro* tests. No endocrine-related effects were reported in any of the acute or repeated dose toxicity studies.

Along with human estrogen, androgen, and thyroid hormone receptor activity, AhR activity has been considered to be an important factor in assessing the endocrine-disrupting potential of environmental contaminants. Postulated effects of AhR activity include metabolic imbalance, developmental toxicity, tumor promotion, and immune response (Fent *et al* 2014, Nagayoshi *et al* 2014). On the basis of the AhR activity observed in two studies, a preliminary score of MODERATE was assigned. As no relationship could be established between the AhR activity observed for bumetrizole and other adverse human health effects, the score was maintained at MODERATE. The low confidence level is assigned because the score is based solely on observed AhR activity, with no estrogenic, androgenic, or thyroid hormone activity observed in any of the other *in vitro* tests.

- Authoritative and Screening Lists (Pharos 2015a)
  - Bumetrizole is not present on any authoritative or screening lists for endocrine activity.
- Estrogenic activity studies –
  - Miller *et al* 2001
    - Bumetrizole and other chemicals were evaluated for estrogenic activity by the yeast two-hybrid *in vitro* assay. Yeast cells transfected with the human estrogen receptor α (ERα) gene, together with expression plasmids (containing estrogen responsive elements and the *lac*-Z reporter gene encoding the enzyme β-galactosidase), were incubated in medium containing the test chemical and the chromogenic substrate, chlorophenol red-β-D-galactopyranoside (CPRG). Active ligands (which bind to the receptor) induce β-galactosidase (β-gal) expression, causing the CPRG (initially yellow) to change into a red product that was measured by absorbance. The relative potencies of test chemicals were determined relative to 17b-estradiol. No estrogenic activity was detected for bumetrizole. The study was well documented and appeared in a peer-reviewed publication.
  - Kawamura *et al* 2003
    - Bumetrizole and other chemicals were evaluated for estrogenic activity by the yeast two-hybrid *in vitro* assay. The assay was based on the ligand-dependent interaction of estrogen receptor α and the coactivator transcriptional intermediary factor 2 (TIF2), and the estrogenic activity was detected as β-galactosidase activity. Two expression plasmids, pGBT-estrogen receptor ligand binding domain (pGBT9-ERLBD) and pGAD424-TIF2 were introduced into yeast cells carrying a β-galactosidase reporter

gene and require tryptophan and leucine for growth. The results were evaluated based on relative activity, expressed as 10% relative effective concentration (REC_{10}), which is the concentration of the test substance showing 10% of the agonist activity level of 10^{-6} M 17β-estradiol. The results for bumetrizole were judged to be negative in that the activity was lower than the REC_{10} (>1.0 x 10^{-4} M) within the concentration tested. This study was well documented, appeared in a peer-reviewed publication, and was assigned a reliability score of 2 (reliable with restrictions) by a secondary source (ECHA 2015a).

- Morohoshi *et al* 2005
  - Bumetrizole and other chemicals were evaluated for estrogen agonistic and/or antagonistic activity using two *in vitro* assays, (1) an ELISA-based estrogen receptor competitive binding assay (ER-ELISA) and (2) a modified yeast two-hybrid estrogen assay, with and without addition of a rat liver preparation, S9 mix. Bumetrizole exhibited no positive effect in either *in vitro* assay, indicating a lack of estrogenic activity. The study was well documented and appeared in a peer-reviewed publication.
- ECHA 2015a
  - Estrogenic activity of bumetrizole was investigated using an *in vitro* (human) MCF-7 cell proliferation assay (Matsumoto, H.; Adachi, S.; and Suzuki, Y. 2005. Yakugaku Zasshi, 125(8): 643-652). The results were negative compared to the vehicle control. The results were not reported in detail and the study was assigned a reliability score of 4 (reliability not assignable) by the secondary source.
- Wielogórska *et al* 2015
  - Bumetrizole and other chemicals were evaluated for potential endocrine disrupting effects at the level of estrogen nuclear receptor transcriptional activity using a mammalian reporter gene assay (RGA) in an *in vitro* study. Bumetrizole exhibited no estrogen agonist or antagonist activity. The study was well documented and appeared in a peer-reviewed publication.

- Other endocrine activity studies –
  - Fent *et al* 2014
    - The estrogenic and androgenic activity of phenolic benzotriazoles (including bumetrizole and the structural analog drometrizole) were investigated using *in vitro* assays. A recombinant yeast assay expressing the human estrogen (hERα in the yeast estrogen screen, YES) and androgen receptor (yeast androgen screen, YAS) was used. Bumetrizole showed no estrogenic activity at concentrations of 0.0001 to 1 g/L, and no significant androgenic activity.
    - The effects of bumetrizole (and the structural analog drometrizole) on the transcription profiles of up to 26 genes associated with different toxicological pathways were studied using *in vivo* tests with zebrafish eleuthero-embryos to elucidate potential modes of action. Embryos were experimentally exposed to the test substances at three different concentrations. In all exposures, no compound-related increase in mortality of embryos was noted, and there were no effects on hatching time or hatching rate as compared to the controls. Among the 26 transcripts, the induction of the aryl hydrocarbon receptor (AhR) pathway by bumetrizole and drometrizole was the most significant finding. The activation of the AhR pathway was less pronounced with bumetrizole as compared to drometrizole. The study was well

documented and appeared in a peer-reviewed publication.

- Nagayoshi *et al* 2014
  - Agonistic activities of phenolic benzotriazoles (including bumetrizole and the structural analogs UV-327 and drometrizole) toward human aryl hydrocarbon receptor (AhR) and thyroid hormone receptors alpha and beta were evaluated using *in vitro* yeast reporter gene assays. None of the phenolic benzotriazoles showed agonist activity towards either of the thyroid hormone receptors. However, both bumetrizole and drometrizole significantly activated AHR, with drometrizole showing the more potent AhR agonist activity. The study was well documented and appeared in a peer-reviewed publication.

Group II and II* Human Health Effects (Group II and II* Human)

Note: Group II and Group II endpoints are distinguished in the v 1.2 Benchmark system (the asterisk indicates repeated exposure). For Systemic Toxicity and Neurotoxicity, Group II and II* are considered sub-endpoints. When classifying hazard for Systemic Toxicity/Organ Effects and Neurotoxicity endpoints, repeated exposure results are required and preferred. Lacking repeated exposure results in a data gap. Lacking single exposure data does not result in a data gap when repeated exposure data are present (shade out the cell in the hazard table and make a note). If data are available for both single and repeated exposures, then the more conservative value is used.*

Acute Mammalian Toxicity (AT) Group II Score (vH, H, M or L): *L*

Bumetrizole was assigned a score of LOW with low confidence (*L*) for acute mammalian toxicity based on study data showing a low acute toxicity by the oral and dermal routes. However, data are lacking to enable unequivocal GHS classification of bumetrizole or the structural analogs by the inhalation route, and therefore the score is assigned as low confidence.

In the only reliable inhalation study with a structural analog, deaths (4/19 animals) were observed after exposure to 0.59 mg/L of the test substance for four hours. Thus classification as GHS Category 3 or 4 by the inhalation route (corresponding to a GreenScreen® score of HIGH or MODERATE) cannot be excluded in a worst-case scenario. As a polymer additive supplied in powder form with a significant fraction of respirable particles, the inhalation route is deemed to be relevant for the purpose of hazard assessment because of the potential for occupational exposure to airborne dust and/or aerosols produced in polymer processing operations.

- Authoritative and Screening Lists (Pharos 2015a, Pharos 2015b, Pharos 2015c)
  - Bumetrizole is not present on any authoritative or screening lists for acute mammalian toxicity by the oral, dermal, or inhalation routes.
  - The structural analogs UV-327 and drometrizole are not present on any authoritative or screening lists for acute mammalian toxicity by the inhalation route.

Summary Table: Acute Mammalian Toxicity (AT) Group II Data.

Route	Animal	Result	Source
Oral	Rat	LD_{50} > 2000 mg/kg – GHS Not Classified	ECHA 2015a
Oral	Rat	LD_{50} > 7750 mg/kg – GHS Not Classified	ECHA 2015a
Oral	Rat	LD_{50} > 2110 mg/kg – GHS Not Classified	ECHA 2015a
Oral	Rat	LD_{50} > 5000 mg/kg – GHS Not Classified	ECHA 2015a
Oral	Mouse	LD_{50} > 5000 mg/kg – GHS Not Classified	ECHA 2015a
Dermal	Rat	LD_{50} > 2000 mg/kg – GHS Not Classified	ECHA 2015a
Inhalation	Rat	Structural analog data (Drometrizole) LC_{50} (4 hr) > 0.59 mg/L	ECHA 2015b

		Not sufficient for unequivocal classification (but excludes GHS Categories 1 and 2)	

- Oral –
  - ECHA 2015a
    - A GLP-compliant acute oral toxicity study was carried out in 2007 according to OECD Guideline 423. Crj: CD(SD) rats (2 groups of 3 females) were dosed with 2000 mg/kg of UV-326 (methylcellulose solution) by oral gavage and observed for 14 days. No mortalities, clinical signs of toxicity, or effects on body weight were observed during the 14-day observation period. Necropsy examination revealed no substance-related findings. The acute oral LD_{50} was greater than 2000 mg/kg of body weight. This study was assigned a reliability score of 1 (reliable without restriction) by the secondary source.
    - An acute oral toxicity study was carried out in 1985 according to a protocol similar to OECD Guideline 401. Wistar rats (5 males and 5 females) were dosed with the test substance (42.2% bumetrizole by weight) at 5000 mg/kg (2110 mg/kg bumetrizole) by oral gavage and observed for 14 days. No mortalities were observed during the 14-day observation period. No clinical signs of toxicity were observed in males during the observation period. In the females, physical signs of ptosis (2 hours to day 4) and chromodacryorrhea (day 1 to day 9) were noted, and one female did not gain a normal amount of weight. Necropsy results were normal in 7/10 animals. Moderate hydronephrosis of the right kidney was noted in one male, and intestinal abnormalities were noted in two females (slight to moderate). The acute oral LD_{50} was greater than 2110 mg/kg of body weight. This study was assigned a reliability score of 2 (reliable with restrictions) by the secondary source.
    - An acute oral toxicity study was carried out in 1978 according to a protocol similar to OECD Guideline 401. Tif:RAIf (SPF) rats (groups of 5 males and 5 females) were dosed with the test substance (TK 10048) at 4640, 6000 or 7750 mg/kg by oral gavage (polyethylene glycol solution) and observed for 14 days. No mortalities or effects on body weight were observed during the 14-day observation period. Within two hours after dosing, the rats in all dosage groups showed sedation, dyspnea, curved position, and ruffled fur. The animals recovered within 8 to 10 days. Necropsy examination revealed no substance related findings. The acute oral LD_{50} was greater than 7750 mg/kg of body weight. This study was assigned a reliability score of 2 (reliable with restrictions) by the secondary source.
    - In an acute oral toxicity study was carried out in 1961, rats (groups of 5, sex and strain unspecified) were dosed with the test substance (TK 10048) at 2500 or 5000 mg/kg orally (gum arabic carrier) and observed for 8 days. No mortalities or clinical signs were observed during the 8-day observation period. The acute oral LD_{50} was greater than 5000 mg/kg of body weight. No further details were provided, and the study was assigned a reliability score of 4 (not assignable) by the secondary source.
    - In an acute oral toxicity study was carried out in 1961, mice (groups of 5, sex and strain unspecified) were dosed with the test substance (TK 10048) at 2500 or 5000 mg/kg orally (gum arabic carrier) and observed for 8 days. No mortalities or clinical signs were observed during the 8-day observation period. The acute oral LD_{50} was greater than 5000 mg/kg of body weight. No further details were provided, and the study was assigned a reliability score of

4 (not assignable) by the secondary source.

- Dermal –
  - ECHA 2015a
    - An acute dermal toxicity study was carried out in 1972 according to a protocol similar to OECD Guideline 402. CFE (RAC; SPF) rats (5 males and 5 females) had 2000 mg/kg of the test material (carboxymethyl cellulose/water carrier) applied to the skin as an occlusive dressing held in place with an adhesive elastic bandage. After a 24-hour period, the test material was removed by washing, and the animals observed for 8 days. Three days later this gauze binder was removed. The test animals were observed for at least 14 days following the initial treatment. No mortalities, clinical signs of toxicity, or effects on body weight gain were observed during the 8-day observation period. The acute dermal LD_{50} was greater than 2,000 mg/kg of body weight. While non-GLP compliant, this study was carried out according to a recognized guideline with the results fully documented, and was assigned a reliability score of 2 (reliable with restrictions) by the secondary source.
- Inhalation –
  - ECHA 2015b – Drometrizole (structural analog data)
    - An acute inhalation toxicity study was carried out in 1973 according to a protocol similar to OECD Guideline 403. Tif. RAI rats (9 males, 9 females), which were exposed to aerosols of the test substance (TK 10047) at a concentration of 0.590 mg/L for four hours and observed for 7 days. The aerosol consisted of 82% of particles smaller than 7 μm. Two males and two females died within 24 hours after exposure, and hemorrhage in the lungs and congested organs were observed in these animals during necropsy. Tachypnoea, asynchronisms of the extremities, lateral or ventral position and apathy were observed in the animals, with the survivors recovering within 48 hours. Necropsy of the surviving animals at the end of the observation period revealed no substance related gross organ changes. The acute inhalation LC_{50} for a four-hour exposure was greater than 0.590 mg/L. This study was assigned a reliability score of 2 (reliable with restrictions) by the secondary source. The result is not sufficient for conclusive classification under GHS criteria. Classification in GHS Category 1 or 2 can be excluded on the basis that the LC_{50} value is greater than 0.5 mg/L, but classification in Category 3 or 4 cannot be ruled out based on the result.
  - Studies of questionable validity –
    - ECHA 2015a – Bumetrizole
      - An acute inhalation toxicity study was carried out in 1969 according to a protocol similar to OECD Guideline 403. Rats (Charles River albino, 5 males, 5 females), which were exposed to aerosols of the test substance (TU 1104) at a concentration of 0.27 mg/L (the maximum attainable concentration) for four hours and observed for 14 days. The particle size characteristics of the aerosol were not reported. No mortalities, clinical signs of toxicity, or effects on body weight were observed during the 14-day observation period. Necropsy of all animals showed a slight amount of lung hyperemia, with no other gross pathological alterations observed in the tissues or organs examined. The acute inhalation LC_{50} for a four-hour exposure was greater than 0.27 mg/L. This study was assigned a reliability score of

3 (not reliable) by the secondary source on the basis that the testing facility (Industrial Bio-Test Laboratories) was found to have falsified other study reports in a US Federal trial. The reliability of the result is also questionable in that the particle size characteristics of the aerosol were not reported, *i.e.* the concentration of respirable particles is unknown.

- Ciba-Geigy 1989 – UV-327 (structural analog data)
  - An acute LC_{50} value in rats of greater than 0.75 mg/L was reported for a four-hour exposure, with no deaths or substance-related gross organ changes. No other study details were reported (including the identity of the test laboratory), and the reliability of the study data is considered not assignable. The reliability of the result is also questionable in that the particle size characteristics of the aerosol were not reported, *i.e.* the concentration of respirable particles is unknown.
- ECHA 2015b – Drometrizole (structural analog data)
  - An acute inhalation toxicity study was carried out in 1965 according to a protocol similar to OECD Guideline 403. Rats (strain unspecified, 5 males, 5 females), which were exposed to aerosols of the test substance (TINUVIN P) for 1.2 hours and observed for 14 days. The particle size characteristics of the aerosol were not reported. No clinical signs of toxicity, or effects on body weight were observed during the 14-day observation period. Necropsy examination revealed no substance-related findings. The acute inhalation LC_{50} for a 1.2-hour exposure was greater than 163 mg/L, which corresponds to an estimated LC_{50} for a four-hour exposure of 48.9 mg/L. This study was assigned a reliability score of 4 (reliability not assignable) by the secondary source. The reliability of the result is also questionable in that the particle size characteristics of the aerosol were not reported, *i.e.* the concentration of respirable particles is unknown.

Systemic Toxicity/Organ Effects incl. Immunotoxicity (ST)
(ST-single) Group II Score (single dose: vH, H, M or L): L

Bumetrizole was assigned a score of LOW with high confidence (**L**) for systemic toxicity/organ effects (single exposure) based on a lack of effects sufficient for GHS classification observed in acute toxicity studies by the oral, dermal, and inhalation routes. The high level of confidence is assigned based on the use of multiple animal data (including the oral, dermal, and inhalation routes) in assigning the LOW score. No data were located for the immunotoxicity endpoint.

- Authoritative and Screening Lists
  - Not present on any authoritative or screening lists for systemic toxicity/organ effects after short-term exposure.
- ECHA 2015a
  - In the acute oral toxicity study in rats carried out in 2007, referenced above in the section on Acute Mammalian Toxicity, no significant adverse clinical signs were observed during the 14-day observation period after a single dose of 2,000 mg/kg bumetrizole. There were also no treatment related signs at necropsy at day 14. This GLP-compliant study was carried out according to a recognized guideline with the results fully documented, and was assigned a reliability score of 1 (reliable without

restriction) by the secondary source.
  - In the acute dermal toxicity study in rats carried out in 1972, referenced above in the section on Acute Mammalian Toxicity, no clinical signs of toxicity or effects on body weight gain were observed during the 8-day observation period after exposure to a single dose of 2,000 mg/kg bumetrizole. While non-GLP compliant, this study was carried out according to a recognized guideline with the results fully documented, and was assigned a reliability score of 2 (reliable with restrictions) by the secondary source.
  - In the acute inhalation toxicity study carried out in 1969, referenced above in the section on Acute Mammalian Toxicity, slight lung hyperemia was observed at necropsy of all animals after the 14-day observation period after exposure to a low dose (0.27 mg/L) of bumetrizole. However, this study was assigned a reliability score of 3 (not reliable) by the secondary source on the basis that the testing facility (Industrial Bio-Test Laboratories) was found to have falsified study reports. At best, the results cannot be relied upon and are provided as supporting information only.

- ECHA 2015b – Drometrizole (structural analog data)
  - In the acute inhalation toxicity study carried out in 1973, referenced above in the section on Acute Mammalian Toxicity, exposure to aerosols of the test substance (TK 10047) at a concentration of 0.590 mg/L for four hours produced tachypnea in the test animals, which cleared within 48 hours. Necropsy of the surviving animals at the end of the observation period revealed no substance related gross organ changes. It is also notable that four of the nineteen test animals died within 24 hours after exposure. The observation of tachypnea was not considered by itself to be sufficient for classification as STOT – SE Category 3 for respiratory irritation under GHS criteria. However, some other effects were observed which are considered in the section on neurotoxicity. This study was assigned a reliability score of 2 (reliable with restrictions) by the secondary source.

(ST-repeat) Group II* Score (repeated dose: H, M, L): *L*

Bumetrizole was assigned a score of LOW with low confidence (*L*) for systemic toxicity/organ effects from repeated exposure based on negative animal test data from multiple studies by the oral route. No effects were observed in any study at doses sufficient for classification as STOT – RE under GHS criteria. However, no high quality data were available for the inhalation or dermal routes, and the low level of confidence is assigned on this basis.

- Authoritative and Screening Lists (Pharos 2015a)
  - Bumetrizole is not present on any authoritative or screening lists for systemic toxicity/ organ effects after repeated exposure.

- ECHA 2015a
  - In the Combined Oral Repeated Dose and Reproductive/Developmental Toxicity Screening study conducted in rats according to OECD Guideline 422 (referenced above in the section on Reproductive Toxicity), no significant dose-related effects were observed in any parameter (including clinical signs, mortality, body weight, weight gain, food consumption, hematology, clinical chemistry, urinalysis, organ weights, gross pathology, and histopathology) at any dose level. The NOAEL (systemic) was 1000 mg/kg/day for both males and females, which is well above the adjusted guidance value of 200 mg/kg/day for GHS STOT – RE Category 2 classification. This study was assigned a reliability score of 1 (reliable without restriction) by the secondary source.
  - In the two-year feeding study in rats (1978) according to a protocol similar to OECD

Guideline 453 (referenced above in the section on Carcinogenicity), the NOEL for systemic toxicity was 3000 ppm, corresponding to 113.2 mg/kg/day for males and 147.7 mg/kg/day for females. These are well above the adjusted guidance value for GHS STOT – RE Category 2 classification of 12.5 mg/kg/day. Some treatment related effects on bodyweight gain, food consumption, and hematology (lower values for red cell parameters) were observed in the high dose group (10,000 ppm, corresponding to a LOAEL of 382.6 mg/kg/day for males and 501.9 mg/kg/day for females). This study was assigned a reliability score of 2 (reliable with restrictions) by the secondary source.

- In the two-year feeding study in mice (1981) according to a protocol similar to OECD Guideline 451 (referenced above in the section on Carcinogenicity), the NOAEL for systemic effects was 500 ppm, corresponding to 59 mg/kg/day for males and 62 mg/kg/day for females. These are well above the adjusted guidance value for GHS STOT – RE Category 2 classification of 12.5 mg/kg/day. This study was assigned a reliability score of 2 (reliable with restrictions) by the secondary source.
- A GLP-compliant oral repeated dose toxicity study was conducted in beagle dogs (1982) according to a protocol similar to OECD Guideline 409 (Repeated Dose 90-Day Oral Toxicity in Non-Rodents). Groups of four animals per sex per dose were administered bumetrizole in feed at doses of 0, 200, 1000, or 5000 ppm (corresponding to 0, 6.2, 29.6, and 168 mg/kg/day for males and 0, 6.5, 32.2, and 153 mg/kg/day for females) once per day for 13 weeks. Satellite groups (one animal per sex from the control and high dose groups) were allowed a post-exposure recovery period of 4 weeks. The NOAEL for systemic effects was 5000 ppm (153-168 mg/kg/day), which is above the guidance value for GHS STOT – RE Category 2 classification of 100 mg/kg/day. This study was assigned a reliability score of 2 (reliable with restrictions) by the secondary source.
- An oral repeated dose toxicity study was conducted in Wistar rats (1969) according to a protocol similar to OECD Guideline 408 (Repeated Dose 90-Day Oral Toxicity in Rodents). Groups of ten animals per sex per dose were administered bumetrizole in feed at doses of 0, 400, 1000, 2500 or 10,000 ppm (corresponding to 0, 25, 62, 153.9, and 637.4 mg/kg/day for males and 0, 28.9, 70.6, 176, and 740.1 mg/kg/day for females) once per day for 13 weeks. No adverse effects seen in any parameter at the highest dose level tested. The NOAEL for systemic effects was 10,000 ppm (637.4-740.1 mg/kg/day), which is well above the guidance value for GHS STOT – RE Category 2 classification of 100 mg/kg/day. This study was assigned a reliability score of 2 (reliable with restrictions) by the secondary source.
- An oral repeated dose toxicity study was conducted in Wistar rats (1969) according to a protocol similar to OECD Guideline 407 (Repeated Dose 28-Day Oral Toxicity in Rodents). Groups of five animals per sex per dose were administered bumetrizole in feed at doses of 0, 400, 1000, 2500 or 10,000 ppm (corresponding to 0, 36.9, 100.2, 235.4, and 996.7 mg/kg/day for males and 0, 41.5, 96.7, 252.5, and 1014.8 mg/kg/day for females) once per day for 28 days. No adverse effects seen in any parameter at the highest dose level tested. The NOAEL for systemic effects was 10,000 ppm (~1000 mg/kg/day), which is well above the adjusted guidance value for GHS STOT – RE Category 2 classification of 300 mg/kg/day. This study was assigned a reliability score of 2 (reliable with restrictions) by the secondary source.

- Studies of Questionable Validity –
  - ECHA 2015a
    - An oral repeated dose toxicity study was conducted in Wistar rats (1968). Groups of 12 rats/sex/dose were administered bumetrizole in feed at doses of

0 and 500 ppm over a period of 4 weeks. No mortality or clinical signs of toxicity were observed during the study, and the NOAEL for systemic effects was 500 ppm (approximately 48 mg/kg/day based on rat default values from TERA 2015). However, the study was assigned a reliability score of 3 (not reliable) by the secondary source on the basis that approximately one-half of the animals showed evidence of chronic infection with round cell infiltrations and, in part, granulomas in the liver and kidneys.

- A dermal repeated dose toxicity study was conducted in rats (1961). Ten rats (5 per sex) were dosed with 0.4 mL of a 5% solution of bumetrizole in gum arabic (corresponding to approximately 50 mg/kg/day based on a mean body weight of 186 g) on intact shaved skin 6 days per week for 4 weeks. Washing was done 3 hours after application. No local irritating or systemic effects were noted during the study. The study was assigned a reliability score of 4 (reliability not assignable) by the secondary source on the basis that the documentation was insufficient for assessment.

- US Department of Health and Human Services 1987
  - An oral repeated dose toxicity study was conducted in Charles River albino rats (1969). Groups of 15 rats/sex/dose were administered bumetrizole in feed at doses of 0, 2500, 5000, 10,000, or 20,000 ppm (approximately 0, 240, 480, 960, and 1,920 mg/kg/day based on rat default values from TERA 2015) for 90 days. Significant treatment-related effects included reduced weight gain in males in the 10,000 and 20,000 ppm groups, elevated serum alkaline phosphatase levels in males in the 5,000, 10,000, and 20,000 ppm groups. Increases in liver weights were considered an adaptive response. The LOAEL for systemic effects was 5,000 ppm (~240 mg/kg/day) for males and the NOAEL was 20,000 ppm (~1,920 mg/kg/day) for females. This study is considered to be of questionable validity on the basis that the testing facility (Industrial Bio-Test Laboratories) was found to have falsified other study reports in a US Federal trial.
  - An oral repeated dose toxicity study was conducted in beagle dogs (1970). Groups of four dogs/sex/dose were administered bumetrizole in feed at doses of 0, 250, 500, 1000, 2500, 5000, or 10,000 ppm for 90 days. Significant treatment-related effects included reduced weight gain, lacrimation, and increased serum alkaline phosphatase activity in the 2500, 5000, and 10,000 ppm groups. Elevated liver to body weight ratios were also observed in the same groups. The LOAEL for systemic effects was 2500 ppm. This study is considered to be of questionable validity on the basis that the testing facility (Industrial Bio-Test Laboratories) was found to have falsified other study reports in a US Federal trial.

Neurotoxicity (N)

(N-single) Group II Score (single dose: vH, H, M or L): *M*

Bumetrizole was assigned a score of MODERATE with low confidence (*M*) for neurotoxicity from a single exposure based on effects observed in an acute inhalation toxicity study in rats on a structural analog, which were considered sufficient for classification as GHS STOT – SE Category 3 for narcotic effects. In an acute toxicity study by the oral route (1978), sedation was observed after dosing, but at doses well above the threshold for classification as STOT – SE by GHS criteria (refer to section on Acute Mammalian Toxicity). The low level of confidence is assigned based on the use of structural analog data in assigning the MODERATE score, and also due to a lack of data from studies specifically investigating neurotoxicity after a single exposure.

- Authoritative and Screening Lists (Pharos 2015a)
    - Bumetrizole is not present on any authoritative or screening lists for neurotoxicity after short-term exposure.
- ECHA 2015b – Drometrizole (structural analog data)
    - In the acute inhalation toxicity study carried out in 1973, referenced above in the section on Acute Mammalian Toxicity, exposure to aerosols of the test substance (TK 10047) at a concentration of 0.590 mg/L for four hours produced asynchronisms of the extremities, lateral or ventral position and apathy in the test animals, which cleared within 48 hours. These are considered sufficient for GHS classification of STOT – SE Category 3 for narcotic effects. This study was assigned a reliability score of 2 (reliable with restrictions) by the secondary source.

(N-repeat) Group II* Score (repeated dose: H, M, L): *L*
Bumetrizole was assigned a score of LOW with low confidence (*L*) for neurotoxicity from repeated exposure based on a lack of effects observed in functional observation batteries carried out as part of an OECD Guideline 422 study. No neurotoxic effects were reported in any of the other repeated dose toxicity studies by the oral route. The low confidence level is assigned on the basis of using the results of a single study by the oral route in assigning the score and a lack of high quality study data by the inhalation and dermal routes.

- Authoritative and Screening Lists (Pharos 2015a)
    - Bumetrizole is not present on any authoritative or screening lists for neurotoxicity after repeated exposure.
- ECHA 2015a
    - The GLP-compliant OECD Guideline 422 (Combined Repeated Dose Toxicity Study with the Reproduction / Developmental Toxicity Screening Test) cited previously included a neurobehavioral assessment. Specifically, this included multiple functional observational batteries (FOB), a sensory assessment, a motor activity assessment, and a grip strength assessment. The FOB were performed at regular intervals during the study, while the other assessments were performed toward the end of the study. No significant differences were observed in any parameters of any group in this study. The NOAEL for neurotoxicity was 1000 mg/kg/day for both males and females. This study was assigned a reliability score of 1 (reliable without restriction) by the secondary source.

Skin Sensitization (SnS) Group II* Score (H, M or L): L
Bumetrizole was assigned a score of LOW with high confidence (**L**) for skin sensitization based on negative data in multiple animal and human studies. The animal and human data are judged sufficiently strong to negate the New Zealand HSNO/GHS – 6.5B classification (corresponding to GHS Category 1 according to NZ EPA 2012), which appears to be based on studies in humans with 1,2,3-benzotriazole (NZ EPA 2015, Stouten *et al* 2000). This substance is considered a weak analog for bumetrizole (<50% similarity, ChemIDplus 2015). The high level of confidence is justified on the basis of using high quality, negative animal and human data in assigning the LOW score.

- Authoritative and Screening Lists
    - *Authoritative:* Not present on any authoritative lists for skin sensitization.
    - *Screening:* New Zealand HSNO/GHS - 6.5B – Contact sensitizers (GHS Category 1)
- ECHA 2015a
    - A GLP-compliant sensitization study was conducted in 1991 according to OECD 406

(Guinea Pig Maximization Test). The animals used were Pirbright White strain (Tif: DHP) guinea pigs (10/sex/dose). Induction exposure was carried out by intradermal injection (0.1 mL of a 5% mixture of bumetrizole in Oleum arachidis) followed seven days later by epicutaneous application (0.4 g of a 30% mixture of bumetrizole in petrolatum) for 48 hours. Challenge exposure was carried out two weeks after epicutaneous induction by epidermal application (0.2 g of a 20% mixture of bumetrizole in petrolatum). Reactions were evaluated at 24 and 48 hours after the challenge exposure. One animal (out of 20) showed reactions after 24 hours and none of the animals showed reactions after 48 hours. None of the animals in a control group inducted with the test substance and challenged with petrolatum alone showed reactions. While sensitization was observed in a single animal, the results are not sufficient for classification as sensitizing under GHS criteria. The study was assigned a reliability score of 1 (reliable without restrictions) by the secondary source.

- The sensitization potential of bumetrizole was assessed in 1993 according to a protocol similar to OECD 429 (Mouse local lymph node assay – LLNA). Deviations from the procedure included injection of the test substance in FCA before topical treatment, sacrifice one day after the last topical treatment, and incorporation of ^{3}HTdR performed *in vitro* instead of injecting the test animals. At least three mice per group were injected intradermally with 50 µL of bumetrizole in FCA (Freund's complete adjuvant) into the shaved abdomen. Five days after the injection, mice were exposed topically (ear) to 25 µL of various concentrations of bumetrizole in vehicle or vehicle alone on both ears daily for 3 consecutive days. The day after the final exposure, mice were sacrificed and the auricular draining lymph nodes were excised. Lymph nodes were pooled per each experimental group and a single cell suspension of LNC was prepared. Cells were cultured (5 culture wells per experimantal group) with 0.5 µCi ^{3}HTdR for 24 h and ^{3}HTdR incorporation was determined by liquid scintillation counting. The result was considered positive in this test if exposure to the test substance resulted in an incorporation of ^{3}HTdR at least three-fold greater than that observed in vehicle treated control mice. The results were interpreted as negative for sensitization on the basis that treatment with the test substance did not affect proliferative response of the auricular draining lymph nodes, although the stimulation index was not determined. The study was assigned a reliability score of 2 (reliable with restrictions) by the secondary source.
- The sensitization potential of bumetrizole was assessed in 1993 according to a mouse ear-swelling test. Groups of 4-5 female mice (Balb/c) were intradermally injected with bumetrizole in FCA into the shaved abdomen and after five days treated topically with the test substance on three consecutive days. Seven days after the final exposure, ear thickness was measured using an engineer's micrometer and the mice were challenged with the test substance in vehicle or vehicle alone. Ear thickness was measured again 24 hours after challenge and the percentage increase was determined. Seven days after the primary challenge, each group of mice was re-challenged with 2% of the test substance in acetone/olive oil (4:1) and elicitation reactions were measured. The result was considered positive if the ear thickness following challenge was at least 20% greater than that before challenge. The test substance did not produce a positive reaction, and the results were interpreted as negative for sensitization. The study was assigned a reliability score of 2 (reliable with restrictions) by the secondary source.
- The sensitization potential of bumetrizole was assessed in 1969 in a skin patch study with 59 human volunteers (26 males, 33 females). Patches containing 0.3% bumetrizole in dimethylphthalate were applied on alternate days, 3 times per week

for 24 hours each (total of 15 applications). After removal of the last application preceding the challenge, the sites were examined immediately and once daily for at least two days. The challenge was applied to the original contact site after 14 days of no contact with test material and was terminated after 24 hours. The sites were examined for immediate reactions, which if present, were graded and recorded. These sites were re-examined after 24 and 48 hours later for delayed reactions. No reactions were noted except for a single male subject exhibiting slight erythema after third application during the induction phase, which did not reoccur after subsequent applications. The results were interpreted as negative for sensitization. The study was assigned a reliability score of 2 (reliable with restrictions) by the secondary source.

- A photo-allergy test was conducted in guinea pigs in 2001 according to OECD Draft Guideline: Acute Dermal Photoirritation Dose-Response Test (February 1995). The protocol differs from the guinea pig maximization test in that the test animals are subjected to UV irradiation after induction and after challenge. Induction exposure was carried out by epicutaneous application of bumetrizole (0.1 g) on days 1, 3, 6, 8, and 10 following FCA/saline intradermal injections. Each epicutaneous application was followed by exposure to UV radiation (10 J/cm^2 UV-A, minimal erythremal dose of UV-B). Challenge exposure was carried out three weeks after induction with 100, 50, or 20% of bumetrizole in petrolatum followed by UV irradiation (10 J/cm^2 UV-A). Evaluations were made 24, 48, and 72 hours after challenge. No indication of sensitizing or photosensitizing potential was observed. The study was assigned a reliability score of 2 (reliable with restrictions) by the secondary source.

- Ikarashi *et al* 1994
  - The sensitizing and cross-sensitizing potentials of bumetrizole and the structural analog drometrizole were evaluated by measuring lymph node cell (LNC) proliferation and ear swelling response in BALB/c mice. Groups of mice received an intradermal injection and subsequent topical challenge application (five days after injection) of the test chemicals. Following the final application, auricular LNC proliferation was measured. In separate experiments, the appearance of contact sensitivity was assessed by increases in ear thickness following challenge with the test chemical. Drometrizole produced positive responses in both LNC proliferation and ear swelling, indicating sensitization. Bumetrizole failed to induce either response under the same conditions and was deemed not sensitizing. Mice that were injected with drometrizole did not show LNC proliferation by challenge with bumetrizole, and those that were injected with bumetrizole did not show positive responses by challenge with drometrizole. The results indicate that drometrizole is sensitizing, bumetrizole is not sensitizing, and the chemicals do not cross-sensitize. The study was well documented and appeared in a peer-reviewed publication.

Respiratory Sensitization (SnR) Group II* Score (H, M or L): DG

Bumetrizole was assigned a score of DATA GAP (DG) for respiratory sensitization based on a lack of data for the substance and structural analogs.

- Authoritative and Screening Lists (Pharos 2015a, Pharos 2015b, Pharos 2015c)
  - Bumetrizole and the structural analogs UV-327 and drometrizole are not present on any authoritative or screening lists for respiratory sensitization.

- No data for bumetrizole or the structural analogs UV-327 and drometrizole were identified in the available GreenScreen® specified lists.

Skin Irritation/Corrosivity (IrS) Group II Score (vH, H, M or L): L
Bumetrizole was assigned a score of LOW with high confidence (**L**) for skin irritation/corrosivity based on negative animal test data in two different primary skin irritation tests and in a dermal phototoxicity test. The substance showed at most mild irritation effects which cleared within 7 days, and none of the results were sufficient for classification as a skin irritant under GHS criteria. The high level of confidence is justified on the basis of using high quality animal data in assigning the LOW score.

- Authoritative and Screening Lists (Pharos 2015a)
    - Bumetrizole is not present on any authoritative or screening lists for skin irritation/ corrosivity.

- ECHA 2015a
    - A primary skin irritation test was conducted in 1979 according to the Proposed Guidelines of the US EPA §163.81-5 'Primary dermal irritation study' (similar to OECD 404). The test substance (0.5 g bumetrizole in a propylene glycol/water carrier) was applied to the intact and abraded skin of six New Zealand white rabbits (3 per sex) under an occlusive dressing. After 24 hours of exposure, the patches and test material were removed, and the resulting reactions were given a Draize score. Readings were also made after 48 and 72 hours. The test substance was at most mildly irritating to intact and abraded skin after the 24-hour exposure. Mean erythrema scores for intact skin were 0.33 for 5/6 animals (reversible within 48 hours), and 1.33 in the sixth animal (reversible within 72 hours). Mean edema scores for intact skin were zero for 5/6 animals and 0.33 for the sixth animal (reversible within 48 hours). The results were not sufficient for classification as a skin irritant under GHS criteria. While non-GLP compliant, this study was carried out according to a recognized guideline with the results fully documented, and was assigned a reliability score of 2 (reliable with restrictions) by the secondary source.
    - A primary skin irritation test was conducted in 1985 under a protocol similar to OECD 404. Deviations from OECD 404 included a 24-hour exposure under occlusive conditions and no scoring at 48 hours. The test substance (42.2% bumetrizole, 0.5 mL) was applied to the intact and abraded skin of six New Zealand white rabbits under an occlusive dressing. After 24 hours of exposure, the patches and test material were removed, and the resulting reactions were given a Draize score. Readings were also made after 72 hours. The maximum mean erythrema score for intact skin was 1.5 for 3/6 animals (reversible within 7 days). The maximum mean edema score for intact skin was 1.0 for a single animal (reversible within 7 days). The results were not sufficient for classification as a skin irritant under GHS criteria. While non-GLP compliant, this study was carried out according to a recognized guideline with the results fully documented, and was assigned a reliability score of 2 (reliable with restrictions) by the secondary source.
    - In a dermal phototoxicity study conducted in 2000 under an unspecified protocol, bumetrizole (0.1 mL, carrier and concentration not specified) was applied to two different sites on the shaved skin of ten male Hartley guinea pigs. The skin on two remaining sites was not treated. After approximately 20 minutes, two sites on each animal (one treated and one not) were exposed to a UV-A dosage of approximately 10.2 J/cm^2. After the exposure period, the animals were returned to their cages, and all sites were graded for erythema and edema after treatment. Mean erythrema and edema scores over 24, 48, 72, and 96 hours off all ten animals were zero for both the UV-exposed and unexposed sites treated with the test substance. The results were interpreted as non-irritating. The study was GLP-compliant and assigned a

reliability score of 2 (reliable with restrictions) by the secondary source.

Eye Irritation/Corrosivity (IrE) Group II Score (vH, H, M or L): L

Bumetrizole was assigned a score of LOW with high confidence (**L**) for eye irritation/corrosivity based on three different animal studies indicating the substance to be at most mildly irritating, with rapid reversal of any effects, and none of which are sufficient for classification as an eye irritant under GHS criteria. The animal data are judged sufficiently strong to negate the New Zealand HSNO/GHS – 6.4A classification (corresponding to GHS Category 2 according to NZ EPA 2012), which appears to be based solely on a statement from a MSDS for an unidentified commercial product (NZ EPA 2015). The high level of confidence is justified on the basis of using high quality animal data supported by less reliable data in assigning the LOW score.

- Authoritative and Screening Lists (Pharos 2015a)
  - *Authoritative:* Not present on any authoritative lists for eye irritation/corrosivity.
  - *Screening:* New Zealand HSNO/GHS - 6.4A - Irritating to the eye (GHS Category 2)
- ECHA 2015a
  - An eye irritation test was conducted in 1972 according to a protocol similar to OECD 405 (Acute Eye Irritation/Corrosion). Deviations included computing of Draize scores for the evaluation of conjunctivae effects by combining redness, swelling and discharge to give a single conjunctivae score, and lacking detailed information on test animals and the test material. The test substance (40 mg TK 10048) was applied to one eye of each of six albino rabbits. The treated eye was not washed after instillation. The untreated eye of each animal served as a negative control. The ocular reaction was scored according to the Draize system at 24, 48 and 72 hours after instillation. Observations with fluorescein staining were made 24 hours after the application of the test substance. Mean Draize scores over 24, 48, and 72 hours were zero for corneal opacity (6/6 animals), iritis (6/6 animals), and conjunctival effects (5/6 animals). A single animal exhibited a mean conjunctival score of 0.67, with effects fully reversible within 72 hours. The results were not sufficient for classification as an eye irritant under GHS criteria. While non-GLP compliant, this study was carried out according to a recognized guideline, and was assigned a reliability score of 2 (reliable with restrictions) by the secondary source.
  - An eye irritation test was conducted in 1985 according to a protocol similar to OECD 405 (Acute Eye Irritation/Corrosion). The test substance (0.1 mL, 42.2% by weight of bumetrizole in a liquid carrier) was applied to one eye of each of six albino rabbits. The treated eye was not washed after instillation. The untreated eye of each animal served as a negative control. The ocular reaction was scored according to the Draize system at 1, 24, 48 and 72 hours after instillation. Observations with fluorescein staining were made 24 and 72 hours after the application of the test substance. Mean Draize scores over 24, 48, and 72 hours were zero for corneal opacity (6/6 animals) and iritis (6/6 animals). Mean scores for conjunctival redness were ≤1 for all animals. Mean scores for chemosis were ≤0.67 for all animals. All effects were fully reversible within 72 hours. The results were not sufficient for classification as an eye irritant under GHS criteria. While non-GLP compliant, this study was carried out according to a recognized guideline, and was assigned a reliability score of 2 (reliable with restrictions) by the secondary source.
- US Department of Health and Human Services 1987
  - An acute eye irritation test was conducted in 1969 according to the Draize method. The test substance (100 mg bumetrizole) was instilled into the conjunctival sac of one eye of each of nine New Zealand albino rabbits. One group of three rabbits had their eyes rinsed with water after a 2 second contact period, a second group of three

rabbits had their eyes rinsed with water after a 4 second contact period, and the eyes of a third group of three rabbits were not rinsed. The left eye of each animal served as a negative control. The ocular reaction was scored according to the Draize system at 1, 24, 48, 72, and 96 hours, and at 7 days. Transient iris and conjunctival irritation were noted in all animals at 1 hour after instillation, but all effects reversed within 24 to 72 hours. Mean Draize scores (over 24, 48, and 72 hours) were zero for corneal opacity. For iris and conjunctival redness, the mean Draize scores were ≤0.67 for all animals and for chemosis the mean scores were ≤0.33 for all animals. Thus the results were not sufficient for classification as an eye irritant under GHS criteria. While this study was well documented, its reliability is questionable on the basis that the testing facility (Industrial Bio-Test Laboratories) was found to have falsified other study reports in a US Federal trial, and the results are provided as supporting information only.

Ecotoxicity (Ecotox)

Acute Aquatic Toxicity (AA) Score (vH, H, M or L): *L*

Bumetrizole was assigned a score of LOW with low confidence (*L*) for acute aquatic toxicity based on a lack of effects at saturation in tests with fish, daphnids, algae, and activated sludge. The LOW score is also supported by modeled data indicating that no effects are expected at saturation in fish, daphnids, and algae. The experimental and modeled data (as well as the low water solubility of bumetrizole) are considered sufficiently strong to negate the New Zealand HSNO/GHS – 9.1D classification and the Environment Canada iT classification, both of which are based solely on modeled data (NZ EPA 2015, OECD 2015). It should be noted that the solubility of bumetrizole in water is very low (4 μg/L), and that all of the observed LC/EC_{50} values are above the limit of solubility, and therefore cannot be reliably used to classify/score the chemical. The results may be best interpreted as providing no evidence of effects at saturation. Given that much of the rationale for classification is based on expert judgment and that the screening list data do not support the LOW score, it is assigned as low confidence.

- Authoritative and Screening Lists (Pharos 2015a)
  - *Authoritative:* Not present on any authoritative lists for acute aquatic toxicity.
  - *Screening:* NZ HSNO/GHS - 9.1D (fish), Acute (GHS Category Acute 3)
    NZ HSNO/GHS - 9.1D (algal), Acute (GHS Category Acute 3)
    Environment Canada – Domestic Substances List – Inherently Toxic in the Environment (iT) on the basis of acute aquatic toxicity

- ECHA 2015a
  - In an acute toxicity study in fish (*Brachydanio rerio*) conducted in 1988 according to OECD Guideline 203 (Fish, Acute Toxicity Test), fish were exposed to bumetrizole (100 mg/L nominal concentration) under static conditions for 96 hours. A dispersing agent (alkylphenol polyglycol ether) was used due to the low water solubility of the test substance. Evidence of undissolved material (precipitate) was noted after 24 hours. The 96-hour LC_{50} was greater than 100 mg/L (nominal concentration). As this is well above the water solubility of bumetrizole, the results are interpreted as providing no evidence of acute toxicity at saturation. The study was assigned a reliability score of 2 (reliable with restrictions) by the secondary source.
  - In a GLP-compliant acute toxicity study in *Daphnia magna* conducted in 2012 according to OECD Guideline 202 (Daphnia sp. Acute Immobilisation Test), daphnids were exposed to bumetrizole (100 mg/L nominal concentration) under static conditions for 48 hours. The test medium was prepared by mixing bumetrizole (100 mg/L) with water, ultrasonicating at 40°C for 15 minutes, stirring using a

mechanical shaker for 24 hours, and filtration to remove particulates. No immobilization of daphnids was observed, and the 48-hour EC_{50} was greater than 100 mg/L (nominal concentration). As this is well above the water solubility of bumetrizole, the results are interpreted as providing no evidence of acute toxicity at saturation. The study was assigned a reliability score of 1 (reliable without restriction) by the secondary source.

- In an acute toxicity study in *Daphnia pulex* conducted in 2011 according to OECD Guideline 202 (Daphnia sp. Acute Immobilisation Test), daphnids were exposed to bumetrizole (0.1, 0.5, 1, 5, or 10 mg/L nominal concentrations) under static conditions for 48 hours. Tetrahydrofuran was used as a solubilizing agent. The 48-hour EC_{50} was greater than 10 mg/L (nominal concentration). As this is well above the water solubility of bumetrizole, the results are interpreted as providing no evidence of acute toxicity at saturation. The study was assigned a reliability score of 4 (reliability not assignable) by the secondary source based on limited details of the experimental conditions.
- In an acute toxicity study in *Daphnia magna* conducted in 1988 according to OECD Guideline 202 (Daphnia sp. Acute Immobilisation Test), daphnids were exposed to bumetrizole (0, 10, 18, 32, 58 or 100 mg/L nominal concentrations) under static conditions for 24 hours. A dispersing agent (alkylphenol polyglycol ether) was used due to the low water solubility of the test substance. Evidence of undissolved material (precipitate) was noted from the start of the experiment. No mortality was observed, and the 24-hour EC_{50} was greater than 100 mg/L (nominal concentration). As this is well above the water solubility of bumetrizole, the results are interpreted as providing no evidence of acute toxicity at saturation. The study was assigned a reliability score of 3 (not reliable) by the secondary source on the basis of no analysis of test material concentration in solution, vehicle concentration (above the 100 mg/L permitted in the Guideline), and an exposure time of only 24 hours instead of 48 hours.
- In an acute toxicity study in algae (*Scenedesmus subspicatus*) conducted in 1992 according to Directive 87/302/EEC, Part C, page 89-94 Algal inhibition test, algae were exposed to bumetrizole (1.23, 3.7, 11, 33 or 100 mg/L nominal concentrations) under static conditions for 72 hours. A dispersing agent (Tween 80) was used due to the low water solubility of the test substance. Some growth inhibition was observed at 100 mg/L (nominal concentration), which is considered to be a consequence of the physical effect of un-dissolved substance reducing the light intensity. The 72-hour EC_{50} based on biomass was greater than 100 mg/L and the 72-hour NOEC was 100 mg/L (both nominal concentration). As this is well above the water solubility of bumetrizole, the results are interpreted as providing no evidence of acute toxicity at saturation. The study was assigned a reliability score of 2 (reliable with restrictions) by the secondary source.
- In a GLP-compliant study acute toxicity study in domestic activated sludge carried out in 2009 according to OECD Guideline 209 (Activated Sludge, Respiration Inhibition Test), activated sludge exposed to bumetrizole (100 mg/L nominal concentration) for 3 hours and evaluated for effects on respiration rate. The 3-hour IC_{50} was greater than 100 mg/L (nominal concentration). As this is well above the water solubility of bumetrizole, the results are interpreted as providing no evidence of acute toxicity at saturation. The study was assigned a reliability score of 2 (reliable with restrictions) by the secondary source.

- EPISuite 2015 (Appendix C)
  - Acute toxicity values were estimated by the ECOSAR v1.11 module:

Fish: LC_{50} (96 hr) = 0.109 mg/L
Daphnid: LC_{50} (48 hr) = 0.160 mg/L
Green Algae: EC_{50} (96 hr) = 0.209 mg/L
Since the estimated LC_{50}/EC_{50} values for fish, daphnids, and green algae are greater than 10x the solubility in water (0.004 mg/L), no effects are expected at saturation (US EPA 2012).

Chronic Aquatic Toxicity (CA) Score (vH, H, M or L): M
Bumetrizole was assigned a score of MODERATE with high confidence (**M**) for chronic aquatic toxicity based on meeting the criteria for classification as GHS Category Chronic 4. This is supported by the classification of HSNO/GHS – 9.1D for chronic toxicity in fish (which corresponds to GHS Category Chronic 4) by New Zealand, and modeled data indicating that chronic effects at saturation in fish and in daphnids cannot be excluded. Experimental data do not show effects at saturation for daphnids or algae but no data for fish exists. The high level of confidence is assigned on the basis of unequivocal classification as GHS Category Chronic 4, supported by screening list data and modeled data.

- Authoritative and Screening Lists (Pharos 2015a)
  - *Authoritative:* Not present on any authoritative lists for chronic aquatic toxicity.
  - *Screening:* NZ HSNO/GHS - 9.1D (fish), Chronic (GHS Category Chronic 4)
- United Nations 2013
  - The criteria for classification as GHS Category Chronic 4 include "*Poorly soluble substances for which no acute toxicity is recorded at levels up to the water solubility, and which are not rapidly degradable and have a log K_{ow} ≥ 4, indicating a potential to bioaccumulate, will be classified in this category unless other scientific evidence exists showing classification to be unnecessary. Such evidence would include an experimentally determined BCF < 500, or a chronic toxicity NOEC > 1 mg/L, or evidence of rapid degradation in the environment*." Bumetrizole unequivocally meets all of the criteria for classification as GHS Category Chronic 4 (see sections on Acute Aquatic Toxicity, Persistence, and Bioaccumulation) and none of the required evidence exists to render classification unnecessary.
- ECHA 2015a
  - A GLP-compliant chronic aquatic toxicity study was conducted in Daphnia magna according to OECD Guideline 211 (Daphnia magna Reproduction Test). The test medium was prepared by mixing bumetrizole (10 mg/L) with water, ultrasonicating at 40°C for 15 minutes, stirring using a magnetic stir plate for 24 hours, and filtration to remove particulates. Fresh test solutions were prepared daily as a precautionary measure to help maintain consistent exposure to the test substance. Analyses of the test media were not conducted, since a reliable method for analyses in the required concentration range could not be developed. The daphnids were exposed under semi-static conditions for 21 days. No significant mortality, reduced reproduction or any other additional significant adverse effects or abnormal behavior were observed. Since no analyses of the test media were conducted, EC_x, NOEC, or LOEC values for reproduction or mortality could not be determined. The results are interpreted as providing no evidence of effects on reproduction or mortality at saturation. This study was assigned a reliability score of 1 (reliable without restriction) by the secondary source.
  - In the acute algae toxicity study cited in the Acute Aquatic Toxicity section, the 72-hour NOEC (based on biomass) was 100 mg/L (nominal concentration). As this is well above the water solubility of bumetrizole, the result is interpreted as providing no

evidence of effects at saturation.

- EPISuite 2015 (Appendix C)
  - Chronic toxicity values (ChV) were estimated by the ECOSAR v1.11 module:
    Fish: ChV = 0.010 mg/L
    Daphnid: ChV = 0.017 mg/L
    Green Algae: ChV = 0.093 mg/L
    Since the ChV value for green algae is greater than 10x the solubility in water (0.004 mg/L), no effects are expected at saturation. The ChV values for fish and daphnids are greater than the solubility in water, but less than the 10x threshold, so effects at saturation cannot be excluded (US EPA 2012). These results are consistent with classification as GHS Category Chronic 4, corresponding to the MODERATE score.

Environmental Fate (Fate)

Persistence (P) Score (vH, H, M, L, or vL): *vH*
Bumetrizole was assigned a score of VERY HIGH with low confidence (*vH*) for persistence based on half-life time data for the biodegradation of structural analogs in sediment ($T_{1/2}$ > 180 days), and modeled data for bumetrizole in sediment ($T_{1/2}$ > 180 days), supported by half-life time data for biodegradation in water ($T_{1/2}$ > 60 days in four reliable studies). Biodegradation data in soil (experimental and modeled) were consistent with a HIGH score. The results of Level III Fugacity Modeling indicate that degradation studies in soil and sediment (and to a lesser extent, water) are the most relevant to assigning the hazard score. Abiotic degradation is possible for phenolic benzotriazoles but is considered less relevant than biodegradation (ECHA 2015c). The low level of confidence is justified on the basis of using analog and modeled data for sediment in assigning the score, and the lack of consistency with the results in soil (which are indicative of a HIGH score).

- Authoritative and Screening Lists
  - Bumetrizole is not present on any authoritative or screening lists for persistence.
- Environmental partitioning –
  - EPI Suite 2015 (Appendix C)
    - The potential environmental distribution of bumetrizole was studied using a series of Level III Fugacity Models (LEVEL3NT module) of EPI Suite (v4.11), using nominal release rates of 1,000 kg/hour initially entering the air, soil and water compartments. Seven different models were produced using every possible combination of release compartments:
      1. 1000 kg/hr to air, soil, and water
      2. 1000 kg/hr to air
      3. 1000 kg/hr to water
      4. 1000 kg/hr to soil
      5. 1000 kg/hr to air and water
      6. 1000 kg/hr to air and soil
      7. 1000 kg/hr to water and soil

      Given the low vapor pressure of bumetrizole, scenarios involving release to water and soil can be regarded as much more relevant than those involving release to air. The models predict that when released to water, bumetrizole will distribute mainly to the sediment compartment with a smaller amount to the water compartment. When released to soil, bumetrizole is predicted to distribute almost exclusively to soil. The results (summarized below) indicate that degradation studies in soil and sediment (and to a lesser extent, water) to be the most relevant to assigning the hazard score.

1000 kg/hr to water:

Air	nil
Water	23.7%
Soil	nil
Sediment	76.3%

1000 kg/hr to soil:

Air	nil
Water	0.02%
Soil	99.9%
Sediment	0.06%

- Abiotic degradation –
  - Hydrolysis –
    - No studies on the hydrolysis of bumetrizole are available. The structural analog UV-327 has been deemed to be hydrolytically stable on the basis that it does not contain any functional groups subject to hydrolysis (ECHA 2015c). The same conclusion would apply to bumetrizole based on expert judgment.
  - Oxidation –
    - Given the structural similarities of phenolic benzotriazoles to hindered phenolic antioxidants (*e.g.* BHT), oxidative degradation cannot be excluded.
    - Hodgeman 1978
      - In a study of the oxidation chemistry of phenolic benzotriazoles, bumetrizole (and the structural analog drometrizole) was reacted with free radicals formed by cobalt-catalyzed decomposition of peroxides. The corresponding phenoxide radical was proposed as a transient intermediate, which is subject to further reactions giving a complex mixture of products that were not fully characterized. One postulated transformation product of bumetrizole was 5-chlorobenzotriazole (CAS No. 94-97-3, also known as 6-chloro-1H-benzotriazole). The study was well documented and appeared in a peer-reviewed publication.
    - ECHA 2015c and EPI Suite 2015 (Appendix C)
      - The AOPWIN module of EPI Suite predicts the generic structure alert "Reaction with Nitrate radicals may be important" for both bumetrizole and the structural analog UV-327 based on the fact that there is a phenolic group in the molecule. However, no experimental studies could be located in the literature showing a reaction of either bumetrizole or UV-327 with atmospheric nitrate radicals.
  - Photolysis and photo-oxidation –
    - ECHA 2015c
      - Phenolic benzotriazoles are used as UV stabilizers in plastics, coatings, and personal care products. At the molecular level, UV-radiation excites the phenolic benzotriazole from its ground state. The energy of excitation is dissipated rapidly and efficiently through radiation-less processes involving the intramolecular hydrogen bond. The UV-protection properties are based on this reversible process. Therefore, it was concluded that degradation through photolysis is negligible for this class of chemicals.
    - Gerlock *et al* 1995
      - The chemical transformation of phenolic benzotriazoles (including the

structural analog drometrizole) exposed to light was investigated in solution photolysis experiments. Photolysis of drometrizole (and other phenolic benzotriazoles) along with the radical generator AIBN in the presence of oxygen led to cleavage of the structure, forming benzotriazole and destroying the phenolic moiety. It was proposed that this pathway accounts for the loss of UV absorbance during outdoor weathering in coatings containing phenolic benzotriazoles. The analogous product that would be formed from bumetrizole is 5-chlorobenzotriazole. The study was well documented and appeared in a peer-reviewed publication.

- Biodegradation –
  - ECHA 2015a
    - A GLP-compliant biodegradation study (2007) was conducted in water according to the OECD Guideline 301B (Ready Biodegradability: CO_2 Evolution Test) over a period of 28 days, using domestic activated sludge as the innoculum. The percentage biodegradation of bumetrizole was 10-20% after 28 days (based on CO_2 evolution). Thus it appears highly probable that the half-life time of the substance would be greater than 60 days, supporting the VERY HIGH score. The study was assigned a reliability score of 2 (reliable with restrictions) by the secondary source.
    - A GLP-compliant biodegradation study (1996) was conducted in water according to the OECD Guideline 301C (Ready Biodegradability: Modified MITI Test (I)) over a period of 28 days, using domestic activated sludge as the innoculum. No biodegradation of bumetrizole was observed after 28 days (based on O_2 consumption). Thus it appears highly probable that the half-life time of the substance would be much greater than 60 days, supporting the VERY HIGH score. The study was assigned a reliability score of 1 (reliable without restriction) by the secondary source.
    - A biodegradation study (1988) was conducted in water according to the OECD Guideline 301B (Ready Biodegradability: CO_2 Evolution Test) over a period of 28 days, using domestic activated sludge as the innoculum. The percentage biodegradation of bumetrizole was 2-10% after 28 days (based on CO_2 evolution). Thus it appears highly probable that the half-life time of the substance would be much greater than 60 days, supporting the VERY HIGH score. The study was assigned a reliability score of 2 (reliable with restrictions) by the secondary source.
  - Liu *et al* 2013
    - Laboratory biodegradation batch studies were performed to investigate the degradation behavior of bumetrizole and other UV filters in an aquifer microcosm (groundwater and aquifer sediment mixture) under aerobic and anaerobic (nitrate, sulfate, and Fe(III) reducing) conditions over 77 days. Bumetrizole showed biological degradation in both aerobic and anaerobic microcosms. The half-life times were 52 days under aerobic conditions, and 72-126 days under anaerobic conditions. The results under aerobic conditions are consistent with a HIGH score, while those under anaerobic conditions support the VERY HIGH score. The study was well documented and appeared in a peer-reviewed publication.
  - Lai *et al* 2014
    - The occurrence and dissipation of phenolic benzotriazoles (including bumetrizole, the structural analogs UV-327 and drometrizole) in soils treated

with benzotriazole-containing sewage sludge ("bio-solid") was investigated. Field trials were conducted with two treatment groups: "Old" groups with bio-solid application at rates of 5, 10, 20 and 40 tons per hectare every year for 5 years, and "New" groups with only a single bio-solid application. Bumetrizole was detected in the bio-solids applied to the fields at an average concentration of 47 ng/g. Phenolic benzotriazoles could be detected in most bio-solid-amended soils, but not in control soils. Based on data for both treatment groups, the dissipation half-life of bumetrizole in soil was determined to be 81-135 days, corresponding to a HIGH hazard score. The study was well documented and appeared in a peer-reviewed publication.

- ECHA 2015c – structural analog data
  - A bio-degradation study (2015) was conducted with the structural analog UV-327 in sediment according to a protocol based on OECD Guideline 308 (Aerobic and Anaerobic Transformation in Aquatic Sediment Systems) over a period of 100 days. Analysis of the soluble and adsorbed concentrations confirmed a high adsorption affinity of UV-327. After 16 days, UV-327 could not be detected in the water phase and recoveries from the sediment phase stabilized. No significant degradation of UV-327 in sediment was observed over the 100-day test period. Therefore it was concluded that the dissipation half-life is much greater than 100 days, suggesting a HIGH to VERY HIGH hazard score.
  - Monitoring studies on the structural analog UV-327 from locations near a former production site in Rhode Island provide evidence for long-term persistence in sediment. Concentration levels in sediment found up to 25 years after production ceased were at levels comparable to or only an order of magnitude lower than at the time of active manufacturing. While it was not possible to derive reliable degradation half-lives from these studies, the results suggest degradation half-life times longer than 180 days, corresponding to a VERY HIGH hazard score.
  - Bio-degradation studies were conducted with the structural analog CG20-568 in sediments according to OECD Guideline 308 (Aerobic and Anaerobic Transformation in Aquatic Sediment Systems). One test was performed under aerobic conditions in a river system, and further tests were performed under both aerobic and anaerobic conditions in a pond system. The dissipation half-lives of CG20-568 were 31.6 days in the river system (aerobic conditions), and 248.2 and 237.7 days in the pond system (aerobic and anaerobic conditions, respectively). The values obtained in the pond system support the VERY HIGH score, while the value in the river system corresponds to a MODERATE score.

- EPISuite 2015 (Appendix C)
  - Bumetrizole was predicted to be not readily biodegradable by the BIOWIN v4.10 module, with an ultimate biodegradation timeframe of months (Biowin3) and a primary biodegradation timeframe of weeks (Biowin4).
  - Half-lives for air, surface water, soil, and sediments were calculated using a series of Level III Fugacity Models. The modeled half-life of 540 days in sediment supports the VERY HIGH score, while the modeled half-lives in water and soil (60 and 120 days, respectively) correspond to a HIGH score.

    1000 kg/hr to water or soil:

Air	$T_{1/2}$ = 17.2 hours
Water	$T_{1/2}$ = 1440 hours (60 days)

Soil	$T_{1/2}$ = 2880 hours (120 days)
Sediment	$T_{1/2}$ = 13,000 hours (540 days)

Bioaccumulation (B) Score (vH, H, M, L, or vL): *H*

Bumetrizole was assigned a score of HIGH with low confidence (*H*) for bioaccumulation based on monitoring data showing the presence of bumetrizole in aquatic life and in human breast milk, which can be considered as evidence of bioaccumulation (and grounds for a HIGH score) under GreenScreen® criteria. The HIGH score also finds support in the result of a bioaccumulation study in fish, which found maximum BCF values (895) close to the threshold for a HIGH score.

While the octanol-water partition coefficient values (Log K_{ow} > 5) and some of the modeled BCF/BAF data correspond to a VERY HIGH hazard score under the GreenScreen® criteria, according to the EPA's DfE Alternatives Assessment criteria these data are only used for evaluation in the absence of measured data (US EPA 2011). The validity of the modeled bioconcentration data is also questionable given the extremely broad range of values obtained. In addition, the screening list data (Environment Canada – DSL Substances that are Bioaccumulative) are discounted on the basis that the listing is based exclusively on modeled data (OECD 2015). The measured bioconcentration data and the monitoring data were considered to be the most relevant in assigning the HIGH hazard score. The low level of confidence is assigned on the basis that all of the data taken together (screening lists, measured and modeled bioaccumulation data, octanol-water partition coefficient, and monitoring data) do not give a consistent hazard score when evaluated according to the GreenScreen® criteria.

- Authoritative and Screening Lists (Pharos 2015a)
  - *Authoritative:* Not present on any authoritative lists for bioaccumulation.
  - *Screening:* Environment Canada – Domestic Substances List – DSL Substances that are Bioaccumulative
- Octanol-water Partition Coefficient –
  - Measured and estimated octanol-water partition coefficient values (Log K_{ow}) for bumetrizole range from from 5.55 to 6.812). All were assigned a reliability score of 2 (reliable with restrictions) by the secondary source.

Summary Table: Octanol-water Partition Coefficient (Log K_{ow}) Values.

Data Type	Method	Value	Reference
Estimated	KOWWIN Program (v1.68)	Log K_{ow} = 5.55	EPISuite 2015 (Appendix C), ECHA 2015a
Measured	OECD Guideline 117 (Partition Coefficient (n-octanol / water), HPLC Method)	Log K_{ow} > 6.5	ECHA 2015a
Estimated	Estimated based on solubilities in n-octanol and water	5.4 < Log K_{ow} < 6.4	ECHA 2015a
Estimated	Calculation using the scientific authoritative software program as recommended in Guidelines under REACH Regulation (EC) No 1907/2006	Log K_{ow} = 6.812	ECHA 2015a

- Bioaccumulation –
  - ECHA 2015a

        - A GLP-compliant bioaccumulation study (1998) was carried out in fish (*Cyprinius carpio*) according to OECD Guideline 305 (Bioconcentration: Flow-through Fish Test). The test utilized bumetrizole in the form of stock solution in the dispersing agent HCO-20. Groups of fish were exposed to bumetrizole at 0.5, 0.05, and 0.005 mg/L (nominal concentrations) under flow-through conditions for 8-10 weeks. BCF (whole body weight basis) of 54-109, 196-802, and 548-895 were determined for the high, medium, and low-dose groups respectively. These measured values correspond to a MODERATE hazard score, but at the lowest test concentration are close to the threshold for the HIGH score. Also, given that it is often observed that the BCF values of poorly water soluble substances increase with decreasing concentration, the possibility that lower concentrations might give a BCF value sufficient for a HIGH score cannot be excluded. The study was assigned a reliability score of 2 (reliable with restrictions) by the secondary source. Note: An extremely small metabolic peak was observed ahead of the test material peak on reverse phase HPLC chromatographic analysis of the high and mid-dose fish, but it was not identified. The BCF obtained by converting the metabolic peak to test material was 1.9-5.5 in the high dose group and 14-90 in the mid-dose group.
    - Modeled data –
        - ECHA 2015a
            - Extensive modeled bioaccumulation data (calculated BCF and/or BAF) were referenced in the REACH dossier with values ranging from 16 to 280,000. All were given reliability scores of 2 (reliable with restrictions) by the secondary source. However, the relevance of the data is questionable given the extremely broad range of values obtained, and it was not possible to independently determine which, if any, of the methods would be considered most reliable.
        - EPI Suite 2015 (Appendix C)
            - Bioconcentration (BCF) and bioaccumulation (BAF) factors were estimated by the BCFBAF v3.01 module using a calculated Log K_{ow} value of 5.55. The BCF and BAF values obtained are all consistent with the HIGH hazard score.
              BCF = 1283 L/kg wet-wt (regression-based method)
              BCF = 1030 L/kg wet-wt (Arnot-Gobas method, upper trophic)
              BAF = 1168 L/kg wet-wt (Arnot-Gobas method, upper trophic)

- Monitoring studies –
    - Nakata *et al* 2009
        - Phenolic benzotriazoles (including bumetrizole and the structural analog UV-327) were analyzed in marine organisms collected from the Ariake Sea, Japan. Fifty-five samples including tidal flat organisms (lugworm, lamp shell, oyster, clam, gastropod, crustaceans (crab and shrimp), fishes (herbivorous and omnivorous mudskippers)), and shallow water species (crustaceans (crab and shrimp), teleost fish (flathead, solefish, right eye flounder, sandperch, sweetlips, mullet, sea bass, hairtail), cartilaginous fish (eagle ray and hammerhead shark), and coastal birds (spot-billed duck and mallard)) were collected during 2004 and 2007. The whole body, soft tissue, hepatopancreas, and liver samples were analyzed, depending on the species. Sixteen coastal and river sediments were also collected around the Ariake Sea during 2006-2007. The phenolic benzotriazoles were detected in

all biota and sediment samples analyzed. The average concentrations of bumetrizole in tidal flat species were 10-20 fold higher than those in shallow water organisms. The tidal flat clam showed the highest concentration of bumetrizole, at 219 ng/g (based on lipid weight). Elevated concentrations of bumetrizole were also found in oysters and gastropods in tidal flat area. These results imply the presence of bumetrizole in sediment, resulting in accumulation in benthic organisms. This was confirmed, with an average concentration of 3.7 ± 3.0 ng/g in the sediment samples analyzed. Possible explanations for the lower concentrations of bumetrizole in shallow water species included the relatively low BCF of this compound as compared with other phenolic benzotriazoles (including the structural analog UV-327), and biodegradation of bumetrizole by shallow water organisms. The study was well documented and appeared in a peer-reviewed publication.

- Kim *et al* 2011
  - Phenolic benzotriazoles (including bumetrizole and the structural analogs UV-327 and drometrizole) were analyzed in fish collected from Manila Bay, Philippines. Fifty-eight different specimens belonging to 20 different species were collected from local fish markets in the Manila area, selecting only those specimens caught in Manila Bay. Muscle tissues were analyzed. Bumetrizole was detected in 19% of the analyzed specimens at a maximum concentration of 71.3 ng/g (based on lipid weight). The study was well documented and appeared in a peer-reviewed publication.
- Nakata *et al* 2012
  - Phenolic benzotriazoles (including bumetrizole and the structural analog UV-327) were analyzed in green and blue mussels collected from Pacific coastal waters. Sixty-eight different specimens were collected and analyzed from Cambodia, China, Hong Kong, India, Indonesia, Japan, Korea, Malaysia, Philippines, Vietnam and the USA during 2003 and 2007. Bumetrizole was detected in 57% of the specimens, including those collected in China, Hong Kong, Indonesia, Japan, Korea, Malaysia, the Philippines, and the USA, at an average concentration of 150 ng/g (based on lipid weight). The highest average concentration (450 ng/g lipid weight) was observed in specimens collected in Japan. The study was well documented and appeared in a peer-reviewed publication.
- Lai *et al* 2014
  - The uptake of phenolic benzotriazoles (including bumetrizole and the structural analogs UV-327 and drometrizole) by plants grown in soils treated with benzotriazole-containing sewage sludge (“bio-solid”) was investigated. Field trials were conducted after a single bio-solid application at 0, 10, 20, or 40 tons/hectare. Bumetrizole was detected in the bio-solids applied to the fields at an average concentration of 47 ng/g. Neither bumetrizole nor any of the other phenolic benzotriazoles were found in the crop plant samples (wheat grain, wheat stalk, corn, corn stalk and corn cob) collected from the treatment plots, indicating no uptake or bioaccumulation by the plants. However, potential risks to soil organisms could not be excluded. The study was well documented and appeared in a peer-reviewed publication.
- Peng *et al* 2015
  - Phenolic benzotriazoles (including bumetrizole and the structural analogs UV-327 and drometrizole) were analyzed in wild aquatic organisms (hairtail, squid, goby, pomfret, and squilla) and farmed red snapper from the Pearl

River estuary in southern China. Bumetrizole was detected in farmed red snapper (average concentrations 7.95-11.38 ng/g dry weight) but not in the wild organisms. The study was well documented and appeared in a peer-reviewed publication.

- Lee *et al* 2015
  - Phenolic benzotriazoles (including bumetrizole and the structural analogs UV-327 and drometrizole) were analyzed in breast milk collected from 87 lactating women in the Children's Health and Environmental Chemicals in Korea Panel. Bumetrizole was detected in 9.1% of the test samples at a maximum concentration of 53.1 ng/g and an average concentration of 1.77 ng/g (both based on lipid weight). The study was well documented and appeared in a peer-reviewed publication.

Physical Hazards (Physical)

Reactivity (Rx) Score (vH, H, M or L): L

Bumetrizole was assigned a score of LOW with high confidence (**L**) for reactivity based on classification data for reactivity hazards from competent authorities (including data for the structural analog drometrizole), information from product safety data sheets (SDS, including NFPA and HMIS scores for instability/physical hazards), and expert judgment. The high level of confidence is assigned based on use of high quality data (classification data from competent authorities) supported by SDS information and expert judgment in assigning the score.

- Authoritative and Screening Lists (Pharos 2015a)
  - Bumetrizole is not present on any authoritative or screening lists for reactivity.
- Ciba Specialty Chemicals Corporation 2004, BASF Corporation 2010
  - The SDS for Tinuvin® 326 (Section 10: Stability and Reactivity) reported the product to be stable with no hazardous reactions expected. The 2004 MSDS assigned a NFPA rating of zero for instability with no known special hazards, and a HMIS rating of zero for physical hazards.

Summary Table: Reactivity Hazard Data.

Reactivity Hazard	Results
Explosives	ECHA 2015a: Bumetrizole was determined not to be explosive based on a read-across from the structural analog drometrizole, which tested negative when tested under EU Method A.14 (Explosive properties). Bumetrizole was classified as "conclusive but not sufficient for classification" under CLP criteria.
Self reactive substances	ECHA 2015a: "Conclusive but not sufficient for classification" under CLP criteria.
Substances which on contact with water emit flammable gases	ECHA 2015a: Determined to be stable in water in solubility tests. "Conclusive but not sufficient for classification" under CLP criteria.
Oxidizing liquids and solids	ECHA 2015a: "Conclusive but not sufficient for classification" under CLP criteria.
Oxidizing gases	Not applicable – This substance is not a gas.
Organic peroxides	Not applicable – This substance is not an organic peroxide.
Self heating substances	ECHA 2015a: "Conclusive but not sufficient for classification" under CLP criteria.
Substances corrosive to metal	ECHA 2015a: "Conclusive but not sufficient for classification" under CLP criteria.

Flammability (F) Score (vH, H, M or L): L
Bumetrizole was assigned a score of LOW with high confidence (**L**) for flammability based on negative burn test data for the structural analog drometrizole, which is not sufficient for classification as a Flammable Solid under GHS criteria, corresponding to a LOW hazard score. The high level of confidence is assigned based on use of high quality data for a strong analog in assigning the score.

- Authoritative and Screening Lists (Pharos 2015a)
    - Bumetrizole is not present on any authoritative or screening lists for flammability.
- ECHA 2015a – Drometrizole (structural analog data)
    - The burning and fire propagation behavior of drometrizole was determined (2010) in testing according to the method of VDI 2263, Part 1, Chapter 1.2. The results were negative in that brief burning of the test substance was followed by rapid extinction, and do not appear sufficient for classification as a Flammable Solid under GHS criteria. It was also pointed out that bumetrizole should be even less flammable due to its chlorine content. The study was assigned a reliability score of 2 (reliable with restrictions) by the secondary source.

References

BASF Corporation. 2010. Safety Data Sheet for Tinuvin® 326. Version 1.1. Revision date 12.05.2010.

ChemIDplus. 2015. Available: http://chem.sis.nlm.nih.gov/chemidplus/.

Ciba-Geigy. 1989. Summaries of Toxicity Reports on Tinuvin 327 with Cover Letter dated 01/10/89. Accessed through the Public National Technical Reports Library (https://ntrl.ntis.gov/NTRL/login.xhtml), U.S. Department of Commerce, reference number OTS05166191.

Ciba Specialty Chemicals Corporation. 2004. Material Safety Data Sheet for Tinuvin 326. MSDS date 27 April 2004.

European Chemicals Agency. 2015a. Bumetrizole (CAS No. 3896-11-5). Registered substance. Registrants: BASF SE and Huntsman Textile Effects (Germany) GmbH. Available: http://apps.echa.europa.eu/registered/data/dossiers/DISS-dffb4072-e26d-47ae-e044-00144f67d031/DISS-dffb4072-e26d-47ae-e044-00144f67d031_DISS-dffb4072-e26d-47ae-e044-00144f67d031.html.

European Chemicals Agency. 2015b. 2-(2H-benzotriazol-2-yl)-p-cresol (CAS No. 2440-22-4). Registered substance. Registrants: 3V Sigma SpA, BASF SE, BASF Lampertheim GmbH. Available: http://apps.echa.europa.eu/registered/data/dossiers/DISS-9d929e03-c530-549e-e044-00144f67d249/DISS-9d929e03-c530-549e-e044-00144f67d249_DISS-9d929e03-c530-549e-e044-00144f67d249.html.

European Chemicals Agency. 2015c. Annex XV report; Proposal for Identification of a Substance of Very High Concern on the Basis of the Criteria Set Out in REACH Article 57; Substance Name: 2,4-Di-tert-butyl-6-(5-chlorobenzotriazol-2-yl)phenol (UV-327); EC Number: 223-383-8; CAS Number: 3864-99-1. Available: http://www.echa.europa.eu/documents/10162/755b24e4-40dc-455b-afc0-b5e4e9045701.

Fent, K.; Chew, G.; Li, J.; and Gomez, E. 2014. Science of the Total Environment, 482-483: 125-136.

Gerlock, J.; Tang, W.; Dearth, M.; and Korniski, T. 1995. Polymer Degradation and Stability, 48: 121-130.

Hodgeman, D. 1978. Journal of Polymer Science: Polymer Letters Edition, 16: 161-165.

Ikarashi, Y.; Tsuchiya, T.; Nakamura, A. 1994. Toxicology Letters, 71: 151-159.

Kawamura, Y.; Ogawa, Y.; Nishimura, T.; Kikuchi, Y.; Nishikawa, J.-i.; Nishihara, T.; and Tanamoto, K. 2003. J. Health. Sci., 49 (3): 205-212.

Kim, J.-W.; Isobe, T.; Ramaswamy, B.; Chang, K.-H.; Amano, A.; Miller, T.; Siringan, F.; and Tanabe, S. 2011. Chemosphere, 85: 751-758.

Lai, H.-J.; Ying, G.-G.; Ma, Y.-B.; Chen, Z.-F.; Chena, F.; and Liu, Y.-S. 2014. Environmental Science: Processes and Impacts, 16: 558-566.

Lee, S.; Kim, S.; Park, J.; Kim, H.-J.; Lee, J.; Choi, G.; Choi, S.; Kim, S.; Kim, S.Y.; Choi, K.; Kim, S.; Moon, H.-B. 2015. Environmental Research, 140: 466-473.

Liu, Y.-S.; Ying, G.-G.; Shareef, A.; and Kookana, R. 2013. Groundwater Monitoring and Remediation, 33(4): 79-88.

Miller, D.; Wheals, B.; Beresford, N.; and Sumpter, J. Environmental Health Perspectives, 109 (2): 133-138.

Morohoshi, K.; Yamamoto, H.; Kamata, R.; Shiraishi, F.; Koda, T.; and Morita, M. 2005. Toxicology in Vitro, 19: 457-469.

Nagayoshi, H.; Kakimoto, K.; Takagi, S.; Konishi, Y.; Kajimura, K.; and Matsuda, T. 2014. Environmental Science and Technology, 49: 578-587.

Nakata, H.; Murata, S.; Filatreau, J. 2009. Environmental Science and Technology, 43: 6920-6926.

Nakata, H.; Shinohara, R-I.; Nakazawa, Y.; Isobe, T.; Sudaryanto, A.; Subramanian, A.; Tanabe, S.; Zakaria, M.; Zheng, G.; Lam, P.; Kim, E.; Min, B.-Y.; We, S.-U.; Viet, P.; Tana, T.; Prudente, M.; Donnell, F.; Lauenstein, G.; and Kannan, K. 2012. Marine Pollution Bulletin, 64: 2211-2218.

New Zealand Environmental Protection Authority (NZ EPA). 2012. Information Sheet. Correlation between GHS and New Zealand HSNO Hazard Classes and Categories. EPA0125. Available: http://www.epa.govt.nz/Publications/hsnogen-ghs-nz-hazard.pdf.

New Zealand Environmental Protection Authority (NZ EPA). 2015. Chemical Classification and Information Database (CCID), Bumetrizole. Available: http://www.epa.govt.nz/search-databases/Pages/ccid-details.aspx?SubstanceID=7083.

Organisation for Economic Co-operation and Development (OECD). 2015. Categorization Results from the Canadian Domestic Substance List; CAS No. 3896-11-5; Phenol, 2-(5-chloro-2H-benzotriazol-2-yl)-6-(1,1-dimethylethyl)-4/methyl-. Available: http://webnet.oecd.org/ccrweb/ChemicalDetails.aspx?ChemicalID=51A168CE-F44F-4B7D-8F3C-58CB906EB4D0.

Peng, X.; Jin, J.; Wang, C.; Ou, W.; Tang, C. 2015. Journal of Chromatography A, 1384: 97-106.

Pharos. 2015a. Pharos Chemical and Material Library entry for bumetrizole (CAS No. 3896-11-5). Available: https://www.pharosproject.net/material/show/2013085.

Pharos. 2015b. Pharos Chemical and Material Library entry for Phenol, 2-(5-chloro-2H-benzotriazol-2-yl)-4,6-bis(1,1-dimethylethyl)- (CAS No. 3864-99-1). Available: https://www.pharosproject.net/material/show/2013084.

Pharos. 2015c. Pharos Chemical and Material Library entry for 2-(2'-hydroxy-5'-methylphenyl) benzotriazole (CAS No. 2440-22-4). Available: https://www.pharosproject.net/material/show/2005393.

Stouten, H.; Rutten, A.; Gevel, I. van de; Vrijer, F. De. 2000. The Nordic Expert Group for Criteria Documentation of Health Risks from Chemicals and The Dutch Expert Committee on Occupational Standards : 126. 1,2,3-Benzotriazole. Available: https://gupea.ub.gu.se/bitstream/2077/4230/1/ah2000_24.pdf.

Toxicology Excellence for Risk Assessment (TERA). 2015. Rat/mouse default values. Available: http://www.tera.org/Tools/ratmousevalues.pdf.

United Nations. 2013. Globally Harmonized System of Classification and Labelling of Chemicals, Fifth revised edition. Available: http://www.unece.org/fileadmin/DAM/trans/danger/publi/ghs/ghs_rev05/English/ST-SG-AC10-30-Rev5e.pdf.

US Department of Health and Human Services. 1987. Toxicology Data and Other Information Pertaining to the Safety of Tinuvin 326 as an Indirect Food Additive with Cover Letter Dated 08/31/87. Accessed through the Public National Technical Reports Library (https://ntrl.ntis.gov/NTRL/login.xhtml), U.S. Department of Commerce, reference number OTS00005720.

US Environmental Protection Agency. 2012. Methodology Document for the Ecological Structure-Activity Relationship Model (ECOSAR) Class Program, MS Windows Version 1.11. Available: http://www.epa.gov/oppt/newchems/tools/ecosartechfinal.pdf.

Wielogórska, E.; Elliott, C.; Danaher, M.; Connolly, L. 2015. Toxicology in Vitro, 29: 211-220.

APPENDIX A: Hazard Benchmark Acronyms (alphabetical order)

(AA) Acute Aquatic Toxicity

(AT) Acute Mammalian Toxicity

(B) Bioaccumulation

(C) Carcinogenicity

(CA) Chronic Aquatic Toxicity

(Cr) Corrosion/ Irritation (Skin/ Eye)

(D) Developmental Toxicity

(E) Endocrine Activity

(F) Flammability

(IrE) Eye Irritation/Corrosivity

(IrS) Skin Irritation/Corrosivity

(M) Mutagenicity and Genotoxicity

(N) Neurotoxicity

(P) Persistence

(R) Reproductive Toxicity

(Rx) Reactivity

(SnS) Sensitization- Skin

(SnR) Sensitization- Respiratory

(ST) Systemic/Organ Toxicity

Appendix B
Optional Hazard Summary Table

Exposure Route	GreenScreen Hazard Ratings: [*Chemical Name*]																			
	Group I Human					Group II and II* Human									Ecotox		Fate		Physical	
	C	M	R	D	E	AT	ST		N		SnS*	SnR*	IrS	IrE	AA	CA	P	B	Rx	F
							single	repeate	single	repeated*										
oral																				
dermal																				
inhalation																				

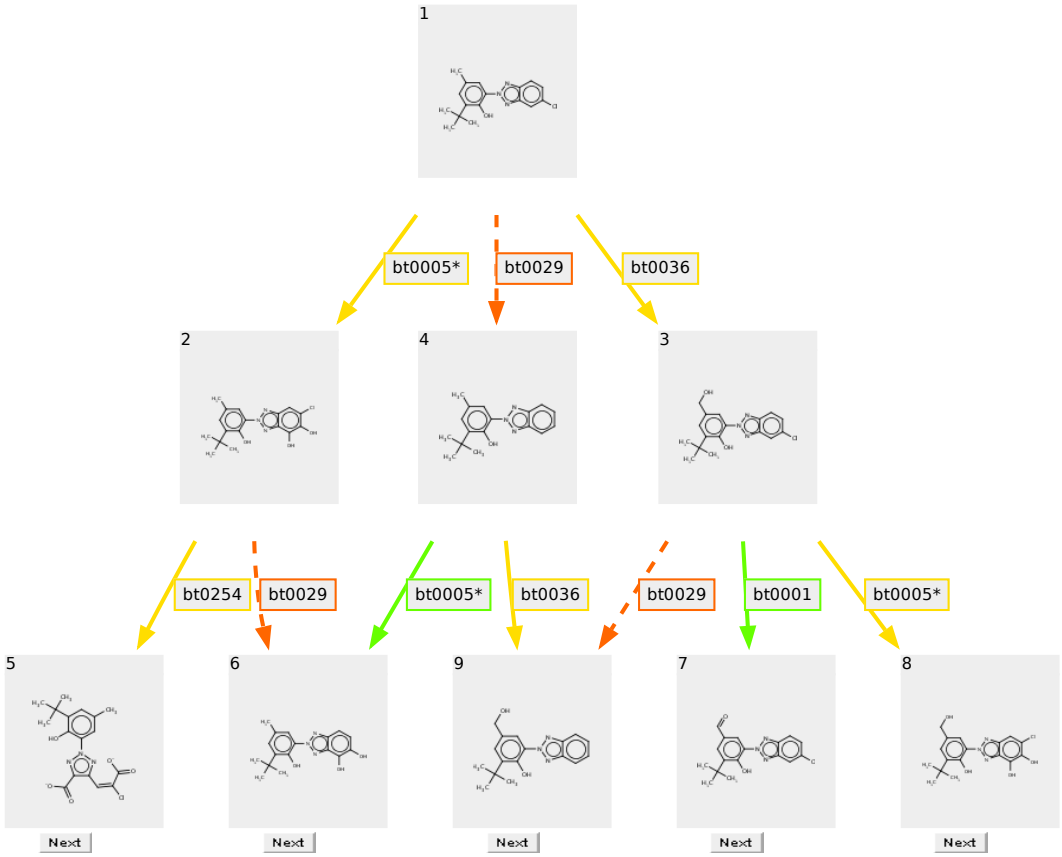
Appendix C
Modeling Results

Attach:

- **EPI Suite Results for Bumetrizole (CAS No. 3896-11-5)**

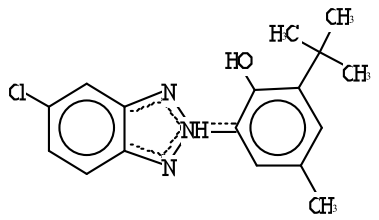
Bumetrizole EPISuite.doc

- **EAWAG-BBD Pathway Prediction System Results for Bumetrizole (CAS No. 3896-11-5)**



Pathway prediction results from EAWAG-PPS, http://umbbd.ethz.ch/predict/ (JobID 2015.09.23-11.57.35-37)

EPI Suite Results For CAS 3896-11-5



SMILES : Oc(c(cc(c1)C)C(C)(C)C)c1n(nc(c2cc(c3)CL)c3)n2
CHEM : Phenol, 2-(5-chloro-2H-benzotriazol-2-yl)-6-(1,1-dimethylethyl)-4-met
hyl-
MOL FOR: C17 H18 CL1 N3 O1
MOL WT : 315.81
---------- EPI SUMMARY (v4.11) ----------
Henry LC (atm-m3/mole) : ------
Log Kow (octanol-water): ------
Boiling Point (deg C) : ------
Water Solubility (mg/L): 0.004
Physical Property Inputs:
Vapor Pressure (mm Hg) : ------
Melting Point (deg C) : 139.70

KOWWIN Program (v1.68) Results:
==========

Log Kow(version 1.68 estimate): 5.55

SMILES : Oc(c(cc(c1)C)C(C)(C)C)c1n(nc(c2cc(c3)CL)c3)n2
CHEM : Phenol, 2-(5-chloro-2H-benzotriazol-2-yl)-6-(1,1-dimethylethyl)-4-met
hyl-
MOL FOR: C17 H18 CL1 N3 O1
MOL WT : 315.81

TYPE	NUM	LOGKOW FRAGMENT DESCRIPTION	COEFF	VALUE
Frag	4	-CH3 [aliphatic carbon]	0.5473	2.1892
Frag	12	Aromatic Carbon	0.2940	3.5280
Frag	1	-CL [chlorine, aromatic attach]	0.6445	0.6445
Frag	1	-OH [hydroxy, aromatic attach]	-0.4802	-0.4802
Frag	3	Aromatic Nitrogen [5-member ring]	-0.5262	-1.5786
Frag	1	-tert Carbon [3 or more carbon attach]	0.2676	0.2676
Factor	1	1,2,3-Triazole correction	0.7525	0.7525
Const		Equation Constant		0.2290

```
-------+-----+-------------------------------------------+---------+--------
Log Kow   =   5.5520



MPBPVP (v1.43) Program Results:
================================
Experimental Database Structure Match:  no data

SMILES : Oc(c(cc(c1)C)C(C)(C)C)c1n(nc(c2cc(c3)CL)c3)n2
CHEM   : Phenol, 2-(5-chloro-2H-benzotriazol-2-yl)-6-(1,1-dimethylethyl)-4-met
hyl-
MOL FOR: C17 H18 CL1 N3 O1
MOL WT : 315.81
---------------------- SUMMARY MPBVP v1.43 --------------------


Boiling Point:  450.11 deg C (Adapted Stein and Brown Method)

Melting Point:  349.84 deg C (Adapted Joback Method)
Melting Point:  149.16 deg C (Gold and Ogle Method)
Mean Melt Pt :  249.50 deg C (Joback; Gold,Ogle Methods)
Selected MP:  189.29 deg C (Weighted Value)

Vapor Pressure Estimations (25 deg C):
(Using BP: 450.11 deg C (estimated))
(Using MP: 139.70 deg C (user entered))
VP:  3.09E-010 mm Hg (Antoine Method)
:  4.12E-008 Pa  (Antoine Method)
VP:  5.64E-009 mm Hg (Modified Grain Method)
:  7.51E-007 Pa  (Modified Grain Method)
VP:  7.52E-008 mm Hg (Mackay Method)
:  1E-005 Pa  (Mackay Method)
Selected VP:  5.64E-009 mm Hg (Modified Grain Method)
:  7.51E-007 Pa (Modified Grain Method)
Subcooled liquid VP:  8.1E-008 mm Hg (25 deg C, Mod-Grain method)
:  1.08E-005 Pa  (25 deg C, Mod-Grain method)

-------+-----+--------------------+----------+---------
TYPE   | NUM |  BOIL DESCRIPTION  |  COEFF   |  VALUE
-------+-----+--------------------+----------+---------
Group |  4  |  -CH3              |   21.98  |   87.92
Group |  1  |  >C<               |    4.50  |    4.50
Group |  1  |  -OH (phenol)      |   70.48  |   70.48
Group |  5  |  CH (aromatic)     |   28.53  |  142.65
Group |  4  |  -C (aromatic)     |   30.76  |  123.04
Group |  3  |  C (3a aromatic)   |   45.46  |  136.38
Group |  3  |  N (aromatic)      |   39.88  |  119.64
Group |  1  |  -Cl (to aromat)   |   36.79  |   36.79
*    |     |  Equation Constant |          |  198.18
=============+====================+==========+=========
RESULT-uncorr|  BOILING POINT in deg Kelvin  |  919.58
RESULT- corr |  BOILING POINT in deg Kelvin  |  723.27
|  BOILING POINT in deg C       |  450.11
-----------------------------------------------------

-------+-----+--------------------+----------+---------
```

```
TYPE  | NUM |  MELT DESCRIPTION  |  COEFF   |  VALUE
------+-----+--------------------+----------+---------
Group |  4  |  -CH3              |   -5.10  |  -20.40
Group |  1  |  >C<               |   46.43  |   46.43
Group |  1  |  -OH (phenol)      |   82.83  |   82.83
Group |  5  |  CH (aromatic)     |    8.13  |   40.65
Group |  4  |  -C (aromatic)     |   37.02  |  148.08
Group |  3  |  C (3a aromatic)   |   37.02  |  111.06
Group |  3  |  N (aromatic)      |   68.40  |  205.20
Group |  1  |  -Cl (to aromat)   |   13.55  |   13.55
*   |     |  Equation Constant |          |  122.50
============+====================+==========+=========
RESULT    |  MELTING POINT in deg Kelvin  |  749.90
RESULT-limit|  MELTING POINT in deg Kelvin  |  623.00
|  MELTING POINT in deg C       |  349.84
-----------------------------------------------------
```

```
Water Sol from Kow (WSKOW v1.42) Results:
=========================================

Water Sol: 0.5979 mg/L

SMILES : Oc(c(cc(c1)C)C(C)(C)C)c1n(nc(c2cc(c3)CL)c3)n2
CHEM   : Phenol, 2-(5-chloro-2H-benzotriazol-2-yl)-6-(1,1-dimethylethyl)-4-met
hyl-
MOL FOR: C17 H18 CL1 N3 O1
MOL WT : 315.81
---------------------------------- WSKOW v1.42 Results -----------------------
Log Kow  (estimated)  :  5.55
Log Kow (experimental):  not available from database
Log Kow used by Water solubility estimates:  5.55

Equation Used to Make Water Sol estimate:
Log S (mol/L) = 0.693-0.96 log Kow-0.0092(Tm-25)-0.00314 MW + Correction

Melting Pt (Tm) = 139.70 deg C (Use Tm = 25 for all liquids)

Correction(s):         Value
--------------------   -----
Phenol                0.961

Log Water Solubility  (in moles/L) :  -5.723
Water Solubility at 25 deg C (mg/L):  0.5979
```

```
WATERNT Program (v1.01) Results:
================================

Water Sol (v1.01 est): 15.021 mg/L

SMILES : Oc(c(cc(c1)C)C(C)(C)C)c1n(nc(c2cc(c3)CL)c3)n2
CHEM   : Phenol, 2-(5-chloro-2H-benzotriazol-2-yl)-6-(1,1-dimethylethyl)-4-met
hyl-
MOL FOR: C17 H18 CL1 N3 O1
```

```
MOL WT : 315.81
-------+-----+-----------------------------------------+----------+---------
TYPE   | NUM |    WATER SOLUBILITY FRAGMENT DESCRIPTION   |  COEFF   |  VALUE
-------+-----+-----------------------------------------+----------+---------
Frag   |  4  |  -CH3    [aliphatic carbon]               |-0.3213   | -1.2851
Frag   |  5  |  Aromatic Carbon  (C-H type)              |-0.3359   | -1.6793
Frag   |  1  |  -CL     [chlorine, aromatic attach]      |-0.4878   | -0.4878
Frag   |  1  |  -OH     [hydroxy, aromatic attach]       | 1.6578   |  1.6578
Frag   |  7  |  Aromatic Carbon  (C-substituent type)    |-0.5400   | -3.7797
Frag   |  3  |  Aromatic Nitrogen [5-member ring]        | 0.5265   |  1.5795
Frag   |  1  |  -tert Carbon  [3 or more carbon attach]  |-0.5774   | -0.5774
Const  |     |  Equation Constant                        |          |  0.2492
-------+-----+-----------------------------------------+----------+---------
Log Water Sol (moles/L) at 25 dec C  =   -4.3227
Water Solubility (mg/L) at 25 dec C  =   15.021



ECOSAR Program (v1.11) Results:
==============================
ECOSAR Version 1.11 Results Page

SMILES : Oc(c(cc(c1)C)C(C)(C)C)c1n(nc(c2cc(c3)CL)c3)n2
CHEM   : Phenol, 2-(5-chloro-2H-benzotriazol-2-yl)-6-(1,1-dimethylethyl)-4-met
hyl-
CAS Num:
ChemID1:
MOL FOR: C17 H18 CL1 N3 O1
MOL WT : 315.81
Log Kow: 5.552      (EPISuite Kowwin v1.68 Estimate)
Log Kow:            (User Entered)
Log Kow:            (PhysProp DB exp value - for comparison only)
Melt Pt: 139.70     (deg C, User Entered for Wat Sol estimate)
Melt Pt:            (deg C, PhysProp DB exp value for Wat Sol estimate)
Wat Sol: 0.5979     (mg/L, EPISuite WSKowwin v1.43 Estimate)
Wat Sol: 0.004      (mg/L, User Entered)
Wat Sol:            (PhysProp DB exp value)


--------------------------------------
Values used to Generate ECOSAR Profile
--------------------------------------
Log Kow: 5.552      (EPISuite Kowwin v1.68 Estimate)
Wat Sol: 0.004      (mg/L, User Entered)



--------------------------------------
ECOSAR v1.11 Class-specific Estimations
--------------------------------------
Benzotriazoles
Phenols
Predicted
ECOSAR Class                 Organism            Duration  End Pt   mg/L (ppm)
==========================  ==================  ========  ======   ==========
Benzotriazoles             : Fish                96-hr     LC50        0.384 *
Benzotriazoles             : Daphnid             48-hr     LC50        0.521 *
```

```
Benzotriazoles             : Green Algae         96-hr     EC50        0.209 *
Benzotriazoles             : Fish                          ChV         0.010 *
Benzotriazoles             : Daphnid                       ChV         0.017 *
Benzotriazoles             : Green Algae                   ChV         0.093 *

Phenols                    : Fish                96-hr     LC50        0.109 *
Phenols                    : Daphnid             48-hr     LC50        0.160 *
Phenols                    : Green Algae         96-hr     EC50        0.522 *
Phenols                    : Fish                          ChV         0.019 *
Phenols                    : Daphnid                       ChV         0.030 *
Phenols                    : Green Algae                   ChV         0.235 *
Phenols                    : Fish (SW)           96-hr     LC50        0.026 *
Phenols                    : Earthworm           14-day    LC50       10.352 *
Phenols                    : Lemna gibba         7-day     EC50        0.032 *

==========================  ==================  ========  ======   ==========
Neutral Organic SAR        : Fish                96-hr     LC50        0.167 *
(Baseline Toxicity)        : Daphnid             48-hr     LC50        0.132 *
: Green Algae         96-hr     EC50        0.382 *
: Fish                          ChV         0.024 *
: Daphnid                       ChV         0.032 *
: Green Algae                   ChV         0.207 *

Note:  * = asterisk designates: Chemical may not be soluble enough to
measure this predicted effect. If the effect level exceeds the
water solubility by 10X, typically no effects at saturation (NES)
are reported.


------------------------------
Class Specific LogKow Cut-Offs
------------------------------
If the log Kow of the chemical is greater than the endpoint specific cut-offs
presented below, then no effects at saturation are expected for those endpoints.

Benzotriazoles:
--------------
Maximum LogKow: 5.0 (LC50)
Maximum LogKow: 6.4 (EC50)
Maximum LogKow: 8.0 (ChV)

Phenols:
-------
Maximum LogKow: 7.0 (Fish 96-hr LC50, Daphnid LC50)
Maximum LogKow: 6.4 (Earthworm, Lemna)
Maximum LogKow: 7.0 (Green Algae EC50
Maximum LogKow: 8.0 (ChV)
Maximum LogKow: 5.0 (Fish (SW) 96-hr LC50, Mysid)

Baseline Toxicity SAR Limitations:
---------------------------------
Maximum LogKow: 5.0 (Fish 96-hr LC50; Daphnid LC50)
Maximum LogKow: 6.4 (Green Algae EC50)
Maximum LogKow: 8.0 (ChV)
```

```
HENRYWIN (v3.20) Program Results:
=============================

Bond Est :  1.17E-013 atm-m3/mole  (1.19E-008 Pa-m3/mole)
Group Est:  Incomplete

SMILES : Oc(c(cc(c1)C)C(C)(C)C)c1n(nc(c2cc(c3)CL)c3)n2
CHEM   : Phenol, 2-(5-chloro-2H-benzotriazol-2-yl)-6-(1,1-dimethylethyl)-4-met
hyl-
MOL FOR: C17 H18 CL1 N3 O1
MOL WT : 315.81
--------------------------- HENRYWIN v3.20 Results --------------------------
----------+-----------------------------------------+---------+----------
CLASS  |     BOND CONTRIBUTION DESCRIPTION           | COMMENT |  VALUE
----------+-----------------------------------------+---------+----------
HYDROGEN |  12  Hydrogen to Carbon (aliphatic) Bonds   |         | -1.4361
HYDROGEN |   5  Hydrogen to Carbon (aromatic) Bonds    |         | -0.7715
HYDROGEN |   1  Hydrogen to Oxygen Bonds               |         |  3.2318
FRAGMENT |   3  C-C                                    |         |  0.3489
FRAGMENT |   2  C-Car                                  |         |  0.3239
FRAGMENT |  12  Car-Car                                |         |  3.1657
FRAGMENT |   1  Car-CL                                 |         | -0.0241
FRAGMENT |   1  Car-OH                                 |         |  0.5967
FRAGMENT |   3  Car-Nar                                |         |  4.8847
FRAGMENT |   2  Nar-Nar                                | ESTIMATE|  6.0000
FACTOR   |   2  Additional aromatic nitrogen(s)        |         | -5.0000
----------+-----------------------------------------+---------+----------
RESULT   |    BOND ESTIMATION METHOD for LWAPC VALUE   |  TOTAL  | 11.320
----------+-----------------------------------------+---------+----------
HENRYs LAW CONSTANT at 25 deg C = 1.17E-013 atm-m3/mole
= 4.79E-012 unitless
= 1.19E-008 Pa-m3/mole

--------+-----------------------------------------------+------------+--------
|        GROUP CONTRIBUTION DESCRIPTION          |   COMMENT  |  VALUE
--------+-----------------------------------------------+------------+--------
|           2  Car (Nar)(Car)(Car)               |  ESTIMATE  | -0.20
|           4  CH3 (X)                           |            | -2.48
|           1  C (C)(C)(C)(Car)                  |            |  0.93
|           5  Car-H (Car)(Car)                  |            |  0.55
|           2  Car (C)(Car)(Car)                 |            |  1.40
|           1  Car (Car)(Car)(Car) external      |  ESTIMATE  |  0.33
|           1  Car (Car)(Car)(CL)                |            |  0.18
|           1  Car (Car)(Car)(O)                 |            | -0.43
|           1  O-H (Car)                         |            |  4.45
|              MISSING Value for:  Nar (Nar)(Nar)(??)
|              MISSING Value for:  Nar (Car)(Nar)
|              MISSING Value for:  Nar (Car)(Nar)
--------+-----------------------------------------------+------------+--------
RESULT |  GROUP ESTIMATION METHOD for LOG GAMMA VALUE  | INCOMPLETE |  4.73
--------+-----------------------------------------------+------------+--------


For Henry LC Comparison Purposes:
Exper Database:  none available
```

```
User-Entered Henry LC:  not entered
Henrys LC [via VP/WSol estimate using User-Entered or Estimated values]:
HLC:  5.859E-007 atm-m3/mole  (5.937E-002 Pa-m3/mole)
VP:   5.64E-009 mm Hg (source: MPBPVP)
WS:   0.004 mg/L (source: User-Entered)



Log Octanol-Air (KOAWIN v1.10) Results:
=======================================

Log Koa: 16.870

SMILES : Oc(c(cc(c1)C)C(C)(C)C)c1n(nc(c2cc(c3)CL)c3)n2
CHEM   : Phenol, 2-(5-chloro-2H-benzotriazol-2-yl)-6-(1,1-dimethylethyl)-4-met
hyl-
MOL FOR: C17 H18 CL1 N3 O1
MOL WT : 315.81
--------------------------- KOAWIN v1.10 Results --------------------------

Log Koa (octanol/air) estimate:  16.870
Koa (octanol/air) estimate:  7.418e+016
Using:
Log Kow:  5.55  (KowWin est)
HenryLC:  1.17e-013  atm-m3/mole (HenryWin est)
Log Kaw:  -11.320  (air/water part.coef.)

LogKow  : ----  (exp database)
LogKow  : 5.55 (KowWin estimate)
Henry LC: --- atm-m3/mole(exp database)
Henry LC: 1.17e-013 atm-m3/mole (HenryWin bond estimate)

Log Koa (octanol/air) estimate:  16.870 (from KowWin/HenryWin)



BIOWIN (v4.10) Program Results:
==============================
SMILES : Oc(c(cc(c1)C)C(C)(C)C)c1n(nc(c2cc(c3)CL)c3)n2
CHEM   : Phenol, 2-(5-chloro-2H-benzotriazol-2-yl)-6-(1,1-dimethylethyl)-4-met
hyl-
MOL FOR: C17 H18 CL1 N3 O1
MOL WT : 315.81
--------------------------- BIOWIN v4.10 Results ---------------------------

Biowin1 (Linear Model Prediction)    :  Does Not Biodegrade Fast
Biowin2 (Non-Linear Model Prediction):  Does Not Biodegrade Fast
Biowin3 (Ultimate Biodegradation Timeframe):  Months
Biowin4 (Primary  Biodegradation Timeframe):  Weeks
Biowin5 (MITI Linear Model Prediction)    :  Does Not Biodegrade Fast
Biowin6 (MITI Non-Linear Model Prediction):  Does Not Biodegrade Fast
Biowin7 (Anaerobic Model Prediction):  Does Not Biodegrade Fast
Ready Biodegradability Prediction:  NO

------+-----+-----------------------------------------+---------+---------
TYPE | NUM |       Biowin1 FRAGMENT DESCRIPTION         |  COEFF  |  VALUE
------+-----+-----------------------------------------+---------+---------
```

Frag	1	Aromatic alcohol [-OH]	0.1158	0.1158
Frag	1	Aromatic chloride [-CL]	-0.1824	-0.1824
Frag	1	Carbon with 4 single bonds & no hydrogens	-0.1839	-0.1839
Frag	1	Alkyl substituent on aromatic ring	0.0547	0.0547
MolWt	*	Molecular Weight Parameter		-0.1503
Const	*	Equation Constant		0.7475
RESULT		Biowin1 (Linear Biodeg Probability)		0.4013

TYPE	NUM	Biowin2 FRAGMENT DESCRIPTION	COEFF	VALUE
Frag	1	Aromatic alcohol [-OH]	0.9086	0.9086
Frag	1	Aromatic chloride [-CL]	-2.0155	-2.0155
Frag	1	Carbon with 4 single bonds & no hydrogens	-1.7232	-1.7232
Frag	1	Alkyl substituent on aromatic ring	0.5771	0.5771
MolWt	*	Molecular Weight Parameter		-4.4844
RESULT		Biowin2 (Non-Linear Biodeg Probability)		0.0235

A Probability Greater Than or Equal to 0.5 indicates --> Biodegrades Fast
A Probability Less Than 0.5 indicates --> Does NOT Biodegrade Fast

TYPE	NUM	Biowin3 FRAGMENT DESCRIPTION	COEFF	VALUE
Frag	1	Aromatic alcohol [-OH]	0.0564	0.0564
Frag	1	Aromatic chloride [-CL]	-0.2066	-0.2066
Frag	1	Carbon with 4 single bonds & no hydrogens	-0.2121	-0.2121
Frag	1	Alkyl substituent on aromatic ring	-0.0749	-0.0749
MolWt	*	Molecular Weight Parameter		-0.6979
Const	*	Equation Constant		3.1992
RESULT		Biowin3 (Survey Model - Ultimate Biodeg)		2.0641

TYPE	NUM	Biowin4 FRAGMENT DESCRIPTION	COEFF	VALUE
Frag	1	Aromatic alcohol [-OH]	0.0397	0.0397
Frag	1	Aromatic chloride [-CL]	-0.1653	-0.1653
Frag	1	Carbon with 4 single bonds & no hydrogens	-0.1534	-0.1534
Frag	1	Alkyl substituent on aromatic ring	-0.0685	-0.0685
MolWt	*	Molecular Weight Parameter		-0.4556
Const	*	Equation Constant		3.8477
RESULT		Biowin4 (Survey Model - Primary Biodeg)		3.0445

Result Classification: 5.00 -> hours 4.00 -> days 3.00 -> weeks
(Primary & Ultimate) 2.00 -> months 1.00 -> longer

TYPE	NUM	Biowin5 FRAGMENT DESCRIPTION	COEFF	VALUE

```
Frag |  1  |  Aromatic alcohol  [-OH]                    |  0.0642 |  0.0642
Frag |  1  |  Aromatic chloride   [-CL]                  |  0.0062 |  0.0062
Frag |  1  |  Carbon with 4 single bonds & no hydrogens  |  0.0676 |  0.0676
Frag |  1  |  Aromatic-CH3                               |  0.0415 |  0.0415
Frag |  5  |  Aromatic-H                                 |  0.0082 |  0.0411
Frag |  3  |  Methyl  [-CH3]                             |  0.0004 |  0.0012
MolWt|  *  |  Molecular Weight Parameter                 |         | -0.9395
Const|  *  |  Equation Constant                          |         |  0.7121
============+=============================================+=========+=========
RESULT   |  Biowin5 (MITI Linear Biodeg Probability)  |         | -0.0056
============+=============================================+=========+=========

------+-----+---------------------------------------------+---------+---------
TYPE | NUM |       Biowin6 FRAGMENT DESCRIPTION          |  COEFF  |  VALUE
------+-----+---------------------------------------------+---------+---------
Frag |  1  |  Aromatic alcohol  [-OH]                    |  0.4884 |  0.4884
Frag |  1  |  Aromatic chloride   [-CL]                  | -0.2191 | -0.2191
Frag |  1  |  Carbon with 4 single bonds & no hydrogens  |  0.3990 |  0.3990
Frag |  1  |  Aromatic-CH3                               |  0.3072 |  0.3072
Frag |  5  |  Aromatic-H                                 |  0.1201 |  0.6007
Frag |  3  |  Methyl  [-CH3]                             |  0.0194 |  0.0583
MolWt|  *  |  Molecular Weight Parameter                 |         | -9.1169
============+=============================================+=========+=========
RESULT   |Biowin6 (MITI Non-Linear Biodeg Probability)|         |  0.0070
============+=============================================+=========+=========

A Probability Greater Than or Equal to 0.5 indicates --> Readily Degradable
A Probability Less Than 0.5 indicates --> NOT Readily Degradable


------+-----+---------------------------------------------+---------+---------
TYPE | NUM |       Biowin7 FRAGMENT DESCRIPTION          |  COEFF  |  VALUE
------+-----+---------------------------------------------+---------+---------
Frag |  1  |  Aromatic alcohol  [-OH]                    |  0.0807 |  0.0807
Frag |  1  |  Aromatic chloride   [-CL]                  | -0.4023 | -0.4023
Frag |  1  |  Carbon with 4 single bonds & no hydrogens  | -0.3342 | -0.3342
Frag |  1  |  Alkyl substituent on aromatic ring         | -0.1145 | -0.1145
Frag |  1  |  Aromatic-CH3                               | -0.2573 | -0.2573
Frag |  5  |  Aromatic-H                                 | -0.0954 | -0.4772
Frag |  3  |  Methyl  [-CH3]                             | -0.0796 | -0.2387
Const|  *  |  Equation Constant                          |         |  0.8361
============+=============================================+=========+=========
RESULT   |   Biowin7 (Anaerobic Linear Biodeg Prob)   |         | -0.9073
============+=============================================+=========+=========

A Probability Greater Than or Equal to 0.5 indicates --> Biodegrades Fast
A Probability Less Than 0.5 indicates --> Does NOT Biodegrade Fast

Ready Biodegradability Prediction: (YES or NO)
----------------------------------------------
Criteria for the YES or NO prediction:  If the Biowin3 (ultimate survey
model) result is "weeks" or faster (i.e. "days", "days to weeks", or
"weeks" AND the Biowin5 (MITI linear model) probability is >= 0.5, then
the prediction is YES (readily biodegradable).  If this condition is not
satisfied, the prediction is NO (not readily biodegradable).  This method
is based on application of Bayesian analysis to ready biodegradation data
(see Help).  Biowin5 and 6 also predict ready biodegradability, but for
```

```
degradation in the OECD301C test only; using data from the Chemicals
Evaluation and Research Institute Japan (CERIJ) database.



BioHCwin (v1.01) Program Results:
=================================
SMILES : Oc(c(cc(c1)C)C(C)(C)C)c1n(nc(c2cc(c3)CL)c3)n2
CHEM   : Phenol, 2-(5-chloro-2H-benzotriazol-2-yl)-6-(1,1-dimethylethyl)-4-met
hyl-
MOL FOR: C17 H18 CL1 N3 O1
MOL WT : 315.81
-------------------------- BioHCwin v1.01 Results --------------------------

NO Estimate Possible ... Structure NOT a Hydrocarbon
(Contains atoms other than C, H or S (-S-))



AEROWIN Program (v1.00) Results:
================================
Sorption to aerosols (25 Dec C)[AEROWIN v1.00]:
Vapor pressure (liquid/subcooled):  1.08E-005 Pa (8.1E-008 mm Hg)
Log Koa (Koawin est  ): 16.870
Kp (particle/gas partition coef. (m3/ug)):
Mackay model           :  0.278
Octanol/air (Koa) model:  1.82E+004
Fraction sorbed to airborne particulates (phi):
Junge-Pankow model     :  0.909
Mackay model           :  0.957
Octanol/air (Koa) model:  1


AOP Program (v1.92) Results:
============================
SMILES : Oc(c(cc(c1)C)C(C)(C)C)c1n(nc(c2cc(c3)CL)c3)n2
CHEM   : Phenol, 2-(5-chloro-2H-benzotriazol-2-yl)-6-(1,1-dimethylethyl)-4-met
hyl-
MOL FOR: C17 H18 CL1 N3 O1
MOL WT : 315.81
------------------- SUMMARY (AOP v1.92): HYDROXYL RADICALS (25 deg C) --------
Hydrogen Abstraction       =   0.6378 E-12 cm3/molecule-sec
Reaction with N, S and -OH =   0.1400 E-12 cm3/molecule-sec
Addition to Triple Bonds   =   0.0000 E-12 cm3/molecule-sec
Addition to Olefinic Bonds =   0.0000 E-12 cm3/molecule-sec
**Addition to Aromatic Rings =  13.4122 E-12 cm3/molecule-sec
**Addition to Fused Rings    =   0.7035 E-12 cm3/molecule-sec

OVERALL OH Rate Constant =  14.8935 E-12 cm3/molecule-sec
HALF-LIFE =     0.718 Days (12-hr day; 1.5E6 OH/cm3)
HALF-LIFE =     8.618 Hrs
.......................  ** Designates Estimation(s) Using ASSUMED Value(s)
------------------- SUMMARY (AOP v1.91): OZONE REACTION (25 deg C) -----------

******  NO OZONE REACTION ESTIMATION ******
(ONLY Olefins and Acetylenes are Estimated)
```

```
NOTE: Reaction with Nitrate Radicals May Be Important!

Experimental Database:  NO Structure Matches
Fraction sorbed to airborne particulates (phi):
0.933 (Junge-Pankow, Mackay avg)
1 (Koa method)
Note: the sorbed fraction may be resistant to atmospheric oxidation



KOCWIN Program (v2.00) Results:
==============================
SMILES : Oc(c(cc(c1)C)C(C)(C)C)c1n(nc(c2cc(c3)CL)c3)n2
CHEM   : Phenol, 2-(5-chloro-2H-benzotriazol-2-yl)-6-(1,1-dimethylethyl)-4-met
hyl-
MOL FOR: C17 H18 CL1 N3 O1
MOL WT : 315.81
---------------------------  KOCWIN v2.00 Results  ---------------------------

Koc Estimate from MCI:
----------------------
First Order Molecular Connectivity Index  ..........  : 10.253
Non-Corrected Log Koc (0.5213 MCI + 0.60)  ..........  :  5.9447
Fragment Correction(s):
*   Multi-Nitrogen aromatic ..............  : -1.2044
1   Aromatic Hydroxy (aromatic-OH)  .......  : -0.0966
Corrected Log Koc  ................................. :  4.6437

Estimated Koc:  4.402e+004  L/kg   <===========

Koc Estimate from Log Kow:
--------------------------
Log Kow  (Kowwin estimate)  ........................ :  5.55
Non-Corrected Log Koc (0.55313 logKow + 0.9251)  .... :  3.9950
Fragment Correction(s):
*   Multi-Nitrogen aromatic ..............  :  0.0729
1   Aromatic Hydroxy (aromatic-OH)  .......  :  0.1668
Corrected Log Koc  ................................. :  4.2347

Estimated Koc:  1.717e+004  L/kg   <===========



HYDROWIN Program (v2.00) Results:
================================
SMILES : Oc(c(cc(c1)C)C(C)(C)C)c1n(nc(c2cc(c3)CL)c3)n2
CHEM   : Phenol, 2-(5-chloro-2H-benzotriazol-2-yl)-6-(1,1-dimethylethyl)-4-met
hyl-
MOL FOR: C17 H18 CL1 N3 O1
MOL WT : 315.81
--------------------------- HYDROWIN v2.00 Results ---------------------------


Currently, this program can NOT estimate a hydrolysis rate constant for
```

```
the type of chemical structure entered!!

ONLY Esters, Carbamates, Epoxides, Halomethanes (containing 1-3 halogens),
Specific Alkyl Halides & Phosphorus Esters can be estimated!!

When present, various hydrolyzable compound-types will be identified.
For more information, (Click OVERVIEW in Help  or  see the User's Guide)

*****   CALCULATION NOT PERFORMED   *****



BCFBAF Program (v3.01) Results:
==============================
SMILES : Oc(c(cc(c1)C)C(C)(C)C)c1n(nc(c2cc(c3)CL)c3)n2
CHEM   : Phenol, 2-(5-chloro-2H-benzotriazol-2-yl)-6-(1,1-dimethylethyl)-4-met
hyl-
MOL FOR: C17 H18 CL1 N3 O1
MOL WT : 315.81
--------------------------------- BCFBAF v3.01 ---------------------------------
Summary Results:
Log BCF (regression-based estimate):  3.11  (BCF = 1.28e+003 L/kg wet-wt)
Biotransformation Half-Life (days) :  2.76  (normalized to 10 g fish)
Log BAF (Arnot-Gobas upper trophic):  3.07  (BAF = 1.17e+003 L/kg wet-wt)

Log Kow (experimental):  not available from database
Log Kow used by BCF estimates:  5.55

Equation Used to Make BCF estimate:
Log BCF = 0.6598 log Kow - 0.333 + Correction

Correction(s):                    Value
Tert-Butyl ortho-phenol type    -0.222

Estimated Log BCF =  3.108  (BCF = 1283 L/kg wet-wt)

============================================================
Whole Body Primary Biotransformation Rate Estimate for Fish:
============================================================
------+-----+-------------------------------------------+---------+---------
TYPE | NUM | LOG BIOTRANSFORMATION FRAGMENT DESCRIPTION |  COEFF  |  VALUE
------+-----+-------------------------------------------+---------+---------
Frag |  1  |  Aromatic alcohol  [-OH]                  | -0.4727 | -0.4727
Frag |  1  |  Aromatic chloride   [-CL]                |  0.3778 |  0.3778
Frag |  1  |  Carbon with 4 single bonds & no hydrogens | -0.2984 | -0.2984
Frag |  1  |  Alkyl substituent on aromatic ring       |  0.1781 |  0.1781
Frag |  1  |  Triazole Ring                            |  0.3225 |  0.3225
Frag |  1  |  Aromatic-CH3                             | -0.0872 | -0.0872
Frag |  5  |  Aromatic-H                               |  0.2664 |  1.3319
Frag |  3  |  Methyl  [-CH3]                           |  0.2451 |  0.7353
Frag |  1  |  Number of fused 6-carbon aromatic rings  | -0.5779 | -0.5779
Frag |  1  |  Number of fused 5-carbon aromatic rings  |  0.0000 |  0.0000
Frag |  1  |  Benzene                                  | -0.4277 | -0.4277
L Kow|  *  |  Log Kow =   5.55 (KowWin estimate)       |  0.3073 |  1.7064
MolWt|  *  |  Molecular Weight Parameter               |         | -0.8098
Const|  *  |  Equation Constant                        |         | -1.5371
============+===========================================+=========+=========
```

```
RESULT   |        LOG Bio Half-Life (days)            |         |  0.4412
RESULT   |            Bio Half-Life (days)            |         |   2.762
NOTE     |  Bio Half-Life Normalized to 10 g fish at 15 deg C   |
===========+============================================+=========+=========

Biotransformation Rate Constant:
kM (Rate Constant):  0.251 /day (10 gram fish)
kM (Rate Constant):  0.1411 /day (100 gram fish)
kM (Rate Constant):  0.07936 /day (1 kg fish)
kM (Rate Constant):  0.04463 /day (10 kg fish)

Arnot-Gobas BCF & BAF Methods (including biotransformation rate estimates):
Estimated Log BCF (upper trophic) =  3.013  (BCF = 1030 L/kg wet-wt)
Estimated Log BAF (upper trophic) =  3.067  (BAF = 1168 L/kg wet-wt)
Estimated Log BCF (mid trophic)   =  3.139  (BCF = 1377 L/kg wet-wt)
Estimated Log BAF (mid trophic)   =  3.352  (BAF = 2247 L/kg wet-wt)
Estimated Log BCF (lower trophic) =  3.175  (BCF = 1496 L/kg wet-wt)
Estimated Log BAF (lower trophic) =  3.599  (BAF = 3971 L/kg wet-wt)

Arnot-Gobas BCF & BAF Methods (assuming a biotransformation rate of zero):
Estimated Log BCF (upper trophic) =  4.214  (BCF = 1.635e+004 L/kg wet-wt)
Estimated Log BAF (upper trophic) =  5.875  (BAF = 7.506e+005 L/kg wet-wt)




Volatilization From Water
=========================

Chemical Name: Phenol, 2-(5-chloro-2H-benzotriazol-2-yl)-6-(1,1-dimethylethyl)-4-
methyl-

Molecular Weight    :  315.81 g/mole
Water Solubility    :  0.004 ppm
Vapor Pressure      :  -----
Henry's Law Constant:  1.17E-013 atm-m3/mole  (estimated by Bond SAR Method)

RIVER             LAKE
---------         ---------
Water Depth     (meters):   1                1
Wind Velocity    (m/sec):   5                0.5
Current Velocity (m/sec):   1                0.05

HALF-LIFE (hours) :   8.893E+009        9.701E+010
HALF-LIFE (days ) :   3.705E+008        4.042E+009
HALF-LIFE (years) :   1.014E+006        1.107E+007


STP Fugacity Model:  Predicted Fate in a Wastewater Treatment Facility
======================================================================
(using 10000 hr Bio P,A,S)
PROPERTIES OF: Phenol, 2-(5-chloro-2H-benzotriazol-2-yl)-6-(1,1-dimethylethyl)-4-
methyl-
-------------
Molecular weight (g/mol)                              315.81
Aqueous solubility (mg/l)                             0.004
```

```
Vapour pressure (Pa)                                    0
(atm)                                  0
(mm Hg)                                0
Henry 's law constant (Atm-m3/mol)                      1.17E-013
Air-water partition coefficient                         4.78495E-012
Octanol-water partition coefficient (Kow)               354814
Log Kow                                                 5.55
Biomass to water partition coefficient                  70963.5
Temperature [deg C]                                     25
Biodeg rate constants (h^-1),half life in biomass (h) and in 2000 mg/L MLSS (h):
-Primary tank        0.00      9930.03       10000.00
-Aeration tank       0.00      9930.03       10000.00
-Settling tank       0.00      9930.03       10000.00

STP Overall Chemical Mass Balance:
---------------------------------
g/h               mol/h          percent

Influent                    1.00E+001         3.2E-002        100.00

Primary sludge              5.60E+000         1.8E-002        55.97
Waste sludge                3.22E+000         1.0E-002        32.16
Primary volatilization      4.19E-012         1.3E-014         0.00
Settling volatilization     9.54E-012         3.0E-014         0.00
Aeration off gas            2.35E-011         7.4E-014         0.00

Primary biodegradation      1.65E-002         5.2E-005         0.16
Settling biodegradation     4.12E-003         1.3E-005         0.04
Aeration biodegradation     5.43E-002         1.7E-004         0.54

Final water effluent        1.11E+000         3.5E-003        11.12

Total removal               8.89E+000         2.8E-002        88.88
Total biodegradation        7.49E-002         2.4E-004         0.75


Level III Fugacity Model (Full-Output):
=======================================
Chem Name   : Phenol, 2-(5-chloro-2H-benzotriazol-2-yl)-6-(1,1-dimethylethyl)-4-
methyl-
Molecular Wt: 315.81
Henry's LC  : 1.17e-013 atm-m3/mole (Henrywin program)
Vapor Press : 5.64e-009 mm Hg  (Mpbpwin program)
Liquid VP   : 7.69e-008 mm Hg  (super-cooled)
Melting Pt  : 140 deg C (user-entered)
Log Kow     : 5.55  (Kowwin program)
Soil Koc    : 4.4e+004  (KOCWIN MCI method)

Mass Amount    Half-Life    Emissions
(percent)        (hr)       (kg/hr)
Air       5.74e-006       17.2         1000
Water     6.05            1.44e+003    1000
Soil      74.4            2.88e+003    1000
Sediment  19.5            1.3e+004     0

Fugacity    Reaction    Advection   Reaction    Advection
(atm)       (kg/hr)      (kg/hr)    (percent)   (percent)
```

```
Air       3.7e-017     0.0245      0.00609     0.000816    0.000203
Water     1.1e-018     309         642         10.3        21.4
Soil      1.54e-019    1.9e+003    0           63.2        0
Sediment  1.81e-018    111         41.4        3.69        1.38

Persistence Time: 3.53e+003 hr
Reaction Time:    4.57e+003 hr
Advection Time:   1.55e+004 hr
Percent Reacted:  77.2
Percent Advected: 22.8

Half-Lives (hr), (based upon Biowin (Ultimate) and Aopwin):
Air:      17.24
Water:    1440
Soil:     2880
Sediment: 1.296e+004
Biowin estimate: 2.064  (months      )

Advection Times (hr):
Air:      100
Water:    1000
Sediment: 5e+004


Level III Fugacity Model (Full-Output):
=======================================
Chem Name   : Phenol, 2-(5-chloro-2H-benzotriazol-2-yl)-6-(1,1-dimethylethyl)-4-
methyl-
Molecular Wt: 315.81
Henry's LC  : 1.17e-013 atm-m3/mole (Henrywin program)
Vapor Press : 5.64e-009 mm Hg  (Mpbpwin program)
Liquid VP   : 7.69e-008 mm Hg  (super-cooled)
Melting Pt  : 140 deg C (user-entered)
Log Kow     : 5.55  (Kowwin program)
Soil Koc    : 4.4e+004  (KOCWIN MCI method)

Mass Amount    Half-Life    Emissions
(percent)        (hr)       (kg/hr)
Air       1.53e-005       17.2         1000
Water     1.48            1.44e+003    0
Soil      93.7            2.88e+003    0
Sediment  4.77            1.3e+004     0

Fugacity    Reaction    Advection   Reaction    Advection
(atm)       (kg/hr)      (kg/hr)    (percent)   (percent)
Air       3.7e-017     0.0245      0.00609     0.00245     0.000609
Water     1.01e-019    28.4        58.9        2.84        5.89
Soil      7.27e-020    899         0           89.9        0
Sediment  1.67e-019    10.2        3.8         1.02        0.38

Persistence Time: 3.98e+003 hr
Reaction Time:    4.25e+003 hr
Advection Time:   6.35e+004 hr
Percent Reacted:  93.7
Percent Advected: 6.27

Half-Lives (hr), (based upon Biowin (Ultimate) and Aopwin):
```

```
Air:      17.24
Water:    1440
Soil:     2880
Sediment: 1.296e+004
Biowin estimate: 2.064  (months      )

Advection Times (hr):
Air:      100
Water:    1000
Sediment: 5e+004


Level III Fugacity Model (Full-Output):
=======================================
Chem Name   : Phenol, 2-(5-chloro-2H-benzotriazol-2-yl)-6-(1,1-dimethylethyl)-4-
methyl-
Molecular Wt: 315.81
Henry's LC  : 1.17e-013 atm-m3/mole (Henrywin program)
Vapor Press : 5.64e-009 mm Hg  (Mpbpwin program)
Liquid VP   : 7.69e-008 mm Hg  (super-cooled)
Melting Pt  : 140 deg C (user-entered)
Log Kow     : 5.55  (Kowwin program)
Soil Koc    : 4.4e+004  (KOCWIN MCI method)

Mass Amount    Half-Life    Emissions
(percent)        (hr)       (kg/hr)
Air       1.59e-014       17.2         0
Water     23.7            1.44e+003    1000
Soil      9.76e-008       2.88e+003    0
Sediment  76.3            1.3e+004     0

Fugacity    Reaction    Advection   Reaction    Advection
(atm)       (kg/hr)      (kg/hr)    (percent)   (percent)
Air       2.38e-026    1.57e-011   3.91e-012   1.57e-012   3.91e-013
Water     9.95e-019    280         582         28          58.2
Soil      4.68e-029    5.78e-007   0           5.78e-008   0
Sediment  1.65e-018    100         37.6        10          3.76

Persistence Time: 2.46e+003 hr
Reaction Time:    6.47e+003 hr
Advection Time:   3.97e+003 hr
Percent Reacted:  38
Percent Advected: 62

Half-Lives (hr), (based upon Biowin (Ultimate) and Aopwin):
Air:      17.24
Water:    1440
Soil:     2880
Sediment: 1.296e+004
Biowin estimate: 2.064  (months      )

Advection Times (hr):
Air:      100
Water:    1000
Sediment: 5e+004
```

```
Level III Fugacity Model (Full-Output):
=======================================
Chem Name   : Phenol, 2-(5-chloro-2H-benzotriazol-2-yl)-6-(1,1-dimethylethyl)-4-
methyl-
Molecular Wt: 315.81
Henry's LC  : 1.17e-013 atm-m3/mole (Henrywin program)
Vapor Press : 5.64e-009 mm Hg  (Mpbpwin program)
Liquid VP   : 7.69e-008 mm Hg  (super-cooled)
Melting Pt  : 140 deg C (user-entered)
Log Kow     : 5.55  (Kowwin program)
Soil Koc    : 4.4e+004  (KOCWIN MCI method)

Mass Amount    Half-Life    Emissions
(percent)        (hr)       (kg/hr)
Air       6.9e-015        17.2         0
Water     0.0196          1.44e+003    0
Soil      99.9            2.88e+003    1000
Sediment  0.0632          1.3e+004     0

Fugacity    Reaction    Advection   Reaction    Advection
(atm)       (kg/hr)      (kg/hr)    (percent)   (percent)
Air       1.75e-026    1.15e-011   2.87e-012   1.15e-012   2.87e-013
Water     1.39e-021    0.391       0.813       0.0391      0.0813
Soil      8.08e-020    999         0           99.9        0
Sediment  2.3e-021     0.14        0.0525      0.014       0.00525

Persistence Time: 4.15e+003 hr
Reaction Time:    4.16e+003 hr
Advection Time:   4.8e+006 hr
Percent Reacted:  99.9
Percent Advected: 0.0865

Half-Lives (hr), (based upon Biowin (Ultimate) and Aopwin):
Air:      17.24
Water:    1440
Soil:     2880
Sediment: 1.296e+004
Biowin estimate: 2.064  (months      )

Advection Times (hr):
Air:      100
Water:    1000
Sediment: 5e+004


Level III Fugacity Model (Full-Output):
=======================================
Chem Name   : Phenol, 2-(5-chloro-2H-benzotriazol-2-yl)-6-(1,1-dimethylethyl)-4-
methyl-
Molecular Wt: 315.81
Henry's LC  : 1.17e-013 atm-m3/mole (Henrywin program)
Vapor Press : 5.64e-009 mm Hg  (Mpbpwin program)
Liquid VP   : 7.69e-008 mm Hg  (super-cooled)
Melting Pt  : 140 deg C (user-entered)
Log Kow     : 5.55  (Kowwin program)
Soil Koc    : 4.4e+004  (KOCWIN MCI method)
```

```
Mass Amount    Half-Life    Emissions
(percent)        (hr)       (kg/hr)
Air       9.45e-006       17.2         1000
Water     9.94            1.44e+003    1000
Soil      58              2.88e+003    0
Sediment  32.1            1.3e+004     0

Fugacity    Reaction    Advection   Reaction    Advection
(atm)      (kg/hr)      (kg/hr)    (percent)   (percent)
Air       3.7e-017     0.0245      0.00609     0.00122     0.000304
Water     1.1e-018     308         641         15.4        32
Soil      7.27e-020    899         0           44.9        0
Sediment  1.81e-018    111         41.4        5.53        2.07

Persistence Time: 3.22e+003 hr
Reaction Time:    4.89e+003 hr
Advection Time:   9.45e+003 hr
Percent Reacted:  65.9
Percent Advected: 34.1

Half-Lives (hr), (based upon Biowin (Ultimate) and Aopwin):
Air:      17.24
Water:    1440
Soil:     2880
Sediment: 1.296e+004
Biowin estimate: 2.064  (months      )

Advection Times (hr):
Air:      100
Water:    1000
Sediment: 5e+004


Level III Fugacity Model (Full-Output):
=======================================
Chem Name   : Phenol, 2-(5-chloro-2H-benzotriazol-2-yl)-6-(1,1-dimethylethyl)-4-
methyl-
Molecular Wt: 315.81
Henry's LC  : 1.17e-013 atm-m3/mole (Henrywin program)
Vapor Press : 5.64e-009 mm Hg  (Mpbpwin program)
Liquid VP   : 7.69e-008 mm Hg  (super-cooled)
Melting Pt  : 140 deg C (user-entered)
Log Kow     : 5.55  (Kowwin program)
Soil Koc    : 4.4e+004  (KOCWIN MCI method)

Mass Amount    Half-Life    Emissions
(percent)        (hr)       (kg/hr)
Air       7.48e-006       17.2         1000
Water     0.734           1.44e+003    0
Soil      96.9            2.88e+003    1000
Sediment  2.37            1.3e+004     0

Fugacity    Reaction    Advection   Reaction    Advection
(atm)      (kg/hr)      (kg/hr)    (percent)   (percent)
Air       3.7e-017     0.0245      0.00609     0.00122     0.000304
Water     1.02e-019    28.7        59.7        1.44        2.99
Soil      1.54e-019    1.9e+003    0           94.9        0
```

```
Sediment  1.69e-019    10.3        3.86        0.515       0.193

Persistence Time: 4.07e+003 hr
Reaction Time:    4.2e+003 hr
Advection Time:   1.28e+005 hr
Percent Reacted:  96.8
Percent Advected: 3.18

Half-Lives (hr), (based upon Biowin (Ultimate) and Aopwin):
Air:      17.24
Water:    1440
Soil:     2880
Sediment: 1.296e+004
Biowin estimate: 2.064  (months      )

Advection Times (hr):
Air:      100
Water:    1000
Sediment: 5e+004


Level III Fugacity Model (Full-Output):
=======================================
Chem Name   : Phenol, 2-(5-chloro-2H-benzotriazol-2-yl)-6-(1,1-dimethylethyl)-4-
methyl-
Molecular Wt: 315.81
Henry's LC  : 1.17e-013 atm-m3/mole (Henrywin program)
Vapor Press : 5.64e-009 mm Hg  (Mpbpwin program)
Liquid VP   : 7.69e-008 mm Hg  (super-cooled)
Melting Pt  : 140 deg C (user-entered)
Log Kow     : 5.55  (Kowwin program)
Soil Koc    : 4.4e+004  (KOCWIN MCI method)

Mass Amount    Half-Life    Emissions
(percent)        (hr)       (kg/hr)
Air       1.03e-014       17.2         0
Water     8.81            1.44e+003    1000
Soil      62.8            2.88e+003    1000
Sediment  28.4            1.3e+004     0

Fugacity    Reaction    Advection   Reaction    Advection
(atm)       (kg/hr)      (kg/hr)    (percent)   (percent)
Air       4.13e-026    2.73e-011   6.78e-012   1.36e-012   3.39e-013
Water     9.96e-019    280         583         14          29.1
Soil      8.08e-020    999         0           49.9        0
Sediment  1.65e-018    101         37.6        5.03        1.88

Persistence Time: 3.31e+003 hr
Reaction Time:    4.79e+003 hr
Advection Time:   1.07e+004 hr
Percent Reacted:  69
Percent Advected: 31

Half-Lives (hr), (based upon Biowin (Ultimate) and Aopwin):
Air:      17.24
Water:    1440
Soil:     2880
```

```
Sediment: 1.296e+004
Biowin estimate: 2.064  (months      )

Advection Times (hr):
Air:      100
Water:    1000
Sediment: 5e+004


....
```