# GreenScreen™ Assessment for for Zinc Borate
# CAS#1332-07-6

**GreenScreen™ Version 1.2 Draft Assessment**
**Note: Validation Has Not Been Performed on *this* Green Screen Assessment**

**Chemical Name: Zinc Borate**

**GreenScreen Assessment Prepared By:**

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Organization: NSF International
Date: December 7th, 2011

**Quality Control Performed By:**

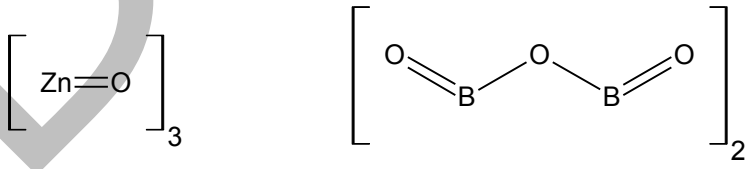
Name: NA
Title: NA
Organization: NA
Date: NA

**Confirm application of the *de minimus* rule[1]: Yes** (if no, what *de minimus* did you use?)

**Chemical Name (CAS #): Zinc Borate (CAS# 1332-07-6)**

**Also Called:**
Alcanex FR 100; Alcanex FRC 600; Bonrex FC; Borax 2335; Climax ZB 467; EINECS 215-566-6; EPA Pesticide Chemical Code 128859; FRC 600; Flamtard Z 10; HSDB 1046; JS 9502; SZB 2335; XPI 187; ZB 112; ZB 237; ZB 467 Lite; ZN 100; ZSB 2335; ZT (fire retardant); Boric acid, zinc salt; Firebrake® ZB

**Chemical Structure(s):** A number of different empirical formulas exist for zinc borate: $4ZnO.6B_2O_3.7H_2O$ or $2ZnO.2B_2O_3.3H_2O$(CEFIC-EFRA, 2006), $3ZnO.2H_3BO_3.3.5H_2O$ (MW= 430) (EPA, 2007), $Zn^{2+}.2H_2BO_3^-$ (MW = 187), and $3ZnO.2B_2O_3$ (MW = 383.5) (Lide, 1983) for the purposes of this review, $3ZnO.2B_2O_3$ will be used to convert from mole equivalents of boric acid or zinc salts to zinc borate.




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

1. Particle size (e.g. silica of respirable size) – 8-20 µm (mean) (for $2ZnO.3B_2O_3.3.5H_2O$; EPA, 1991).
2. Structure (e.g. amorphous vs. crystalline) – white and granular (for $2ZnO.3B_2O_3.3.5H_2O$; EPA, 1991).

[1] Every chemical in a material or formulation should be assessed if it is:
1. intentionally added and/or
2. present at greater than or equal to 100 ppm.

3. Mobility (e.g. Water solubility, volatility) – water solubility for zinc borate at 23°C is very low (0.1% at pH 5 and 7, and 0.03% at pH 9), (EPA, 1991). Volatility and vapor pressure have not been identified, however based on physical state (solid) and high melting point of 980°C (HSDB), vapor pressure is expected to be negligible, and volatility is not expected.
4. Bioavailability – Empirical data examining bioavailability of zinc borate were not identified. In the acidic environment of the stomach, zinc borate is anticipated to dissociate into the zinc ion / zinc chloride ($ZnCl_2$) and boric acid/borate ion ($BH_3O_3/BO_3^{3-}$). Systemic bioavailability of ingested zinc ranges from 20 to 30% (ATSDR, 2005); whereas gastrointestinal absorption of borates is >90% (USDA, 2006). Acute oral toxicity data suggest that zinc borate is less toxic than its presumed dissociation products. Quantitative studies regarding absorption of zinc and zinc compounds after inhalation exposure in humans are limited (ASTDR, 2005). Inhalation of borate dust can result in some absorption of boron (USDA, 2006). Studies are very limited regarding the absorption of zinc through the skin (ATSDR, 2004). Borates are not readily absorbed through intact skin but are more quickly absorbed across abraded skin (USDA, 2006).

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

1. Fungicide (EPA, 1991)
2. Fire retardant with interior applications such as PVC carpet backing, shower curtains, wall coverings, etc., and exterior uses in PVC tenting and awnings, polyolefin wire and cable coverings, etc. Application rates vary, typical use levels in plastics is 3-30 parts product per hundred parts resin , and in coatings is 1.25-3.0 lb/gal (EPA, 1991).

**GreenScreen Rating[2]:** Zinc borate was assigned a **Benchmark Score of 1** based on high concern level for reproductive and developmental toxicity. Zinc borate also has a very high concern level for environmental persistence[2] and very high concern for chronic aquatic toxicity of zinc borate, and high or moderate concern level for respiratory sensitization of zinc oxide as a potential combustion or biodegradation product. A data gap exists for neurotoxicity.

| GreenScreen Hazard Ratings: Zinc Borate | | | | | | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| 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[2] | B | Rx |
| L | M | H | H | *M* | L | S / DG | R* / M | S / DG | R* / DG | L | *H or M* | L | M | H or *vH* | *vH* | **vH** | *L* | *L* |

Note: Hazard levels (Very High (vH), High (H), Moderate (M), Low (L), Very Low (vL)) in *italics* reflect estimated values and lower confidence. Hazard levels in **BOLD** font reflect values based on test data (See Guidance). For the purposes of this report, hazard levels derived from test data on boric acid or zinc salts were given a high level of confidence. Data on analogs or predicted data were given a low level of confidence.

[2]For inorganic chemicals with low human and ecotoxicity across all hazard endpoints and low bioaccumulation potential, persistence alone will not be deemed problematic. Inorganic chemicals that are only persistent will be evaluated under the criteria for Benchmark 4.

**Transformation Products and Ratings:**
**Identify relevant fate and transformation products** (i.e., dissociation products, transformation products, valence states) **and/or moieties of concern**[3]

| Functional Use | Life Cycle Stage | Transformation Pathway | Transformation Products | CAS # | On CPA Red List[4]? | Green Screen Rating[5] |
|---|---|---|---|---|---|---|
| **Flame Retardant** | **End of Life** | **Biotrans-formation** | Boric acid/ borate ion ($BH_3O_3$/$BO_3^{3-}$) MW = 59g/mol | 10043-35-3/3920 1-27-9 | **Y** | **1** |
| **Flame Retardant** | **End of Life** | **Biotrans-formation** | Zinc ($Zn^{+2}$) MW=65g/mol | 23713-49-7 | **N** | |
| **Flame Retardant** | **End of Life** | **Biotrans-formation** | Zinc hydroxide [$Zn(OH)_2$] MW= 99g/mol | 20427-58-1 | **N** | |
| **Flame Retardant** | **End of Life** | **Biotrans-formation** | zinc chloride ($ZnCl_2$) MW=136g/mol | 7646-85-7 | **N** | |
| **Flame Retardant** | **End of Life** | **Biodegradation or Combustion** | Zinc oxide (ZnO); MW=81g/mol | 1314-13-2 | **N** | |

- Chemical reactions of zinc borate can form a composite of oxides of zinc and boron. Both occur naturally in soil and are essential plant nutrients. They are also artificially added to agricultural crops (EPA, 1991).

**Introduction**

Since toxicity data for zinc borate were limited, potential hazards are inferred through knowledge of its potential byproducts or dissociation products, such as zinc (as various salts) and boron (as borate/boric acid). Zinc is an essential nutrient that is integral to many physiological processes. Boron is a trace element for which essentiality is suspected but has not been directly proven in humans (EPA, 2004).

If incidental ingestion of zinc borate occurs during treated-product use, zinc borate, zinc chloride and borate/boric acid may be of exposure concern.. Under physiological conditions, the acidic environment of the stomach is likely to facilitate solubility of the zinc borate complex and its dissociation into zinc (i.e. ionic or as the chloride salt) and borate/boric acid. Although there are limited empirical systemic toxicity data for zinc chloride, zinc is an essential nutrient and tolerable upper intake levels for zinc range from 4 mg/day in infants (0-6 months) to 40 mg/day for elderly, pregnant or lactating women (NRC, 2001; NRC, 2004). Tolerable upper intake levels of 25 mg/day for adults (including pregnant and lactating women) and 7 mg/day for children ages 1 to 3 years have also been recommended (European Commission, 2003). Further, the European Population Reference Intake (PRI) for zinc for adult males and females is 9.5 mg/day and 7.0 mg/day, respectively (European Commission, 2003). Thus, it is unlikely that incidental ingestion of zinc borate from its commercial use as a flame retardant will result in systemic

[3] 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.
[4] The CPA "Red List" refers to chemicals 1. flagged as Benchmark 1 using the GreenScreen™ List Translator or 2. flagged as Benchmark 1 or 2 using the GreenScreen™ List Translator and further assessed and assigned as Benchmark 1. The most recent version of the GreenScreen™ List Translator should be used.
[5]The way you conduct assessments for transformation products depends on the Benchmark Score of the parent chemical (See Guidance).

zinc exposure that exceeds these recommended tolerable intake levels. With respect to the boron (as borate or boric acid) moiety, identified toxicity data are discussed in each respectively section.

Although the zinc borate complex may be an exposure concern for a handler of powderorliquid formulations in manufacturing and commercial settings (inhalation concerns for workers spraying paint/coatings), it is unclear whether the parent compound or its potential biotransformation products (such as zinc ion or borate/boric acid) would be of greater toxicological concern following inhalation exposure. Similar to incidental oral exposure, it is unlikely that incidental inhalation of zinc borate from its manufacture or commercial use as a flame retardant will result in systemic zinc exposure that exceeds the recommended tolerable intake levels described previously. With respect to the boron (as borate or boric acid) moiety, available data were insufficient to serve as the basis for characterizing potential risk (EPA, 2004). However, since boron is absorbed following inhalation exposure, is uniformly distributed in soft tissues as boric acid, and is not metabolized, route-specific differences in systemic targets are not anticipated (EPA, 2004). Therefore, systemic target tissues identified in oral studies comprise the potential systemic targets following inhalation exposure.

Although dermal contact of zinc borate with healthy skin is not anticipated to result in appreciable dermal absorption, contact with damaged skin may increase the potential for absorption and/or for skin irritation.

Boron is a naturally-occurring element that is widespread in the environment and always found chemically bound to oxygen, usually as alkali or alkaline earth borates, or as boric acid (EPA, 2004). Thus, dose levels of borates can be expressed in terms of Boron equivalents (B) based on the fraction of B on a molecular weight basis. The B equivalents used are a generic designation rather than a designation of the element B. When the boron moiety of zinc borate served as the basis of the hazard score, the B dose was back-calculated to a zinc borate dose. Likewise, when the zinc moiety served as the basis of the hazard score, the Zn dose was back-calculated a zinc borate dose. The dose expressed as mg/kg zinc borate was used to compare to GHS or DfE criteria.



**Chemical Structure of Surrogate**

**Chemical Name (CAS #)**

Zinc borate can exist in various hydration states that according to CEFIC-EFRA (2006) include:

- Zinc borate Firebrake® ZB ($2ZnO.3B_2O_3.3.5H_20$), CAS # 138265-88-0
- Zinc borate Firebrake® 500 ($2ZnO.3B_2O_3$), CAS# 1338265-88-0
- Zinc borate Firebrake® 415 ($4ZnO.B_2O_3.H_20$), CAS# 149749-62-2
- ZB-467 ($4ZnO.6B_2O_3.7H_2O$), CAS# 1332-07-6
- ZB-223 ($2ZnO.2B_2O_3.3H_2O$), CAS# 1332-07-6

**Group I Human Health Effects (Group I Human)**

**Carcinogenicity (C) Score (H, M or L):**
Zinc borate was assigned a score of **Low** for carcinogenicity based on: negative results in two chronic studies on boricacid.

Authoritative and Screening Lists:

- Zinc borate, zinc, zinc hydroxide, zinc chloride and zinc oxide were all classified as Group D - Not classifiable as to human carcinogenicity (EPA, 2004).

Zinc borate data:

- Carcinogenicity data were not identified for zinc borate (CAS #1332-07-6).

Zinc salts and Boric acid data:

- No adequate experimental evidence has been found to indicate that zinc salts administered orally or parenterally are tumorigenic (WHO/IPCS, 2001).
- Carcinogenic effects were not observed in 2-year and 38-week feeding studies on boric acid or sodium borate in rats and dogs treated with up to 1170ppm B. This corresponds to approximately 213-333mg $BO_3$/kg-day. and 340-532mg $3ZnO.2B_2O_3$/kg-day based on boron equivalents. (Weir and Fisher, 1972).
- Carcinogenicity was not observed in a 2-year National Toxicology Program (NTP, 1987) dietary study in mice at boric acid doses up the highest dietary dose of 5,000 ppm boric acid (550 mg boric acid/kg-day or 96 mg B/kg-day as estimated by IRIS), which is on a boron equivalent basis approximately **837mg $3ZnO.2B_2O_3$/kg-day.**

**Mutagenicity/Genotoxicity (M) Score (H, M or L):**
Zinc borate was assigned a score of **Moderate** for mutagenicity/genotoxicity based on: positive results for zinc chloride in an *in vivo* chromosomal aberration assay.

Authoritative and Screening Lists:

- Zinc Chloride (CAS# 7646-85-7) is classified by GHS Japan as GHS Category 2 for Germ Cell Mutagenicity (NITE, 2011). This translates to a **Moderate** concern for mutagenicity.

Zinc Borate Data:

- Zinc borate (CAS# 138265-88-0) was negative in *Salmonella* reverse mutation (Ames) assay when tested with and without metabolic activation (EPA, 1991).
- The weak positive observed for zinc borate (CAS# 149749-62-2) in a chromosomal aberration assay in Chinese hamster lung cells was attributed to high zinc concentrations in the media (Hubbard, 1998), which are not physiologically relevant.

Boric Acid and Zinc Salts Data:

- Boric acid tested with and without metabolic activation was not mutagenic in the *Salmonella*/microsome assay to strains TA98, TA100, TA1535 or TA1537. Boric acid was negative in the mouse lymphoma assay and did not induce sister-chromatid exchanges or chromosomal aberrations in Chinese hamster ovary cells (NTP, 1987).
- The weight of evidence from a variety of test systems suggests that zinc is not mutagenic but there are indications of some weak clastogenic effects (WHO/IPCS, 2001).
- Zinc chloride was not mutagenic to mouse lymphoma cells (ECHA, 2011a).
- In an *in vivo* chromosomal aberration assay zinc chloride caused severe chromosomal anomalies, particularly in animals kept on a low calcium diet under the conditions of the test (ECHA, 2011b).
- In an *in vivo* bone marrow chromosomal aberration test zinc chloride was a potent clastogen (ECHA, 2011c).
- Zinc is not considered to be genotoxic *in vivo* (Hubbard, 1998).

**Reproductive Toxicity (R) Score (H, M, or L):**
Zinc borate was assigned a score of **High** for reproductive toxicity based on: known concern for reproductive effects for boric acid.

Note: the Green Screen does not use guidance values for reproductive toxicity, therefore a dose adjustment for zinc borate was not applied here and the zinc borate as a whole is considered a **High** for reproductive toxicity based on boric acid.

If cutoff values were applied, zinc borate may earn a lower score. For example, a similar tool, the US EPA's Design for the Environment Alternatives Assessment Criteria for Hazard Evaluation (EPA, 2011), uses guidance values of <50mg/kg-day for High concern; 50-250mg/kg-day for Moderate concern; >250-1000mg/kg-day for Low concern; >1000mg/kg-day for Very Low concern. Under these criteria zinc borate would be assigned a score of Moderate considering the NOAEL of 105mg zinc borate/kg-day based on B equivalents.

Authoritative and Screening Lists:

- Boric Acid (CAS #s 10043-35-3 and 11113-50-1) are both classified as Category 2 for reproductive toxicity under EU CMR (ECHA, 2011).
- Boric Acid (CAS #s 10043-35-3 and 11113-50-1) carry an EU Risk Phases R60 code. This translates to **High** concern for reproductive toxicity (ECHA, 2011).
- Boric Acid (CAS # 10043-35-3) is Classified by GHS Japan as GHS category 1B for reproductive toxicity. This translates to **High** concern for reproductive toxicity (NITE, 2011).
- Boric Acid (CAS # 10043-35-3) is Classified by GHS New Zealand as Category 6.8B (GHS Category 2) for reproductive or developmental toxicity (New Zealand EPA, 2011). This translates to a **Moderate** concern for reproductive toxicity.
- Zinc Chloride (CAS # 7646-85-7) is classified by GHS Japan as GHS Category 2 for reproductive toxicity (NITE, 2011). This translates to a **Moderate** concern for reproductive toxicity.

Zinc Borate Data:

- Studies assessing potential reproductive toxicity for zinc borate (CAS #1332-07-6) were not identified.

Boric Acid and Zinc Salts Data:

- Reproductive toxicity is a concern for boron (from boric acid or borate) exposure and dogs were the most sensitive species evaluated (EPA, 2004). A 2-year systemic toxicity study in Sprague-Dawley rats and Beagles treated with a diet containing borax and boric acid at 117, 350 and 1170ppm as boron equivalent or 58, 117 and 350ppm as boron equivalent respectively, reported testicular effects, and was subsequently followed by a 38-week study with Beagles treated with borax and boric acid in the diet at 1170ppm for further examination of testicular effects (Weir and Fisher, 1972). Both species showed no clinical or histological alterations at doses up to 350ppm. At 1170ppm caused testicular atrophy in rats and dogs and spermatogenic arrest in dogs. Weir and Fisher (1972) continued with a three generation reproductive toxicity study in Rats treated with Borax or Boric acid at 117, 350 and 1170ppm as boron equivalent in the diet. No adverse effects were observed at 117 and 350ppm boron and rats at the high dose level were sterile due to lack of viable sperm and evidence of decreased ovulation. In both studies, for dogs, the NOAEL = 350ppm Boron LOAEL = 1170ppm boron (NOAEL = 8.8mg B/kg-day; LOAEL = 29.2mg B/kg-day as cited in EPA IRIS, 2004). In boron equivalents, the **NOAEL corresponds to approximately 48mg $B0_3$/kg-day and 75mg $3ZnO.2B_2O_3$/kg-day.** Although these studies had numerous deficiencies, they are the most conservative reproductive NOAEL and LOAEL amongst the available studies.

  Note: A reproductive NOAEL of 75mg zinc borate/kg-day is considered a **"Moderate"** concern according to the EPA's Design for the Environment Alternatives Assessment Criteria for Hazard Evaluation (EPA, 2011).
- Reproductive and systemic toxicity studies have identified the testis as a sensitive target of boron toxicity in rats and mice, although at higher doses than in the dog study (Weir and Fisher, 1972; Seal and Weeth, 1980; NTP, 1987; Fail et al., 1991, as reviewed by EPA, 2004). Testicular effects included reduced organ weight and organ:body weight ratio, atrophy, degeneration of the spermatogenic epithelium, impaired spermatogenesis, reduced fertility, and sterility (Weir and Fisher, 1972; Seal and Weeth, 1980; NTP, 1987; Fail et al., 1991; Dixon et al., 1979; Linder et al., 1990; Treinen and Chapin, 1991; Ku et al., 1993a; Ku et al., 1993b as reviewed by EPA, 2004).
- A human study of occupational exposure to borate dust (as the sodium salt) showed no adverse effect on some reproduction parameters (Whorton et al., 1994).
- No effect on testicular development was seen in rats fed zinc chloride at up to 500 mg/kg-day from 8 weeks of age until weanlings (Evenson et al., 1993).

**DevelopmentalToxicity incl. developmental neurotoxicity (D) Score (H, M or L):**

Zinc borate was assigned a score of **High** for developmental toxicity based on: known concern for developmental toxicity for boric acid.

Note: the Green Screen does not use guidance values for developmental toxicity, therefore a dose adjustment for zinc borate was not applied here and the zinc borate as a whole is considered a **High** for developmental toxicity based on boric acid.

If cutoff values were applied, zinc borate may earn a lower score. For example, a similar tool, the US EPA's Design for the Environment Alternatives Assessment Criteria for Hazard Evaluation (EPA, 2011), uses guidance values of <50mg/kg-day for High concern; 50-250mg/kg-day for Moderate concern; >250-1000mg/kg-day for Low concern; >1000mg/kg-day for Very Low concern. Under these criteria zinc borate would be assigned a score of Moderate considering the NOAEL of 105mg zinc borate/kg-day based on B equivalents.

Authoritative and Screening Lists:

- Boric Acid (CAS#s 10043-35-3 and 11113-50-1) carries an EU Risk Phrase of R61. This translates to **High** concern for developmental toxicity (ECHA, 2011).

Zinc Borate Data:

- Studies assessing potential developmental toxicity of zinc borate ($4ZnO.6B_2O_3.7H_2O$ or $2ZnO.2B_2O_3.3H_2O$, CAS #1332-07-6) were not identified.

Boric acid and Zinc Salts Data:

- Developmental toxicity is the critical effect of boron (from boric acid or borate) exposure and rats were the most sensitive species evaluated (EPA, 2004). A chronic reference dose (RfD) of 0.2 mg/kg-day for boron (from boric acid and borates) was derived based on a benchmark dose (BMDL) of 10.3 mg B/kg-day for a 5% decrease in fetal weight from two developmental toxicity studies. A composite uncertainty factor of 66 was applied to the BMDL and this uncertainty factor considered both toxicokinetic and toxicodynamic differences between humans (intraspecies extrapolation) and between humans and rats (interspecies extrapolation). The resulting chronic RfD was 0.2 mg B/kg-day.
- The $BMDL_{05}$ of 10.3 mg B/kg-day estimated by EPA (2004) based partly on the Price et al. (1996a, 1994) study is supported by the NOAEL of 9.6 mg B/kg-day from the Price et al. (1996a, 1994) study. When expressed on a boron equivalent molecular weight basis **9.6mg B/kg-day corresponds to a NOAEL of approximately 52mg $B0_3$/kg-day (mw = 59) and 84mg $3ZnO.2B_2O_3$/kg-day (MW= 187).** These studies do not appear to have any major deficiencies with respect to current developmental toxicity testing guidelines, recognizing that the study authors did not cite a specific protocol.

  Note: A developmental NOAEL of 84 mg/kg-day is considered a **"Moderate"** concern according to the EPA's Design for the Environment Alternatives Assessment Criteria for Hazard Evaluation (EPA, 2011).
- Intraperitoneal injection of zinc chloride at 12.5, 20.5 or 25 mg/kg-day on GD 8, 9, 10 or 11 was associated with a dose-related increase in skeletal defects, usually ripple ribs at all doses (Chang et al., 1977). The intraperitoneal exposure route is not directly relevant to oral exposure.
- Dose-related reductions in pup body weight and some changes in iron and copper distribution were seen in the offspring of rats fed zinc oxide at 0.25 or 0.5% Zn (estimated to result in approximately 250 or 500 mg Zn/kg-day which corresponds on a zinc equivalent basis to approximately 492 or 983mg **$3ZnO.2B_2O_3$./kg-day**) during gestation and 14 days of lactation (Ketcheson et al., 1969). Since no NOAEL was identified in this study, a concern level cannot be derived.

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

Zinc borate was assigned a score of *Moderate* for endocrine activity based on: boric acid listed as a substance of "Medium concern" on the EU ED list.

Authoritative and Screening Lists:

- Boric acid (10043-35-3, 11113-50-1 and 39201-27-9) is listed as a category 1 substance of "Medium concern" on European Union Priority List of suspected endocrine disruptors (Petersen et. al., 2007). This translates to a **Moderate** or **High** concern for endocrine activity.

Zinc Borate Data:

- Studies assessing potential endocrine activity for any zinc borate compound were not identified.

Boric Acid and Zinc Salts Data:

- Results of systemic, reproductive and developmental toxicity studies for zinc or borate salts do not suggest that exposure to zinc borate is of potential concern for endocrine disruption.

**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. For Systemic Toxicity and Neurotoxicity, Group II and II* are considered sub-endpoints and test data for single or repeated exposures may be used. If data exist for single OR repeated exposures, then the endpoint is not considered a data gap. 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):**

Zinc borate was assigned a score of **Low** for acute mammalian toxicity based on: low concern levels for oral, dermal and inhalation acute toxicity for zinc borate.

Authoritative and Screening Lists:

- Boric Acid (CAS #10043-35-3) is classified by GHS Japan as GHS Category 5 for acute oral toxicity (NITE, 2011). This translates to a **Low** concern for acute mammalian toxicity.
- Boric Acid (CAS # 10043-35-3) is classified by GHS New Zealand as 6.1E (GHS Category 5) for acute oral toxicity (New Zealand EPA, 2011). This translates to a **Low** concern for acute mammalian toxicity.
- Zinc Chloride (CAS # 7646-85-7) carries an EU H-Statement of H302 (ECHA, 2011). This translates to a **Moderate** concern for acute mammalian toxicity.
- Zinc Chloride (CAS # 7646-85-7) carries an EU Risk Phrase of R22(ECHA, 2011). This translates to a **Moderate** or **High** concern for acute mammalian toxicity.
- Zinc Chloride (CAS # 7646-85-7) is classified by GHS Japan as GHS Category 4 for acute oral toxicity and Category 1-5 for acute inhalation toxicity-dust (NITE, 2011). This translates to a **Moderate** concern for acute oral mammalian toxicity and **unknown** concern for inhalation toxicity.
- Zinc Chloride (CAS # 7646-85-7) is classified by GHS New Zealand as 6.1C (GHS Category 3) for acute oral toxicity and category 6.1E (GHS Category 5) for acute inhalation toxicity (New Zealand EPA, 2011). This translates to a **High** concern for acute oral toxicity and a **Low** concern for acute inhalation mammalian toxicity.
- Zinc Oxide (CAS # 1314-13-2) is classified by GHS Japan as GHS Category 5 for acute inhalation toxicity (NITE, 2011). This translates to a **Low** concern for acute inhalation mammalian toxicity.

Zinc Borate Data:

- $LD_{50}$ or $LC_{50}$ values for zinc borate (CAS #1332-07-6) were not identified.
- Rat oral $LD_{50}$ (males only) for zinc borate ($2ZnO3B_2O_33.5H_2O$, CAS#138265-88-0) is > 10 g/kg (EPA, 1991; Hubbard, 1998).
- Rat oral $LD_{50}$ for zinc borate ($4ZnOB_2O_3H_2O$, CAS#149749-62-2) is > 5 g/kg (Hubbard, 1998).
- The rat 4-hr $LC_{50}$ for zinc borate ($4ZnOB_2O_3H_2O$, CAS#149749-62-2) is >4.95 mg/$m^3$(Hubbard, 1998).
- Albino rabbit dermal $LD_{50}$for zinc borate ($2ZnO.3B_2O_3.3.5H_2O$, CAS #138265-88-0) is > 10 g/kg (EPA, 1991; Hubbard, 1998).
- Albino rabbit dermal $LD_{50}$ for zinc borate ($4ZnOB_2O_3H_2O$, CAS#149749-62-2) is >2 g/kg (Hubbard, 1998).
- Based on $LD_{50}$ values for acute oral and dermal toxicity, zinc borate was considered a Pesticide Toxicity Category III or IV (EPA, 1991), respectively, which means it is considered to have **Low** Toxicity or **Very Low** Toxicity, respectively (NPIC, 2008).

Boric Acid and Zinc Salts Data:

- Boric Acid (CAS No. 10043-35-3) has a rat oral $LD_{50}$ value of 2660 – 4100 mg/kg (Pfeiffer et al., 1945 and Weir and Fisher, 1972) equivalent to ~4245 – 6541 mg/kg $3ZnO.2B_2O_3$ on a B equivalent basis.
- Zinc Chloride (CAS No. 7646-85-7) has a mouse oral $LD_{50}$ value of 1260 mg/kg in an OECD 401 test and a SD Rat oral $LD_{50}$ value of 1100 mg/kg in an OECD 401 test (ECHA, 2011d). These values convert to $LD_{50}$s of approximately 1510 and 1730mg $3ZnO.2B_2O_3$/kg (zinc equivalent basis).
- Zinc Chloride (CAS No. 7646-85-7) has a female SD Rat inhalation LC50 value of 2000 mg/$m^3$ or 2 mg/L with a median diameter of 2.3µm (ECHA, 2011e). This value corresponds to approximately 2.75 mg/L $3ZnO.2B_2O_3$ /kg (zinc equivalent basis).

**Systemic Toxicity/Organ Effects incl. immunotoxicity (ST)**
**Group II Score (single dose: vH, H, M or L):**
Zinc borate was assigned a score of **DG** for systemic toxicity/organ effects-single exposure, based on: a lack of relevant data. Screening lists indicate *very high* concern level for boric acid, zinc oxide and zinc chloride for single exposure, however no data were found to support that assignment and to enable conversions on a zinc- or boron-equivalent basis to zinc borate concern levels.

**Group II* Score (repeated dose: H, M or L);**
Zinc borate was assigned a score of **Moderate** for systemic toxicity/organ effects-repeated exposure, based on: NOAELs for zinc salts, which, when converted to zinc borate on a zinc equivalent basis, translate to moderate or low levels of concern.

Authoritative and Screening Lists:

- Boric Acid (CAS # 10043-35-3) is classified by GHS Japan as Category 1 (oral) and category 3 (inhalation) for target organ toxicity, single exposure (NITE, 2011). This translates to a **Very High** concern for Systemic Toxicity.
- Boric Acid (CAS # 10043-35-3) is classified by GHS Japan as a Category 1 for target organ toxicity repeated exposure (NITE, 2011). This translates to a **High** concern for Systemic Toxicity.
- Zinc Chloride (CAS # 7646-85-7) is classified by GHS Japan as GHS Category 1 for target organ toxicity single exposure (respiratory, liver and pancreas) and repeated exposure (Lung, Liver) (NITE, 2011). This translates to a **High or Very High** concern for Systemic Toxicity.
- Zinc Oxide(CAS # 1314-13-2) is classified by GHS Japan as GHS Category 1 for target organ toxicity single exposure (inhalation, systemic toxicity) and repeated exposure (inhalation, Lung) (NITE, 2011). This translates to a **High or Very High** concern for Systemic Toxicity.

Zinc Borate Data:

- Studies assessing the systemic toxicity of zinc borate (CAS #1332-07-6) were not identified.

Boric acid and Zinc Salts Data:

- Inhaled zinc oxide is of theoretical exposure potential as a result of combustible zinc borate. Zinc oxide does not produce lung damage even when administered at relatively high concentrations (WHO/IPCS, 2001).
- Borax and boric acid was administered to rats and dogs in a 2-year and 38 week study (Weir and Fisher 1972). See the summary of this study under the reproductive toxicity section. **The dog NOAEL of 8.8mg B/kg-day was equivalent in boron equivalents to approximately 75mg $3ZnO.2B_2O_3$/kg-day.** This corresponds to a **Moderate** concern for Systemic Toxicity.
- Boric Acid was evaluated in 14-day, 13-week and 2-year studies in $B6C3F_1$ mice (NTP 1987). In the 14-day studies, mortality occurred in mice fed doses over 25,000ppm boric acid in feed. No compound related gross pathologic or histopathologic effects were observed in mice exposed up to 12,500ppm boric acid. In the 13 week study, mortality occurred in 1/10 female and 8/10 males at the 20,000ppm level and 1/10 male at the 10,000ppm level. At 20,000ppm testicular atrophy occurred in 8/10 male mice, hyperkeratosis and acanthosis

of the stomach in 8/10 male and 3/9 female mice and extramedullary hematopoiesis of the spleen in all male and female mice.
In the 2 year assay, groups of 50 male and 50 female rats were treated with 0, 2500 or 5000ppm boric acid in feed. Male mice showed reduced survival at both dose levels. Body weight gain was reduced in both sexes after week 30. No compound related clinical signs were reported. At the high dose male mice showed increased incidence of testicular atrophy and interstitial cell hyperplasia. Low dose males also showed increased testicular atrophy. Low dose males showed increases in incidences of hepatocellular carcinomas or adenomas and an increased incidence of subcutaneous tissue tumors. These effects were not dose related and were within the historical control range. The authors concluded that the tumors were not considered to be related to the administration of boric acid. The LOAEL was 2500ppm, the NOAEL was <2500ppm boric acid (225mg boric acid/kg-day or 48 mg B/kg-day as estimated by IRIS), and **418mg $3ZnO.2B_2O_3$/kg-day in boron equivalents.**

- Zinc chloride was administered to Wistar rats orally at a concentration of 11.7-12.8 mg Zn/kg-day daily for 28 days. This study only measured haematological effects. Significant increase in percentage of recticulocytes and polychromatophilic erythrocytes and statistically significant decrease in the erythrocyte count and haemoglobin level in the peripheral blood was observed. No major changes in the percentage composition of bone marrow cells between the control and treated animals were observed. The LOEL was 11.7-12.8mg Zn/kg-day or in zinc equivalents, **~23mg $3ZnO.2B_2O_3$/kg-day** (ECHA, 2011f).
- Zinc oxide was administered to male and female ferrets (3-5/group) at 0, 500, 1500 or 3000 mg zinc oxide/kg feed (equivalent to be 0, 81.3, 243.8 or 487.5 mg ZnO/kg bw, respectively) for 180 days. All high dose animals died within 13 days. At the mid dose level the animals (n=4) were killed on days 7, 14 and 21 and showed severe to mild diffuse nephrosis, extramedullary haematopoesis in the spleen, macrocytic hypochromic anaemia and an increased in level of zinc in the liver and kidney tissue. At the lowest dose level the animals (n=3) were killed on days 48, 138 and 191, respectively. No clinical signs of toxicity or pathological changes were seen, apart from an extramedullary heamatopoiesis in the spleen. The authors do not state a LOAEL or NOAEL. If the NOAEL is assumed to be 500ppm or 81.3mg ZnO/kg-day this is equivalent on a zinc basis to **~128 mg $3ZnO.2B_2O_3$/kg-day** (ECHA, 2011g).
- In an EU Risk Assessment Report on Zinc Chloride (2004), analogs zinc oxide, zinc sulfate and zinc monoglycerolate were considered as analogs for zinc toxicity. The lowest oral NOAEL was from a 13-week study in rats with a NOAEL of 31.52mg zinc monoglycerolate/kg-day (13.26 mg Zn/kg-day) which calculates on a zinc equivalent basis to **~26mg $3ZnO.2B_2O_3$/kg-day** (EU RAR, 2004).

**Neurotoxicity (N)**
**Group II Score (Single Dose vH, H, M or L):**
Zinc borate was assigned a score of **DG** for neurotoxicity-single exposure, based on: a lack of relevant data.

**Group II *Score (Repeated Dose H, M or L):**
Zinc borate was assigned a score of **DG** for neurotoxicity-repeated exposure, based on: a lack of relevant data.

Authoritative and Screening Lists:

- Zinc borate, boric acid and zinc salts were not found on relevant screening or authoritative lists.

Zinc Borate Data:

- Studies designed to assess the potential neurotoxicity of any zinc borate compound were not identified.

Boric Acid and Zinc Salts Data:

- Although neurological effects were noted in human case reports after ingestion of high levels of boron (EPA, 2004), animal data are limited to increased brain succinate dehydrogenase activity after 10-14 weeks of oral exposure to sodium tetraborate, equivalent to 20.8 mg B/kg-day (Settimi et al., 1982- as reviewed by EPA, 2004).

- There is an uncertainty about neurological effects at lower boron doses and other than acute duration because no data are available (EPA, 2004). This is identified as an area where further research may be beneficial.
- Chronic studies with boric acid in rats (Weir and Fisher, 1972) and mice (NTP, 1987) failed to identify clinical signs or histopathological changes indicative of neurotoxicity, however, comprehensive neurological evaluations were not conducted.

**Skin Sensitization (SnS) Group II* Score (H, M or L):**
Zinc borate was assigned a score of **Low** for skin sensitization based on: negative results in skin sensitization tests on zinc borate.

Authoritative and Screening Lists:
- Zinc borate, boric acid and zinc salts were not found on relevant screening or authoritative lists.

Zinc Borate Data:
- Skin sensitization has not been observed for any borate compound that has been tested for such effects (Hubbard, 1998), including zinc borate ($2ZnO.3B_2O_3.3.5H_20$, CAS # 138265-88-0; Kreuzmann, 1990- as reviewed by Hubbard, 1998).

Boric Acid and Zinc Salts Data:
- No information assessing the potential for skin sensitization was identified for zinc or its salts other than zinc borate.
- Boric acid (CAS # 10043-35-3) was not sensitizing in guinea pigs per OECD 406 (ECB, 2000).

**Respiratory Sensitization (SnR) Group II* Score (H, M or L):**
Zinc borate was assigned a score of *High or Moderate* for respiratory sensitization based on: AOEC's "Rs" code for zinc oxide.

Authoritative and Screening Lists:
- Zinc oxide (CAS No. 1314-13-2) carries an "Rs" on the AOEC Asthmagen list (AOEC, 2011). This translates to a **High** or **Moderate** concern for Respiratory Sensitization.

Zinc Borate Data:
- Although occasional mild irritation effects to the nose and throat may occur from inhalation of zinc borate dust at levels greater than 10 $mg/m^3$ (Borax, 2000), studies designed to assess potential respiratory sensitization associated with exposure to any zinc borate compound were not identified.
- An EU Risk Assessment Report on Zinc Oxide indicated no data are available for respiratory sensitization (ECB, 2004), andno other data for respiratory sensitization were identified for zinc oxide. Therefore no modification was made to the initial assignment of a High or Moderate concern level for zinc borate based on the "Rs" code for Zinc Oxide on the AOEC Asthmagen List.

**Skin Irritation/Corrosivity (IrS) Group II Score (vH, H, M or L):**
Zinc borate was assigned a score of **Low** for skin irritation/corrosivity based on: low concern for irritation from zinc borate.

Authoritative and Screening Lists:
- Boric acid (CAS # 10043-35-3) is classified by GHS Japan as GHS category 2 for Skin Irritation which translates to a **High** concern for skin irritation (NITE, 2011)
- Boric acid (CAS # 10043-35-3) is classified by GHS New Zealand as Category 6.3B (GHS Category 3) for skin irritation (New Zealand EPA, 2011). This translates to a **Moderate** concern for skin irritation.
- Zinc Chloride (CAS # 7646-85-7) carries an EU H-Statement of H314 (ECHA, 2011). This translates to a **Very High** concern for Skin irritation.

- Zinc Chloride (CAS # 7646-85-7) carries an EU Risk Phrase of R34 (ECHA, 2011). This translates to a **Very High** concern for Skin irritation.
- Zinc Chloride (CAS # 7646-85-7) is a DOT hazard Class 8 (DOT, 2011). This translates to a **High** concern for Skin irritation.
- Zinc Chloride (CAS # 7646-85-7) is classified by GHS Japan as GHS Category 1A-1C for skin irritation (NITE, 2011). This translates to a **Very High** concern for Skin irritation.
- Zinc Chloride (CAS # 7646-85-7) is classified by GHS New Zealand as 8,2C (GHS Category 1C) for skin irritation (New Zealand EPA, 2011). This translates to a **Very High** concern for Skin irritation.

Zinc Borate Data:

- Zinc borate (unspecified CAS#) does not cause irritation to intact skin (Borax, 2000)
- Zinc borate (unspecified CAS#) was not irritating to Albino rabbits in a primary dermal irritation/corrosivity study (EPA, 1991).

Boric Acid and Zinc Salts Data:

- 1 % w/v zinc chloride was found to be moderately irritating to guinea-pig skin (ECHA, 2011h).
- 1 % w/v zinc chloride was found to be severely irritating to rabbit skin or mouse skin (ECHA, 2011h).

**Eye Irritation/Corrosivity (IrE) Group II Score (vH, H, M or L):**
Zinc borate was assigned a score of **Moderate** for eye irritation/corrosivity based on: data indicating zinc borate can be mildly irritating to the eyes.

Authoritative and Screening Lists:

- Boric acid (CAS # 10043-35-3) is classified by GHS Japan as GHS category 2A-2B for Eye Irritation which translates to a **High** or **Moderate** concern for eye irritation (NITE, 2011)
- Boric acid (CAS # 10043-35-3) is classified by GHS New Zealand as Category 6.4A (GHS Category 2A or 2B) for eye irritation (New Zealand EPA, 2011). This translates to a **Moderate** or **High** concern for eye irritation.
- Zinc chloride (CAS # 7646-85-7) is classified by GHS Japan as GHS Category 1 for eye irritation (NITE, 2011). This translates to a **Very High** concern for eye irritation.
- Zinc chloride (CAS # 7646-85-7) is classified by GHS New Zealand as 8.3A (GHS Category 1) for eye irritation (New Zealand EPA, 2011). This translates to a **Very High** concern for eye irritation.

Zinc Borate Data:

- Since many years of occupational exposure to zinc borate (unspecified CAS#) suggest no adverse effects on human eyes, it is not considered to be a human eye irritant in normal industrial use (Borax, 2000).
- While U.S. EPA (1991) reported that other zinc borate compounds (unspecified but not CAS#1332-07-6) were irritating to Albino rabbit eyes since mild conjunctivitis was observed, zinc borate ($4ZnO.B_2O_3.H_20$, CAS #149749-62-2) was not irritating to rabbit eyes (Cerven, 1992- as reviewed by Hubbard, 1998).

Boric Acid and Zinc Salts Data:

- Boric acid was evaluated in OECD 405 in rabbit eyes. It was classified as not irritating Toxicity Category III - corneal involvement or irritation clearing in 7 days or less (ECHA, 2011i).
- Anhydrous boric acid was an ocular irritant when applied directly to the eyes of rabbits. The irritation was reversible after 24 h with a return to near normal by 72 h after exposure to the test article (ECHA, 2011i).
- Boric acid (100mg) applied to rat eyes resulted in mild to moderate erythema which subsided by Day 4. The test substance was classified as non-irritating (ECHA, 2011i).

**Ecotoxicity (Ecotox)**

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

Zinc borate was assigned a score of **High** or *Very High* for acute aquatic toxicity based on: a score of *Very High* is possible based on the R-phrase R50/53 assigned to zinc borate, however data on aquatic toxicity indicates **High** concern may be more accurate.

Authoritative and Screening Lists:

- Boric acid (CAS # 10043-35-3) is classified by GHS New Zealand as Category 9.1D (GHS Category 2 or 3) for aquatic toxicity (New Zealand EPA, 2011). This translates to a **Moderate** or **High** concern for acute aquatic toxicity.
- Zinc chloride (CAS # 7646-85-7) is classified by GHS Japan as GHS Category 1 for acute and chronic aquatic toxicity (NITE, 2011). This translates to a **Very High** concern for acute and chronic aquatic toxicity.
- Zinc chloride (CAS # 7646-85-7) is classified by GHS New Zealand as 9.1A (GHS Category 1) for aquatic toxicity (New Zealand EPA, 2011). This translates to a **Very High** concern for acute and chronic aquatic toxicity.
- Zinc oxide (CAS # 1314-13-2) is classified by GHS New Zealand as 9.1A (GHS Category 1) for aquatic toxicity (New Zealand EPA, 2011). This translates to a **Very High** concern for acute and chronic aquatic toxicity.
- Zinc oxide (CAS # 1314-13-2) is classified by GHS Japan as GHS Category 1 for aquatic toxicity acute & chronic (NITE, 2011). This translates to a **Very High** concern for acute and chronic aquatic toxicity.

Zinc Borate Data:

- Zinc borates are classified as Dangerous to the Environment, with the EU Risk Phrases of R50/R53, Very toxic to aquatic organisms/May cause long-term effects in the aquatic environment. However, both boron and zinc are essential micronutrients for the healthy growth of plants and other aquatic organisms (CEFIC-EFRA, 2006).
- 96-hr $LC_{50}$ to *Lepomismacrochirus* (bluegill sunfish) under static conditions was >335 ppm. (ECOTOX, 2000)
- 96-hr $LC_{50}$ S. gairdneri (rainbow trout) under static conditions was 2.4 mg/L (Borax, 1992, 2000).
- Boric acid – zinc salt (CAS # not specified) 48-hr $EC_{50}$ in Daphnia magna = 75 mg/L (ECOTOX, 2000).
- Data supporting R50/53 could not be identified; the above noted $LC/EC_{50}$s support a GHS classification 2.

Other

- In avian dietary studies, the $LC_{50}$ of zinc borate in mallard ducklings (*Anasplatyrhynchos*) was > 5620 ppm (EPA, 1991).

**Chronic Aquatic Toxicity (CA) Score (vH, H, M or L):**
Zinc borate was assigned a score of *Very High* for chronic aquatic toxicity based on: R50/53 code for zinc borate.

Authoritative and Screening Lists:

- Zinc powder (CAS # 7440-66-6), zinc chloride (CAS # 7646-85-7) and zinc oxide (CAS # 1314-13-2) all carry EU Risk Phrases of R50/53 phrases (ECHA, 2011). This translates to a **Moderate** concern for chronic aquatic toxicity.
- Zinc chloride (CAS # 7646-85-7) is classified by GHS Japan as GHS Category 1 for acute and chronic aquatic toxicity (NITE, 2011). This translates to a **Very High** concern for acute and chronic aquatic toxicity.
- Zinc chloride (CAS # 7646-85-7) is classified by GHS New Zealand as 9.1A (GHS Category 1) for aquatic toxicity (New Zealand EPA, 2011). This translates to a **Very High** concern for acute and chronic aquatic toxicity.
- Zinc oxide (CAS # 1314-13-2) is classified by GHS New Zealand as 9.1A (GHS Category 1) for aquatic toxicity (New Zealand EPA, 2011). This translates to a **Very High** concern for acute and chronic aquatic toxicity.
- Zinc oxide (CAS # 1314-13-2) is classified by GHS Japan as GHS Category 1 for aquatic toxicity acute & chronic (NITE, 2011). This translates to a **Very High** concern for acute and chronic aquatic toxicity.

Zinc Borate Data:

- Zinc borates are classified as Dangerous to the Environment, with the EU Risk phrase of R50/R53, Very toxic to aquatic organisms/May cause long-term effects in the aquatic environment (CEFIC-EFRA, 2006).
- Data supporting R50/53 could not be identified.

**Environmental Fate (Fate)**

**Persistence (P) Score (vH, H, M, L, or vL):**
Zinc borate was assigned a score of **Very High** for persistence based on:

- Under certain environmental conditions, zinc borate will slowly hydrolyze to form zinc hydroxide and boric acid (Borax, 2000) or a composite of oxides of zinc and boron (EPA, 1991).
- Oxides of zinc and boron occur naturally in soil and are essential plant nutrients (EPA, 1991). As such, half-life estimates in soil, sediment, water or air are not likely to be a reliable prediction of the potential for zinc borate to persist in the environment.
- Boron is not transformed or degraded in the environment, but depending on environmental conditions (e.g., pH, moisture level), changes in the specific form of boron and its transport can occur (EPA, 2004).

**Bioaccumulation (B) Score (vH, H, M, L, or vL):**
Zinc borate was assigned a score of *Low* for bioaccumulation based on: no evidence of bioaccumulation.

- Zinc is an essential metal and is naturally concentrated by living organisms and thus the bioconcentration factor (BCF) for zinc bears no relationship to toxicity (WHO/IPCS, 2001). Further, bioaccumulation measurements do not differentiate between zinc adsorbed to the outer surface of organisms, and the zinc within organisms.
- Since zinc bioavailability is affected by biotic and abiotic factors, e.g., organism age and size, prior history of exposure, water hardness, pH, dissolved organic carbon and temperature; the toxicity of zinc will depend on environmental conditions and habitat types which vary locally (WHO/IPCS, 2001).
- Boron has been known to be an essential micronutrient for the growth of all plants and in humans, boron is a trace element for which essentiality is suspected but has not been directly proven (U.S. EPA, 2004).

**Physical Hazards (Physical)**

**Reactivity (Rx) Score (vH, H, M or L):**
Zinc borate was assigned a score of *Low* for reactivity based on: zinc borate's HMIS reactivity score of 0.

Authoritative and Screening Lists:
- Zinc chloride (CAS # 7646-85-7) is classified by GHS New Zealand as a 8.1A Code (GHS category 1), Corrosive to metals (New Zealand EPA, 2011). This translates to a **Moderate** concern for reactivity.
- Zinc borate (2ZnO.2B2O3.3H2O, CAS #1332-07-6) has a HMIS reactivity score of 0 (Borax, 2000).

**Flammability (F) Score (vH, H, M or L):**
Zinc borate was assigned a score of *Low* for flammability based on: zinc borate's NFPA flammability rating score of 0.

Authoritative and Screening Lists
- The estimated NFPA flammability rating for zinc borate is 0 indicating that it is not combustible (Borax, 2000; Fischer Scientific, 2007).

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ECHA 2011e. Zinc Chloride CAS# 7646-85-7, Exp Key Acute toxicity: inhalation.001
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**Appendix 1**

**Modeling Results**

EPI Suite and ECOSAR modeling results were not used because these modeling programs and not currently suitable for inorganic compounds.