BEFORE THE
U.S. ENVIRONMENTAL PROTECTION AGENCY

PETITION OF THE DOW CHEMICAL COMPANY UNDER CLEAN AIR ACT SECTION 112(b)(3) TO REMOVE 2-BUTOXYETHYL BENZOATE FROM THE GLYCOL ETHERS CATEGORY IN THE LIST OF HAZARDOUS AIR POLLUTANTS

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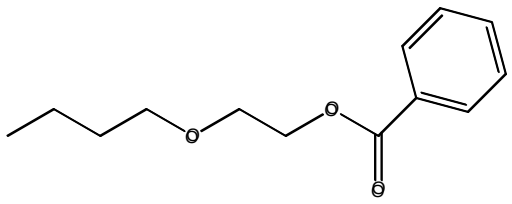
INTRODUCTION AND SUMMARY

The Dow Chemical Company respectfully submits this petition to the U.S. Environmental Protection Agency (EPA) to remove 2-butoxyethyl benzoate (2-BEB) from the category of glycol ethers in the list of hazardous air pollutants (HAP) under Section 112(b)(3) of the Clean Air Act (CAA), 42 U.S.C. § 7412(b)(3).

2-BEB (Chemical Abstracts Service Registry Number (CAS RN) 5451-76-3) has a molecular formula of $C_{13}H_{18}O_3$. 2-BEB is also known as ethylene glycol butyl ether benzoate. 2-BEB has also been referred to in some historical Dow documents and reports as Butyl CELLOSOLVE™ Benzoate, but this is currently not an officially recognized name for this product. The chemical formula of 2-BEB is $C_4H_9OCH_2CH_2OOCC_6H_5$.



2-BEB is a glycol ether ester of benzoic acid. Ethylene oxide-based glycol ethers are listed as HAP compounds because they are included in the glycol ethers category in CAA Section 112(b)(1), as that category was redefined by 40 C.F.R. § 63.62. It should be noted that 2-BEB is not currently sold in commercial quantities in the U.S., and that it is not expected to be a large volume chemical; however, due to the potential advantages described below, 2-BEB would be a preferred product over its targeted replacements.

- Glycol ethers category (no CAS RN)
  - 40 C.F.R. § 63.62 (as revised by 65 Fed. Reg. 47348 (Aug 2, 2000)) defines the glycol ether category in the HAP list as follows:
    - Glycol ethers include mono- and di-ethers of ethylene glycol, diethylene glycol, and triethylene glycol R-(OCH2CH2)n-OR′.
      - Where: n = 1, 2, or 3; R = alkyl C7 or less; or
      - R = phenyl or alkyl substituted phenyl;
      - R′= H or alkyl C7 or less; or
      - OR′ consisting of carboxylic acid ester, sulfate, phosphate, nitrate, or sulfonate.

2-BEB rapidly metabolizes to form ethylene glycol monobutyl ether (EGBE) (2-butoxyethanol; CAS RN 111-76-2) in mammals. In 2004, EPA promulgated a final rule deleting EGBE from the glycol ethers category in the HAP list. 40 C.F.R. § 63.63 (69 Fed. Reg. 69325 (Nov. 29, 2004)). Esters related to EGBE were not deleted from the glycol ethers category at that time. As a derivative of and precursor to EGBE that is even less likely to cause any adverse health or environmental effects, 2-BEB should also be considered for deletion from the glycol ethers category in the HAP list.

2-BEB is produced through the esterification of EGBE and benzoic acid. 2-BEB is rapidly metabolized to EGBE and benzoic acid in mammals. These two metabolites are both considered to be non-HAP compounds. As will be explained in detail in the following sections, 2-BEB has many environmental and sustainability benefits compared to the products it is targeted to

replace. Many of 2-BEB's physical and chemical properties provide clear advantages over the targeted products that would be replaced for the intended uses. Additionally, 2-BEB has a better environmental fate, environmental effects, and mammalian toxicology profile compared with its replacement targets.

The primary intended applications of 2-BEB are those of a coalescing solvent for water-based coatings, and as a replacement for phthalate-based plasticizers used in the formulations of caulking compounds and in some polyvinyl chloride (PVC) formulations where dioctyl phthalate (DOP), butyl benzyl phthalate (BBP), and diisononyl phthalate (DINP) are currently used. Water-based coatings are preferred over solvent-based coatings since they are considered more environmentally friendly and have a much lower volatile organic compound (VOC) content. Phthalate-based plasticizers are under regulatory scrutiny and are being deselected by industry.

The conservative proposed reference concentration (RfC) and reference dose (RfD) for 2-BEB have been determined in Section V to be 3 mg/m^3 and 0.19 mg/kg bw/day, respectively. There is no scientific reason to believe that exposures below the proposed RfC/RfD for 2-BEB would pose any potential health hazard. Thus, it is appropriate to use the proposed RfC/RfD as a health benchmark below which exposures to 2-BEB will not likely cause adverse health effects. The risk assessments for exposures via inhalation, ingestion, and dermal pathways both for workers and consumers result in Hazard Quotients (HQ) that are substantially below 1. These low HQs reflect low to minimal risk associated with the manufacture and processing of 2-BEB. As noted in Section VI, there is a high level of conservatism built into the modeling used to

derive 2-BEB exposure estimates and the corresponding HQ values. The Risk Quotient (RQ) values for the aquatic and soil compartments were 3.07E-10 and 4.75E-11, respectively. Thus, it can be concluded that any health or environmental risk from exposure to 2-BEB associated with potential air emissions from manufacturing and use scenarios will be negligible.

In summary, even with conservative assumptions and large production volumes, the anticipated HQs and RQs are substantially below 1, indicating low to minimal risk for human exposures and to the environment. As Dow will demonstrate in the analysis below, "there is adequate data on the health and environmental effects of the substance to determine that emissions, ambient concentrations, bioaccumulation or deposition of the substance may not reasonably be anticipated to cause any adverse effects to human health or adverse environmental effects." As such, the statutory standard for deleting a unique substance from the glycol ethers category in the HAP list has been satisfied and 2-BEB should therefore be delisted as a HAP.

I. THE STATUTORY CRITERIA FOR DELISTING

When Congress adopted the 1990 Amendments to the CAA, it placed 189 chemicals and chemical categories on the "initial list" of substances to be regulated as HAP. Congress recognized, however, that this initial list was not necessarily definitive, but should be reviewed and, if appropriate, revised based on the best available scientific information. Significantly, Congress acknowledged the possibility that some substances on the initial list should not be regulated as HAPs and authorized the Agency to remove substances from the original list.

Under CAA Section 112(b)(3), Congress established the criteria to be applied to add or remove chemicals from the HAP list. Under CAA Section 112(b)(3)(C), EPA is required to remove a substance from the HAP list "upon a showing" that:

> there is adequate data on the health and environmental effects of the substance to determine that emissions, ambient concentrations, bioaccumulation or deposition of the substance may not reasonably be anticipated to cause any adverse effects to the human health or adverse environmental effects. 42 U.S.C. § 7412(b)(3)(C).

The substantive standard for removing one or more unique chemical substances from a listed category (*e.g.*, glycol ethers) is the same. CAA Section 112(b)(3)(D), 42 U.S.C. § 7412(b)(3)(D).

A. Standard of Proof for Delisting

The standard for HAP delisting in Section 112(b)(3)(C) requires that there be "adequate" data to show that adverse effects to human health and the environment "may not reasonably be anticipated." As EPA has recognized, this standard does not require absolute proof that a substance will not cause adverse effects.

EPA does not interpret Section 112(b)(3)(C) to require absolute certainty that a pollutant will not cause adverse effects on human health or the environment before it may be deleted from the list. The use of the terms "adequate" and "reasonably" indicate that the Agency must weigh the potential uncertainties and their likely significance. *See* 66 Fed. Reg. 21929, 21930 (May 2, 2001).

In its evaluation of both the exposure data and health and environmental effects data, EPA should use a weight-of-the-evidence approach to determine whether it is "reasonable" to anticipate that emissions of 2-BEB will cause adverse health or environmental effects.

B. A Substance Should Not Be Retained as a Listed HAP Unless It Reasonably Can Be Anticipated to Cause Adverse Effects under Normal Conditions

At high exposure levels, virtually all chemicals can cause adverse health or environmental effects. Under Section 112(b)(3)(C), however, the inquiry is whether a substance's "emissions, ambient concentrations, bioaccumulation or deposition" can "reasonably be anticipated" to result in such effects. EPA must consider the exposure potential, not just the potential hazard, in deciding whether to delist a substance. If emissions of a listed substance are not reasonably expected to result in ambient levels, deposition, or bioaccumulation that reasonably can be anticipated to cause adverse health or environmental effects, then that substance meets the standard for delisting set forth at CAA Section 112(b)(3)(C) regardless of its toxicity.

2-BEB is unlikely to present any concern regarding occupational or accidental hazards, but occupational exposures and accidental chemical releases are not relevant to the statutory delisting criteria. CAA Section 112(b)(2) specifically states that accidental releases that are subject to regulation under Section 112(r) are not to be considered in HAP listing decisions. Likewise, workplace exposures are regulated by the Occupational Safety and Health Administration (OSHA), not EPA, and should not be a factor in making HAP delisting decisions. By excluding consideration of accidental releases or workplace exposure, EPA's analysis is

focused on the direct and indirect risks to the public from air emissions that are regulated under the CAA.

C. The CAA Authorizes EPA to Delist Specific Substances from Certain Listed Categories

Under CAA Section 112(b)(3)(D), EPA may delete specific substances from certain listed categories. Glycol ethers is one of the listed categories of compounds that are subject to substance-specific deletions.

EPA has on two prior occasions deleted specific substances from the glycol ethers category. In 2000, EPA issued a final rule deleting from the glycol ethers category a group of individual substances called the surfactant alcohol ethoxylates (SAED), and redefining the glycol ethers category accordingly. 65 Fed. Reg. 47342, 47348 (Aug. 2, 2000). The SAED group of substances was included in the original statutory definition of glycol ethers in the HAP list, which was incorporated in the CAA verbatim from the Emergency Planning and Community Right-to-Know Act (EPCRA), and EPA subsequently determined based on conservative worst-case assumptions that each individual substance in the SAED group has very low potential toxicity and very low exposure potential. In 2004, in response to a petition by the Ethylene Glycol Ethers Panel of the American Chemistry Council, EPA issued another final rule removing EGBE from the redefined glycol ethers category. 69 Fed. Reg. 69320, 69325 (Nov. 29, 2004). In 2004, 2-BEB was not yet in commercial production or use, and the 2004 rule did not include any ester of EGBE as a deleted substance. As a consequence, 2-BEB still is included within the definition of

glycol ethers, even though the available scientific evidence indicates that 2-BEB will consistently present lesser toxicity and lower exposures than EGBE.

To our knowledge, this petition to delete 2-BEB from the glycol ethers category represents a matter of first impression for EPA, because it constitutes the first instance where a newly introduced chemical substance is already defined as a listed HAP. Dow believes that 2-BEB is defined as a HAP solely as an unintended artifact of the current definition of the glycol ethers category, not because there is any substantive reason to conclude that emissions, ambient concentrations, bioaccumulation, or deposition of 2-BEB would present any potential health or environmental hazard.

II. DELISTING 2-BEB IS WARRANTED BASED ON ITS RELATIONSHIP WITH A PREVIOUSLY DELISTED SUBSTANCE

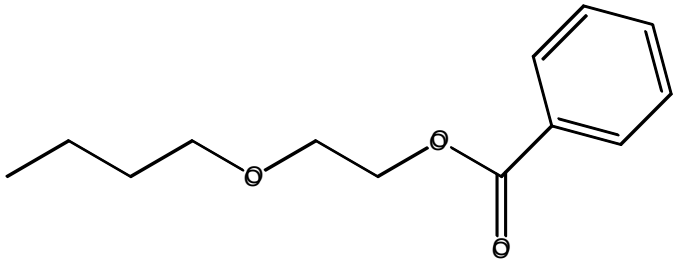
2-BEB forms EGBE (2-butoxyethanol) when hydrolyzed. As a derivative of and precursor to EGBE, there is a sound scientific basis for concluding that 2-BEB will also meet the criteria for HAP delisting. As noted in the following table comparing physical/chemical property data and toxicology classifications of 2-BEB and EGBE, there are added advantages when assessing the physical property data and the classifications associated with acute and chronic mammalian toxicology and environmental fate and effects data. 2-BEB is less likely to be evaporated to enter and reside in the atmosphere (*i.e.*, air) compartment in the environment, therefore, 2-BEB is less likely to have the characteristics of a HAP.

Table 1: Comparison of parameters between 2-BEB and EGBE			
Parameter	**2-BEB (CAS 5451-76-3)**	**EGBE (CAS 111-76-2)**	**2-BEB Advantaged or Equivalent to EGBE**
Vapor Pressure@ 20 degC	0.00029 mmHg	0.87 mmHg	YES
Evaporation Rate	0.0001	0.06	YES
Boiling Point	292 degC	171 degC	YES
Flash Point	146.2 degC	67 degC	YES
Water Solubility	<1% @ 25 degC	100% @ 25 degC	YES
Acute Oral Toxicity	Cat. 4	Cat. 4	YES
Acute Dermal Toxicity	not classified via GHS	Cat. 4	YES
Acute Inhalation	not classified via GHS	Cat. 4	YES
Eye Irritation	not classified via GHS	Cat 2A	YES
Skin Irritation	not classified via GHS	Cat 2	YES
Skin Sensitization	not classified via GHS	not classified via GHS	YES
Target Organ Toxicity	not classified via GHS	not classified via GHS	YES
In vitro/In Vivo Genotoxicity	not classified via GHS	not classified via GHS	YES
Carcinogenicity	not classified via GHS (based on read across)	not classified via GHS (tumors not relevant to humans)	YES
Reproductive Toxicity	not classified via GHS	not classified via GHS	YES
Aquatic Toxicity -- Acute and Chronic	Cat 2	not classified via GHS	NO
Biodegradation	Readily biodegradable	Readily biodegradable	YES

III. THE POTENTIAL FOR EXPOSURE TO 2-BEB IN THE ENVIRONMENT IS LIMITED DUE TO ITS PRODUCTION PROCESS AND END USE

A. Physical Characteristics

2-BEB has a molecular formula and weight of $C_{13}H_{18}O_3$ and 222.28, respectively, and its structural formula is depicted below. 2-BEB is a clear, colorless liquid with a very low vapor pressure and evaporation rate, along with a high boiling point. The vapor pressure is 0.00029 mmHg at 20 ^{o}C, relative evaporation rate of 0.00015 (butyl acetate = 1), and the boiling point is 292 ^{o}C. These and other physical properties are summarized in the Technical Data Sheet (Attachment 1).



B. 2-BEB's Production and Use Limits Its Environmental Releases

1. Projected Uses of 2-BEB

Laboratory tests have demonstrated that 2-BEB is a highly efficient coalescing aid for latex emulsion based on acrylic, styrene-acrylic, and other polymers that are typically used in the formulation of water-based architectural and industrial coatings. In these formulations, 2-BEB helps to achieve the desired minimum film formation temperatures (MFFT) at lower concentrations (1 - 2% by weight of the paint) than those required with other commercial coalescents (2 - 4%). This translates into fewer solvent emissions and lower VOC from paints.

Paints with lower coalescent concentrations can also have much lower odor, a benefit that is highly appreciated by painters and consumers.

Laboratory tests have also shown that 2-BEB can be 25 - 40% more efficient than BBP or DINP at lowering the glass transition temperature (Tg) of typical water-based acrylic latexes when used as plasticizers in the formulation of water-based caulking compounds. This translates into nearly half the volume of plasticizer required to achieve the same low temperature properties specified for the products. Water is used to make up the volume lost in the formulation by the reduction in the plasticizer concentration.

Given the general industry effort to replace phthalates and less efficient coalescents in the aforementioned formulations, various products have been introduced or will be introduced in these markets. 2-BEB is aimed at filling the need in niche applications within these markets, and it is not anticipated to become a high volume chemical; perhaps reaching a sales volume of about 5 million pounds a year by 2028. The default classification of 2-BEB as a HAP based on its chemical structure, however, is a significant commercial barrier to material substitution by those coatings formulators. Dow is seeking deletion of 2-BEB from the glycol ethers category not because use of 2-BEB would require new emission controls, but because customers strongly prefer to avoid using any listed HAP in manufacturing or formulating their products.

2. Production Volume

All volume of 2-BEB (about 200,000 pounds) produced to date since 2016 has been for export, since 2-BEB is exempt from VOC status outside of the U.S. No sales have

currently taken place in the U.S. due to the current HAP listing. As aforementioned, 2-BEB is expected to fill the need in niche applications, and it is not expected to become a high volume chemical in the U.S. Details for the production process and associated potential emissions are given in Section VI.

IV. 2-BEB CANNOT REASONABLY BE ANTICIPATED TO CAUSE ADVERSE ENVIRONMENTAL EFFECTS

Under CAA Section 112(b)(3)(C) and 112(b)(3)(D), EPA must consider whether emissions of a substance may reasonably be anticipated to cause "adverse environmental effects." The CAA defines "adverse environmental effect" as:

> any significant and widespread adverse effect, which may reasonably be anticipated, to wildlife, aquatic life, or other natural resources, including adverse impacts on populations of endangered or threatened species or significant degradation of environmental quality over broad areas. CAA Section 112(a)(7), 42 U.S.C. § 7412(a)(7).

As discussed below, 2-BEB emissions clearly do not cause "significant or widespread" adverse effects on the environment.

A. 2-BEB Does Not Persist in the Environment

Experimental data on 2-BEB indicate that it is readily biodegradable and thus, would not be expected to persist in the environment (*see* Attachment 2). Two tests have been conducted according to the "OECD, Guidelines for the Testing of Chemicals. Ready Biodegradability 301 F: Manometric Respirometry Test, 1992." Both tests concluded that 2-BEB

met the criteria to be considered readily biodegradable. The 10-day window for ready biodegradability was met with >60% biodegradation within 4 days of the start of biodegradation (test 1) and 91% biodegradation within 10 days of the start of biodegradation (test 2), respectively. In both cases, the test substance was fully degraded by the end of the 28-d incubation. Therefore, 2-BEB can be classified as "readily biodegradable" and would not be expected to persist in the aquatic environment.

Estimated data from environmental modeling also indicate a short residence time for 2-BEB in the environment. Modeling data presented in Appendix B of Attachment 2 estimate degradation half-lives of 11.8 hours, 82.8 hours, and 166 hours in air, water, and soil, respectively. Additional modeled data from the EPA Comptox Dashboard for the water compartment calculated a similar aqueous half-life of 112 hours.

Based on the available information, 2-BEB is not expected to persist in the environment and therefore not expected to pose a chronic hazard.

B. 2-BEB's Potential for Bioaccumulation Is Low

The available information demonstrates that 2-BEB is not expected to bioaccumulate in the environment (*see* Attachment 2). The EPA Comptox Dashboard tool was employed to evaluate the bioconcentration and subsequent bioaccumulation potential of 2-BEB. A measured log K_{ow} value of 3.37 was determined at 30 °C but due to lack of temperature dependence data on K_{ow}, calculation of a value at 20 °C was not possible. The EPA Comptox

Dashboard predicted an average log K_{ow} of 3.09 with a range of 2.59 to 3.37. The Dashboard tool also predicted a bioconcentration factor (BCF) and a fish biotransformation half-life for 2-BEB. The predicted BCF value was 11.9, with a range of 10.7 to 13.6. A separate BCF value of 46.2 L/kg was predicted using the BCFBAF v3.01 model in the EPA EPI Suite tool.

In addition, the Dashboard tool estimated a fish biotransformation half-life of 0.778 days. The predicted log K_{ow} values indicate 2-BEB would be of low to moderate bioconcentration potential. Estimated air, water, soil, and sediment half-lives of 11.8, 82.8, 166, and 745 hours, respectively, are presented in Appendix B of Attachment 2, indicating fairly rapid dissipation of 2-BEB in the environment. The EPA Comptox Dashboard calculated a similar aqueous half-life of 112 hours (4.67 days). Considering the predicted BCF values (11.9 - 46.2) and fish biotransformation half-life, in conjunction with a lack of persistence in the environment (*i.e.*, ready biodegradability, short predicted half-lives in environmental media), 2-BEB would not be expected to bioaccumulate in the aquatic or terrestrial food chain and therefore would not constitute a chronic hazard to ecological receptors.

C. 2-BEB's Environmental Risk Is Low

An evaluation of the potential for exposure and risk was conducted for 2-BEB to evaluate the potential for environmental effects as a result of future releases of 2-BEB to the air (*see* Attachment 2). A risk characterization phase brings together information on the chemical stressors, potential effects, and ecological receptors to clarify these relationships and identify the potential areas of risk concern, *i.e.*, reach conclusions regarding the occurrence of exposure and the adversity of anticipated effects. Thus, the results of the analysis phase (exposure and effect)

are integrated to yield an estimate of potential risk resulting from exposure to 2-BEB from manufacturing emissions.

Equilibrium partitioning (EQP) modeling based on manufacturing and use volumes, estimated potential worst-case exposure estimates for air, water, soil, and sediment compartments resulting from projected releases to air under the prescribed scenario. The exposure estimates for all these compartments were 5.43E-14 g/m^3, 2.02E-12 mg/L, 1.19E-10 mg/kg dw, and 2.31E-11 mg/kg dw, respectively. These estimates are extremely low and no risk can be anticipated based on these estimates and the ecotoxicity values available for 2-BEB. For this screening level risk characterization, however, risks to aquatic and terrestrial receptors were calculated to demonstrate the negligible risk.

According to standard screening level risk methodologies, risk was evaluated by comparing the estimated environmental concentrations with derived predicted no effect concentration (PNEC) values (ratio of exposure/toxicity). The resulting RQs describe the potential for ecological risks. Using PNECs, which incorporate sufficient safety factors based on the available data set, a level of concern of one is set. Where RQs are less than one, it can be concluded that ecological risks are unlikely to occur. RQs greater than one suggest the potential for adverse effects to individual organisms. As indicated earlier, the purpose of a screening level risk assessment is to identify areas of potential for risk for further consideration. An RQ that exceeds one cannot be inferred to indicate that harm will occur to individuals, populations, or communities but helps to focus resources for further evaluation (*e.g.*, higher tier assessment, additional data needs, etc.). The resulting RQ values for the aquatic and soil compartments were

3.07E-10 and 4.75E-11, respectively. Thus, it can be concluded that potential environmental risk from exposure to 2-BEB resulting from air emissions under manufacturing and use scenarios will be negligible.

V. THE PROPOSED RfC FOR 2-BEB IS THE THRESHOLD BELOW WHICH NO ADVERSE HEALTH EFFECTS ARE REASONABLY EXPECTED

There is at present no RfC established by EPA for 2-BEB. There is, however, an RfC established for EGBE, which due to its direct relationship to 2-BEB via metabolism (*see* Attachment 3), can be used in one method for determining a proposed RfC for 2-BEB. The RfC for EGBE offers a highly conservative health benchmark for setting the RfC value for 2-BEB to evaluate whether its emissions may reasonably be expected to cause adverse human health effects. Another way to derive a proposed RfC for 2-BEB is to utilize studies performed with 2-BEB and adjusted by the inclusion of uncertainty factors (UF). Using either method, 2-BEB does not pose an unreasonable risk to human health for the reasons set forth below.

A. 2-BEB's Health Effects Are Well Understood

Available toxicological data on 2-BEB include:

- A radiolabeled pharmacokinetic study;
- A subchronic toxicity study, including toxicokinetics;
- A rat developmental study, including toxicokinetics;
- A repeated dose, reproductive, and developmental probe study, including toxicokinetics;

- Several mutagenicity studies, including bacterial, mammalian cell, and in vivo studies;
- Oral, dermal, and inhalation acute toxicity studies; and
- Skin and eye irritation, and sensitization studies.

A summary of the toxicology studies performed on 2-BEB are in Attachment 4.

B. Route of Potential Human Exposure to Ambient 2-BEB Emissions

CAA Section 112(b)(2) indicates that, in making listing decisions, the Agency should consider whether a substance may reasonably be anticipated to cause adverse effects "through inhalation or other routes of exposure." Due to the low vapor pressure of 2-BEB (0.00029 mmHg), deposition of 2-BEB in water will also be a source of exposure. This deposition into water will lead to potential dermal and oral exposure after release from the manufacturers/formulators.

C. Potential Human Health Effects

The primary effect seen in laboratory rodents after exposure to 2-BEB was hematotoxicity. This toxicity is the same effect seen in laboratory rodents after treatment with EGBE. Based on pharmacokinetic/toxicokinetic studies with 2-BEB, it has been shown that 2-BEB is rapidly metabolized to EGBE in the body of mammals (*see* Attachment 3). EGBE induced hemolysis has been extensively studied in many different species, which has shown that humans are at least 10x less susceptible to this hemolysis than laboratory rodents (like rats and

mice) (Attachment 5). Based on this, the hematotoxicity seen in rats after 2-BEB treatment is expected to exhibit the same difference in sensitivity in humans as EGBE.

1. 2-BEB Cannot Reasonably Be Expected to Pose a Risk of Carcinogenicity

2-BEB is non-genotoxic and does not show any evidence of pre-neoplastic lesions in repeated dose studies. No carcinogenicity study has been conducted for 2-BEB. As mentioned above, however, 2-BEB readily metabolizes to EGBE and benzoic acid in the mammalian body. Sodium benzoate (the sodium salt of benzoic acid) and EGBE have carcinogenicity data. In the EPA Integrated Risk Information System (IRIS) document for EGBE (US EPA, 2010), it indicates for both oral and inhalation exposures that doses of EGBE below the RfD/RfC would not be expected to produce an increased cancer risk. Sodium benzoate, which is considered Generally Recognized As Safe (GRAS) by the U.S. Food and Drug Administration (FDA), had a drinking water study performed at 0 and 2% (corresponding to a dose of up to 6,200 mg/kg-day) and had no effect on survival rate when compared to controls and no pathological or statistical evidence of tumor induction (Toth, 1984). Therefore, 2-BEB is not expected to pose a risk of carcinogenicity.

D. The RfC Is Extremely Conservative and Is Considered Protective of Human Health

The primary finding in rodents with 2-BEB is hemotoxicity (hemolysis) which is consistent with the primary toxicity for EGBE, the main initial metabolite of 2-BEB (along with benzoic acid). An IRIS RfC and RfD value for EGBE was derived in 2010. The IRIS record for EGBE is located in Attachment 6. The RfC and RfD for EGBE can be used to derive

corresponding values for 2-BEB (*see* Attachment 3). In the alternative, a proposed, RfC and RfD can be derived from 2-BEB studies using the appropriate UFs (*see* next section).

According to the EPA definition, the RfC/RfD is the concentration/dose of a pollutant which the human population, including sensitive subgroups, can continuously inhale or ingest on a daily exposure, and is likely to be without any appreciable risk of deleterious effects during a lifetime (IRIS website). The EGBE values were derived using benchmark dose, 95% lower bound, based on hemosiderin accumulation in the liver which is secondary to hemolysis. A UF of 10 was used to include a safety factor for intraspecies variability (sensitive subpopulations). The basis for derivation of the RfC/RfD for 2-BEB is explained below.

E. Derivation of RfC and RfD for 2-BEB

2-BEB currently does not have a RfC or RfD derived for it. Therefore, two possible ways to derive these values are presented: (1) using data from 2-BEB toxicology studies, and (2) using molar correction of the EGBE RfC and RfD.

1. Approach 1: 2-BEB Data

UFs

UF = 90

$= 10(UF_H) \times 3(UF_A) \times 1(UF_S) \times 1(UF_L) \times 3(UF_D)$

A UF of 10 was selected associated with the variability of the human response uncertainty (UF_H) to the effects of 2-BEB to match that used for EGBE RfD determination. The selection of a UF of 10 is based on the potential susceptibility of subpopulations, including people with enhanced metabolism or lower excretion of BAA (butoxyacetic acid) (cause of hemolysis) and people whose red blood cell (RBC) membranes have higher sensitivity to BAA-induced lysis. In vitro studies with human RBC from the elderly and patients with fragile RBCs have shown they would not be more sensitive to the hemolytic effects of EGBE (BAA) than normal adults. Animal studies suggest that neonates are less sensitive than older animals and females are more sensitive than males. Studies of the developmental toxicity of 2-BEB and EGBE do not show increased susceptibility of pups, although none of the studies examined fetal/pup blood for signs of hemolytic effects for either compound. Finally, humans who have been exposed over a broad range of conditions, along with potential sensitive subjects, have not had observed responses to EGBE.

A UF of 3 was selected to account for the uncertainty associated with interspecies variability resulting from toxicokinetic and toxicodynamic differences between animals and humans (UF_A). A partial UF of 3 was selected for toxicokinetics because the rat no observed adverse effect level (NOAEL) could not be converted to a human equivalent in the absence of a physiologically based pharmacokinetic (PBPK) model for 2-BEB. A value of 1 is used for the toxicodynamic portion since several studies have been performed indicating that humans are significantly less susceptible than rats to the hemolytic effects of BAA (Carpenter et al., 1956; Ghanayem and Sullivan, 1993; Udden, 2000; Udden and Patton, 1994). There has also been a

number of accidental exposures and poisoning reported that have shown the hemolytic potential of EGBE (major metabolite of 2-BEB) in humans occurs only at very high doses (Bauer et al., 1992; Butera et al., 1996; Burkhart and Donovan, 1998; Dean and Krenzelok, 1992; Gijsenbergh et al., 1989; Gualtieri et al., 1995; Gualtieri et al., 2003; Hung et al., 2010; McKinney et al., 2000; Rambourg-Schepens et al., 1988).

A UF to account for extrapolation from subchronic to chronic exposure (UF_S) was not needed because the effect used as the basis of the RfC/RfD, hemolysis, does not increase with longer exposure. Pre-treatment of animals to EGBE gives a "protective" effect by shifting the average age of reticulocytes to be younger, which is what happens with longer exposures (Sivarao and Mehendale, 1995). This can also be seen when comparing the hematology endpoints between the shorter OECD 422 study and the 90-day treatment with 2-BEB.

A UF to account for the extrapolation from a lowest observed adverse effect level (LOAEL) to a NOAEL (UF_L) was not applied because the RfC was derived using a NOAEL.

A UF of 3 was selected to account for deficiencies in the database (UF_D). 2-BEB is missing a chronic study and also subchronic studies in a second species, however, since 2-BEB is rapidly metabolized to EGBE and benzoic acid, read-across can be used to fill the data gaps (*see* Attachment 3 for justification).

RfC

There are no repeated dose inhalation studies performed on 2-BEB due to its low volatility. To generate a RfC value, since one does not exist, data from an oral repeated dose study will be utilized. The NOAEL for both the OECD 422 and 90-day studies is 1500 ppm 2-BEB in diet. The effects seen in the OECD 422 were lower body weights and hematology effects (representative of regenerative anemia) in females and in the 90-day study lower body weights in females. The average exposures at the NOAEL over the full OECD 422 and 90-day studies were calculated to be 117 and 94.9 mg/kg-bw/day, respectively. Therefore, the NOAEL value being used as the point of departure to derive the RfC will be 100 mg/kg-day. During the 90-day study, the 1500 ppm NOAEL females had body weight gains either similar to or higher than the control animals whether the mg/kg-day dose was above or below 100, therefore, 100 mg/kg-day is being used. There is no PBPK model for 2-BEB; therefore, the NAOEL value cannot be converted from a rat dose to a human exposure concentration via a model. Based on the PBPK model for EGBE, for inhalation, the dose needed for humans is higher than rats to get the same blood concentration for the main metabolite BAA. Therefore, using the rat NOAEL dose to determine the RfC would provide a more conservative estimate. So, the air concentration that would provide a 70 kg person, who breathes 20 m^3 of air (US EPA, 1994), that amount of daily intake is 350 mg/m^3 as follows:

$$Air\ HEC_{NOAEL} = Oral\ HED_{NOAEL} \times 70\ kg \div (day/20m^3)$$

$$= (100\ mg / kg - day) \times 70\ kg \div (day/20m^3) = 350\ mg / m^3$$

$$RfC = Air\ HEC_{NOAEL} \div UF$$

$$= 350\ mg / m^3 \div 90 = 3.9\ mg / m^3$$

RfD (oral and dermal)

A RfD for oral and dermal is needed due to the potential for 2-BEB emissions released from manufacturers or formulators to deposit into water. The RfD is derived based on the oral toxicity studies for 2-BEB. As explained in the previous section, the point of departure for oral toxicity is 100 mg/kg-day, therefore, the RfD will also be 100 mg/kg-day (Oral/Dermal HED_{NOAEL}). To convert the oral value into a dermal value, the dermal absorption factor (AF) is used. Based on the predicted 82.4% permeability using IH SkinPerm, a conservative 100% absorption will be used.

$$RfD_{oral} = Oral\ HED_{NOAEL} \div UF$$

$$= 100\ mg/kg\text{-}day \div 90 = 1.1\ mg/kg\text{-}day$$

$$RfD_{dermal} = RfD_{oral} \text{ X } AF$$

$$= 1.1\ mg/kg\text{-}day \text{ X } 1.0 = 1.1\ mg/kg\text{-}day$$

2. Approach 2: EGBE RfC Molar Equivalent

RfC

Since 2-BEB is metabolized rapidly into EGBE (and benzoic acid), a conservative RfC would be to convert the EGBE RfC (1.6 mg/m^3) (US EPA, 2010) to the molar equivalent of 2-BEB. Using this method, the RfC for 2-BEB would be 3.0 mg/m^3.

2-BEB Inhalation *RfC* = EGBE Inhalation *RfC* X (2-BEB *MW*/EGBE *MW*)

= 1.6 *mg* / m^3 X (222.28/118.2) = 3.0 *mg* / m^3

RfD (oral and dermal)

Since 2-BEB is metabolized rapidly into EGBE (and benzoic acid), a conservative RfD would be to convert the EGBE RfD (0.1 mg/kg-day) (US EPA, 2010) to the molar equivalent of 2-BEB. To convert the oral RfD into a dermal value, the dermal AF is used. Based on the predicted 82.4% permeability using IH SkinPerm, a conservative 100% absorption will be used. Based on this method, the RfD for 2-BEB would be 0.19 mg/kg-day.

RfD_{oral} = EGBE Oral *RfD* X (BEB *MW*/EGBE *MW*)

= 0.1 *mg*/*kg-day* X (222.28/118.2) = 0.19 *mg*/*kg-day*

$RfD_{dermal} = RfD_{oral}$ X AF

= 0.19 *mg*/*kg-day* X 1.0 = 0.19 *mg*/*kg-day*

F. The RfC Is an Appropriate Threshold to Use in a Delisting Petition

EPA has recognized the appropriateness of relying on an RfC when reviewing substances proposed for HAP delisting. In the context of its review of methanol, EPA noted that:

> Usually the RfC is considered protective of all noncancer adverse health effects. Therefore, exposures at or below the RfC are generally not expected to result in any adverse noncancer health effects. (66 Fed. Reg. 21929, 21939 (May 2, 2001).)

The proposed RfC/RfD for 2-BEB is conservative for the reasons discussed above, and there is no scientific reason to believe that exposures below the proposed RfC/RfD pose health hazards. Thus, it is appropriate to use the proposed RfC/RfD as a health benchmark below which exposures to 2-BEB will not likely cause adverse health effects.

VI. MANUFACTURING AND PROCESSING OF 2-BEB

A. Approach to Estimate Exposure

Since 2-BEB is a chemical intended for prospective substitution in water-based coatings, there are no emissions or monitoring data available that are pertinent to the manufacture, use, and release of 2-BEB. In lieu of such emission/monitoring data, models can be utilized to estimate the worst-case release into the environment from unit operations and resulting exposures to the community. Worst-case estimates have previously been used by EPA when it promulgated a rule deleting the SAED compounds from the glycol ethers category.

One model that provides conservative emissions estimates is the US EPA's Chemical Screening Tool for Exposures and Environmental Releases (ChemSTEER) model. ChemSTEER is a computer-based software program developed by EPA's Office of Pollution Prevention and Toxics (OPPT) that can be used to conduct a screening-level workplace exposure and release assessment. This model is appropriate because it was developed by EPA as a screening tool for newly introduced chemical substances. ChemSTEER generates screening-level estimates for environmental releases of and worker exposures to a chemical manufactured and

used in industrial and commercial operations (*i.e.*, workplaces). The model's default emission factors were used to estimate emissions to air and water except when required to estimate the vapor generation rate. Methodology to calculate the vapor generation rate is provided separately below.

ChemSTEER does not include methods for estimating exposures to chemicals to the general public, to consumers, or to other species in the environment. To assess exposures to the general public and consumers, another US EPA model was used, Exposure and Fate Assessment Screening Tool (E-FAST V2.0). E-FAST V2.0 is a screening-level computer tool that allows users to estimate chemical concentrations in water to which aquatic life may be exposed, as well as generate human inhalation, drinking water ingestion, and fish ingestion exposures resulting from chemical releases to air, water, and land. Here, E-FAST V2.0 was used to estimate the maximum ground-level air concentrations. The exposed populations assessed by the model are either some segment of the general population or consumers. Because E-FAST V2.0 incorporates defaults of either a combination of upper percentile and mean exposure parametric values or all upper percentile parametric values, the exposure/dose estimates are considered to be conservative high-end estimates. E-FAST V2.0 is appropriate for use as a screening tool to assess potential exposures from chemical discharges to air (stack or fugitive releases), surface water, or land.

E-FAST V2.0 uses EPA's SCREEN3 Model for estimating ambient air concentrations from stack and fugitive releases. SCREEN3 is a single source Gaussian plume model that provides maximum ground-level concentrations for point, area, flare, and volume

sources, as well as concentrations in the cavity zone, and concentrations due to inversion break-up and shoreline fumigation. To maximize the ground-level concentrations of 2-BEB, it was assumed that all emissions are fugitive and that no control techniques are applied to reduce the emissions. Thus, if 2-BEB is used by any facility with existing emission controls, the resultant emission estimates will be conservative. The model default parameters were used in the emissions model.

In SCREEN3, stability and wind speed are the two most important parameters of meteorological conditions that affect ambient pollutant concentrations emitted from an elevated stack. In this modeling, it was assumed that all emissions are released as fugitive and not from a point source or stack. For simple elevated or flat-terrain screening, which is what was selected in this modeling exercise, there are three choices of meteorological conditions: (1) full meteorological description, including all stability classes and wind speeds; (2) specification of a single stability class; and (3) specification of both stability class and wind speed. Full meteorology, selected for this modeling, is recommended for a combination of stability and wind speed that will result in maximum ground-level concentrations.

For land use, the default value is rural. The selection of an urban or rural land use parameter dramatically affects the estimate of concentrations by giving a different wind speed profile at the same stability category. If more than 50% of an area 3 km around the source is of land use types heavy or medium industrial, commercial, or multi-family residential, the site is deemed to be in an urban setting. In this model, the land selection was set to urban. It is expected that in both the manufacturing and process scenarios, since the operations are expected to be in

industrial areas, the option best suited for land use is an urban setting. Urban land use type results in a higher estimate of ground-level concentration.

Air quality models are most accurate when simulating long-term averages in areas with relatively simple topography. Terrain sometimes significantly affects ambient ground-level pollutant concentrations through its effects on plume behavior. The important topographic features to note are the location and height of the elevated terrain. SCREEN3 uses two types of terrain: simple or complex. Simple terrain is considered to be an area where terrain features are all lower in elevation than the top of the stack of the source(s) in question. Complex terrain is defined as terrain exceeding the height of the stack being modeled. If terrain height is higher than stack height, the modeling techniques required to simulate such a situation become more demanding. Because of the potential for providing inappropriate information in such a circumstance, only the simple terrain option of SCREEN3 has been incorporated into E-FAST V2.0.

In summary, default emission estimates generated by ChemSTEER were fed into E-FAST to estimate maximum ground-level air concentrations and were combined with the EQuilibrium Criterion (EQC) model to estimate the contributions into water bodies. Based on these concentrations, exposure estimates were generated for expected exposure pathways and compared to the proposed RfCs and/or RfDs.

B. Manufacture of 2-BEB

2-BEB is manufactured in an enclosed reactor with the following unit operations. The unit operations described below are expected to be part of the manufacturing process and thus emissions from these unit operations are estimated.

1. Aqueous Wash of Organic Mass

The aqueous wash of organic material containing the chemical is the activity in which the chemical is transferred from the organic material into the aqueous phase. The amount of chemical that is transferred into the aqueous phase is estimated based on its water solubility, by default. This activity uses default models to estimate the release of the chemical and worker exposure to the chemical.

2. Distillation Column Bottoms Disposal

This activity is the disposal of waste collected from distillation column bottoms that contains the chemical, which is estimated to result primarily in the release of the chemical.

3. Sampling of Liquid Product

This activity is the sampling of liquids that results in a release of the chemical and/or worker exposure to the chemical.

4. Loading of Liquid Product into Drums

The activity is loading of liquid product or raw material into transport containers/vessels that results in a release of the chemical and/or worker exposure to the chemical.

5. Equipment Cleaning Losses of Liquids from Multiple Vessels

This activity is the cleaning of product residues from one or more process vessels with a liquid cleaning medium that results in a release of the chemical and/or worker exposure to the chemical.

The schematic shows the different activities and potential releases to air, water, or both media types from manufacturing operations. The projected maximum production volume of 2-BEB is expected to be 275,000 kg/yr. The approximate production time is 48-50 hours per batch and total quantity of 2-BEB will be manufactured in approximately 10 batches. Thus, the approximate production time for the entire quantity of 2-BEB will range from 480-500 hours. Distillation bottoms are incinerated and, thus, minor releases from manufacturing operations to the environment are expected. For this screening level assessment, however, it was assumed that distillation bottoms are not incinerated and rather discharged into water. This is an extremely conservative assumption.

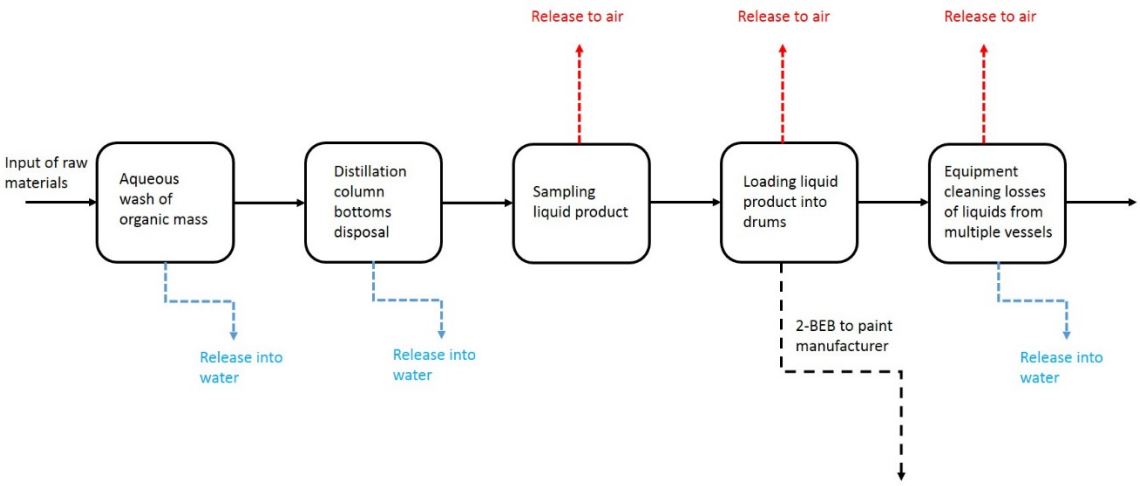


Figure 1. Simplified Process Flow Diagram for the Manufacturing of 2-BEB

C. Incorporation (Processing) of 2-BEB into Water-Based Paints

These unit operations are unique to a vendor that will utilize 2-BEB in the production of water-based paints. Due to the variability associated with the manufacture of paints, a generic description of the water-based paint manufacturing process was used to identify activities that would result in releases of 2-BEB to the environment. Although unit operations will vary depending on the paint formulator, the following set of generic unit operations provides a reasonable estimate of 2-BEB release. The unit operations are listed and described below:

1. Unloading Liquid Raw Material from Drums

This activity is the unloading of liquid product or raw material from transport containers/vessels that results in a release of the chemical and/or worker exposure to the chemical.

2. Vapor Release from Open Liquid Surfaces

This activity is the release of chemical vapors as a result of a pool of volatile liquid or other liquid surface that is open to the environment.

3. Sampling Liquid Product

This activity is the sampling of liquids that results in a release of the chemical and/or worker exposure to the chemical.

4. Loading Liquid Product into Drums

This activity is the loading of liquid product or raw material into transport containers/vessels that results in a release of the chemical and/or worker exposure to the chemical.

5. Equipment Cleaning Losses of Liquids from Multiple Vessels

This activity is the cleaning of product residues from one or more process vessels with a liquid cleaning medium that results in a release of the chemical and/or worker exposure to the chemical.

6. Cleaning Liquid Residuals from Drums Used to Transport the Raw Material

This activity is the cleaning of raw material or product residues from "empty" transport containers/vessels with a liquid cleaning medium that results in a release of the chemical and/or worker exposure to the chemical. This release source/worker activity is also relevant to the disposal of liquid residues with the empty container/vessel.

The schematic shows the different activities and potential releases to air, water, or both media types from processing (paint formulation) operations. The projected maximum usage volume of 2-BEB is expected to be 265,000 kg/yr (total production volume less emission during manufacturing). In the absence of specific information, it is expected that paint formulation or processing of 2-BEB will occur over 50 weeks/yr x 5 days/week x 8 hrs/day = 2,000 hrs/yr.

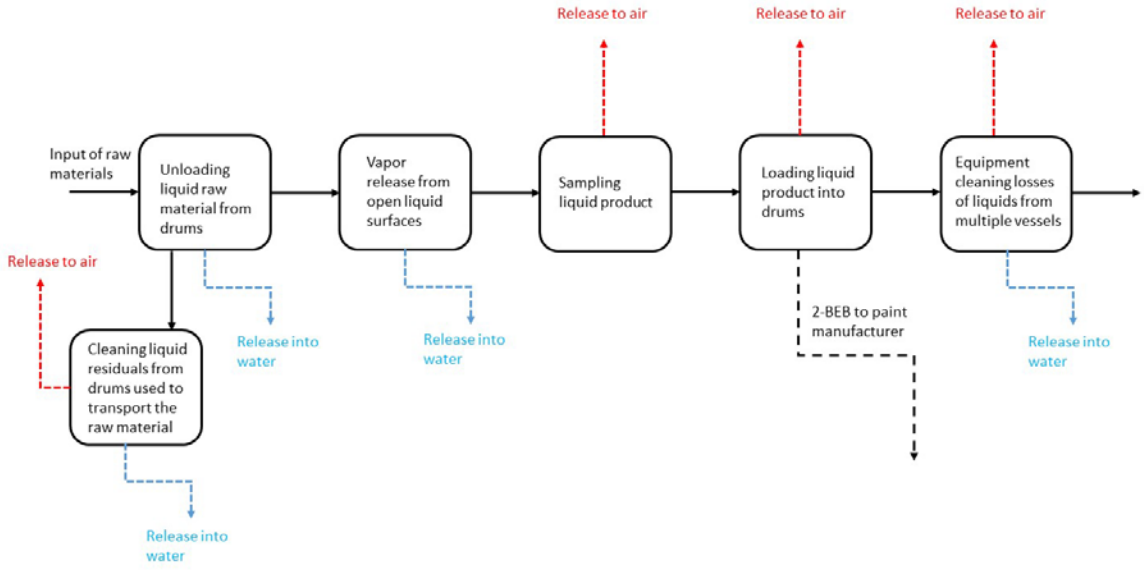


Figure 2. Simplified Process Flow Diagram for the Processing (Paint Formulation) of 2-BEB

D. Environmental Releases of 2-BEB

1. Emissions Releases from Manufacturing of 2-BEB

Based on the unit operations involved in the manufacture of 2-BEB and default values provided in ChemSTEER, emission estimates were determined.

As discussed above, the Chemical Screening Tool for Exposures and Environmental Releases (ChemSTEER, v3.0)[1] is a computer-based software program developed by EPA OPPT that can be used to conduct a screening-level workplace exposure and release assessment. ChemSTEER generates screening-level estimates for environmental releases of and worker exposures to a chemical manufactured and used in industrial and commercial operations (*i.e.*, workplaces). The tool also contains data and estimation methods to assess chemical use in common industrial/commercial sectors (*e.g.*, automotive refinishing) and chemical functional uses (*e.g.*, tackifier in adhesive). ChemSTEER does not contain methods for estimating exposures to chemicals to the general public, consumers, or other species in the environment.

ChemSTEER was developed for technically knowledgeable users to support EPA in assessing the potential exposures and risks to chemicals. A primary application is for assessing new chemicals that are submitted to EPA under Section 5 of the Toxic Substances Control Act (TSCA). ChemSTEER's methods and models are primarily intended to assess common sources of workplace releases and activities with worker exposure potential that are specific to a particular

[1] Available at https://www.epa.gov/tsca-screening-tools/chemsteer-quick-start-guide-and-user-guide-tsca-predictive-screening-tool.

industry and other sources of workplace releases and activities with worker exposure potential that are "broadly applicable" across many workplaces. The "broadly applicable" sources/activities available in ChemSTEER are only a subset of all possible sources and activities and cover the sources/activities that are often overlooked or considered to be non-routine or insignificant. The methods and models in ChemSTEER have undergone internal EPA review and most have been used extensively in EPA assessments for over ten years.

a. Aqueous Wash of Organic Mass

Release of the chemical to non-air media with the aqueous phase is calculated using the EPA/OPPT Water Saturation Loss Model. No default model exists for releases to air from this source in ChemSTEER. OPPT assumes that releases to air from this source are insignificant when compared to other sources.

b. Distillation Column Bottoms Disposal

Release of the chemical to the environment with the disposal of distillation column bottoms waste is calculated using the User-Defined Loss Rate Model.

c. Sampling of Liquid Product

It is assumed that these activities are performed indoors (*i.e.*, air speed is $\leq$ 100 feet/min) and the EPA/OPPT Penetration Model is used as a default for releases to air. No default

model exists for releases to non-air media from these sources in ChemSTEER. OPPT assumes that releases from these sources are insignificant when compared to other sources.

d. Loading of Liquid Product into Drums

All sources/activities involving loading liquids into transport containers/vessels use the EPA/OAQPS AP-42 Loading Model as the default for calculating releases of a volatile chemical to air. The EPA/OAQPS AP-42 Loading Model estimates releases to air from the displacement of air containing chemical vapor as a container/vessel is filled with liquid. This model determines a vapor generation rate (G) based in part upon the chemical's physical-chemical properties and assumes that the rate of evaporation is negligible compared to the loss from displacement.

e. Equipment Cleaning Losses of Liquids from Multiple Vessels

The amount of chemical release into the air from this source is thus calculated using the EPA/OPPT Mass Transfer Coefficient Model. Release of the residual product contained in multiple vessels into water is calculated using the EPA/OPPT Multiple Process Vessel Residual Model.

Emissions for releases to water and air are obtained from Attachment 8, Emissions from Manufacturing.

Table 2. Release of 2-BEB into Air from Manufacturing Activities					
Stage	Activity	Emissions Release Model	Release into Media	Typical Emissions (kg/site yr)	Worst Case Emissions (kg/site yr)
Manufacturing	Sampling Liquid Product	EPA/OPPT Penetration Model	Air	8.10E-07	6.50E-06
Manufacturing	Loading Liquid Product into Drums	EPA/OAQPS AP 42 Loading Model	Air	4.70E-04	9.30E-04
Manufacturing	Equipment Cleaning Losses of Liquids from Multiple Vessels	EPA/OPPT Mass Transfer Coefficient Model	Air	1.80E-03	1.80E-03
			Total	2.27E-03	2.74E-03

Table 3. Release of 2-BEB into Water from Manufacturing Activities					
Stage	Activity	Emissions Release Model	Release into Media	Typical Emissions (kg/site yr)	Worst Case Emissions (kg/site yr)
Manufacturing	Aqueous Wash of Organic Mass	EPA/OPPT Water Saturation Loss Model	Water	2.40E+01	2.40E+01
Manufacturing	Distillation Column Bottoms Disposal	User Defined Loss Rate Model	Water	5.50E+03	5.50E+03
Manufacturing	Equipment Cleaning Losses of Liquids from Multiple Vessels	EPA/OPPT Multiple Process Vessel Residual Model, CEB standard 2% residual	Water	5.50E+03	5.50E+03
			Total	1.10E+04	1.10E+04

Thus, the total mass is reduced by 1.1E4 kg/yr, and the amount of 2-BEB sent to the paint formulator is 275,000 kg/yr - 11,000 kg/yr ≈ 265,000 kg/yr.

2. Emissions Releases from Incorporation (Processing) of 2-BEB into Water-Based Paint

a. Unloading Liquid Raw Material from Drums

The EPA/OAQPS AP-42 Loading Model is the default for calculating releases of the chemical to air during unloading. It is assumed that as the container is unloading, another is being loaded. The default model provides a conservative estimate of chemical releases that occur during this activity. No default model exists for releases to non-air media from this source in ChemSTEER. OPPT assumes that releases from this source are insignificant when compared to other sources.

b. Vapor Release from Open Liquid Surfaces

Release of the chemical to air is calculated using the User-Defined Vapor Generation Rate Model as a default. No default model exists for releases to non-air media from this source in ChemSTEER. OPPT assumes that releases from this source are insignificant when compared to other sources.

As per EPA,[2] the rate of vaporization of a liquid can be modeled as a function of several characteristic factors of the compound being considered (Crowl and Louvar, 2002).

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[2] EPA, Methods for Estimating Air Emissions from Paint, Ink, and Other Coating Manufacturing Facilities (Feb. 2005).

$$E_{n-i} = \frac{M_i K_i A\left(P_i^{sat} - P_i\right)}{RT_L}$$

Where

- E_n is the evaporation rate (mass/time).
- M_i is the molecular weight of the volatile substance,
- K_i is a mass transfer coefficient (length/time),
- A is the evaporation surface area,
- P_i^{sat} is the saturated solvent vapor pressure,
- P_i is the actual vapor pressure near the liquid surface,
- R is the ideal gas constant, and
- T_L is the absolute temperature of the liquid.

For many cases, $P_{sat} >> P_i$, and thus the following equation can be used to estimate the vapor generation rate of a volatile liquid from an open vessel:

$$E_{n-1} = \frac{M_i K_i A P_i^{sat}}{RT_L}$$

The ratio of the mass transfer coefficients between the compound of interest Ki and reference compound Ko is expressed as follows:

$$\frac{K_i}{K_o} = \left(\frac{D_i}{D_o}\right)^{2/3}$$

The gas-phase diffusion coefficient D for a compound is estimated from the ratio of molecular weight of the compound of interest and a known compound (normally water) as follows:

$$\frac{D_i}{D_o} = \left(\frac{M_o}{M_i}\right)^{1/2}$$

The above two equations can be combined and the result can be used to estimate the mass transfer coefficient of a given volatile compound. Water is commonly used as a base reference for estimating the mass transfer coefficient for many compounds of interest. The mass transfer coefficient of water at 77 °F and 760 mm Hg. is 0.83 cm/s.

$$K_i = K_o\left(\frac{M_o}{M_i}\right)^{1/3}$$

The vapor release from open liquid surfaces is calculated using the methodology given above. Using the vapor pressure predicted by the MpBp module from EPA's EPISuite, the vapor generation rate is estimated to be approximately 4 x 10^{-4} g/s (Attachment 7).

c. Sampling Liquid Product

It is assumed that these activities are performed indoors (*i.e.*, air speed is ≤ 100 feet/min) and the EPA/OPPT Penetration Model is used as a default for releases to air. No default model exists for releases to non-air media from these sources in ChemSTEER. OPPT assumes that releases from these sources are insignificant when compared to other sources.

d. Loading Liquid Product into Drums

All sources/activities involving loading liquids into transport containers/vessels use the EPA/OAQPS AP-42 Loading Model as the default for calculating releases of a volatile chemical to air. The EPA/OAQPS AP-42 Loading Model estimates releases to air from the displacement of air containing chemical vapor as a container/vessel is filled with liquid. This model determines a vapor generation rate (G) based in part upon the chemical's physical-chemical properties and assumes that the rate of evaporation is negligible compared to the loss from displacement.

e. Equipment Cleaning Losses of Liquids from Multiple Vessels

The amount of chemical release into the air from this source is thus calculated using the EPA/OPPT Mass Transfer Coefficient Model. Release of the residual product contained in multiple vessels into water is calculated using the EPA/OPPT Multiple Process Vessel Residual Model.

f. Cleaning Liquid Residuals from Drums Used to Transport the Raw Material

It is assumed that cleaning activities for bottles, small containers, drums, and totes are performed indoors (*i.e.*, air speed is ≤ 100 feet/min). The amount of chemical release from these sources is thus calculated using the EPA/OPPT Penetration Model. Release of the residual raw material/product in the "empty" container is calculated using either EPA/OPPT Small Container Residual Model, EPA/OPPT Drum Residual Model, or EPA/OPPT Bulk Transport Residual Model, depending on the container size.

Emissions releases to water and air are obtained from Attachment 9, Emissions from Processing.

Table 4. Release of 2-BEB into Air from Processing Activities

Stage	Activity	Emissions Release Model	Release into Media	Typical Emissions (kg/site yr)	Worst Case Emissions (kg/site yr)
Processing	Unloading Liquid Raw Material from Drums	EPA/OAQPS AP 42 Loading Model	Air	2.20E-02	4.50E-02
Processing	Vapor Release from Open Liquid Surfaces	User defined Vapor Generation Rate Model	Air	6.30E-01	6.30E-01
Processing	Sampling Liquid Product	EPA/OPPT Penetration Model	Air	2.00E-05	1.60E-04
Processing	Loading Liquid Product into Drums	EPA/OAQPS AP 42 Loading Model	Air	2.20E-02	4.50E-02
Processing	Equipment Cleaning Losses of Liquids from Multiple Vessels	EPA/OPPT Mass Transfer Coefficient Model	Air	4.40E-02	4.40E-02
Processing	Cleaning Liquid Residuals from Drums Used to Transport the Raw Material	EPA/OPPT Penetration Model	Air	7.30E-04	7.30E-04
			Total	7.19E-01	7.65E-01

Table 5. Release of 2-BEB into Water from Processing Activities					
Stage	Activity	Emissions Release Model	Release into Media	Typical Emissions (kg/site yr)	Worst Case Emissions (kg/site yr)
Processing	Equipment Cleaning Losses of Liquids from Multiple Vessels	EPA/OPPT Multiple Process Vessel Residual Model, CEB standard 2% residual	Water	5.30E+03	5.30E+03
Processing	Cleaning Liquid Residuals from Drums Used to Transport the Raw Material	EPA/OPPT Drum Residual Model, CEB standard 3% residual	Water	6.60E+03	8.00E+03
			Total	1.19E+04	1.33E+04

Using the information from Tables 4 and 5, the net emission rates into air and water on an annual, daily, and hourly basis are determined:

Table 6. Release Rates of 2-BEB into Air					
Source	Quantity of 2-BEB released into environment (kg/yr)	Days of Operation	Quantity of 2-BEB released into environment (kg/day)	Hours of Operation	Release rate of 2-BEB into environment (kg/hr)
Manufacturing	2.74E-03	20	1.37E-04	480	5.70E-06
Processing	7.65E-01	250	3.06E-03	500	1.53E-03
Total	7.68E-01		3.20E-03		1.54E-03

Table 7. Release Rates of 2-BEB into Water		
Source	Quantity of 2-BEB released into environment (kg/yr)	Days of Operation
Manufacturing	1.10E+04	20
Processing	1.33E+04	250
Total	2.43E+04	

E. Contribution of 2-BEB into Air from Releases into Water by Manufacturing- and Processing-Related Unit Operations

To determine the contribution of 2-BEB from water to air, the EQuilibrium Criterion (EQC, v1.0) model was used to estimate the mass transfer rate from water to air.[3] The EQC model, as described in Section V, uses chemical-physical properties to quantify a chemical's behavior in an evaluative environment. The environment is fixed to facilitate a chemical-to-chemical comparison. This model is useful for establishing the general features of a new or existing chemical's behavior, *i.e.*, the media into which the chemical will tend to partition, the primary loss mechanisms, and its tendency for intermedia transport. The result of various emission scenarios can be explored. The EQC model estimated that 0.4% of the mass of 2-BEB released into water will transfer into air. This is shown in Figure 3 below:

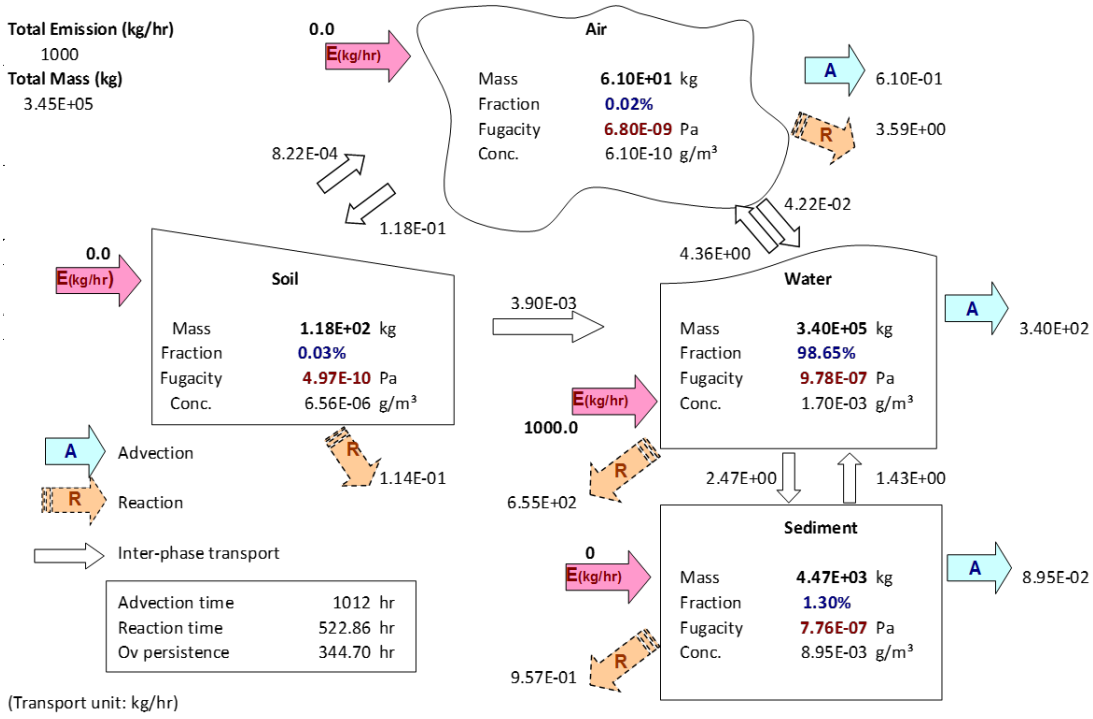

Figure 3. EQC model showing the partitioning of 2-BEB from water into air (assumes release rate of 1,000 kg/hr into water)

[3] Available at http://www.trentu.ca/academic/aminss/envmodel/models/NewEQCv100.html.

Thus, the net contribution of 2-BEB into air from releases into water is shown below:

Table 8. Contribution of 2-BEB into Air Arising from Releases into Water

Source	Worst Case Emissions (kg/site yr)	Net Intermediate Transport Predicted by EQC (%)	Contribution of 2-BEB into Air Arising from Release into Water (kg/site yr)	Num of hrs in 1 year (365 days/yr)	Contribution of 2-BEB into Air Arising from Release into Water (kg/hr)
Manufacturing	1.10E+04	0.4	4.41E+01	8760	5.03E-03
Processing	1.33E+04		5.32E+01		6.07E-03
		Total	9.73E+01		1.11E-02

It was assumed that once released into the water, 2-BEB will slowly partition into the air over a period of 1 year. Thus, the daily partitioning rate of 2-BEB into air is:

97.3 kg/site yr ÷ 365 days/yr = 2.67E-01 kg/day

1. Contribution of 2-BEB into Water from Manufacturing and Processing Related Unit Operations Releases into Air

The EQC model also estimates that 1% of the mass of 2-BEB released into the air will transfer into water. This has been depicted in Figure 4 shown below.

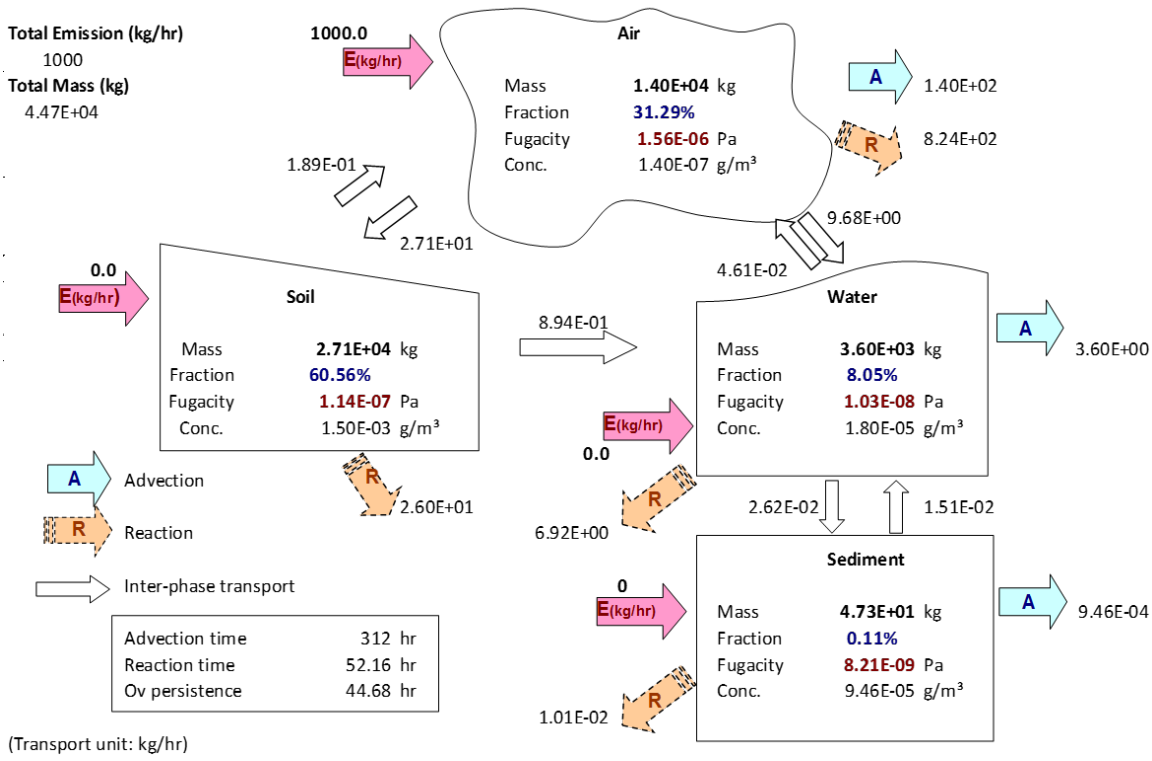

Figure 4. EQC model showing the partitioning of 2-BEB from air into water (assumes release rate of 1,000 kg/hr into air)

Accordingly, the contributions to water and the resulting concentrations are shown below:

Table 9. Contribution of 2-BEB into Water Arising from Releases into Air and Resulting Concentrations

Source	Worst Case Emissions (kg/site yr)	Net Intermediate Transport Predicted by EQC (%)	Contribution of 2-BEB into Water Arising from Release into Air (kg/site yr)	Contribution of 2-BEB into Water Arising from Release into Air (mg/site yr)	EQC Volume of Water Body (m^3)	Concentration of 2-BEB in Water due to Air Releases (mg/m^3)
Manufacturing	2.74E-03	1	2.74E-05	2.74E+01	2.00E+11	1.37E-10
Processing	7.65E-01		7.65E-03	7.65E+03		3.82E-08
		Total	7.68E-03	7.68E+03		3.84E-08

F. Air Dispersion Modeling of 2-BEB and Inhalation Exposures

1. Results from Air Dispersion Modeling for a Manufacturing Facility

EPA's SCREEN3 model, embedded into EPA's Exposure and Fate Assessment Screening Tool (EFAST), was used to estimate the ground-level air concentration of 2-BEB.[4] This modeling scenario, applicable to both manufacturing and processing, assumes that the mass of 2-BEB is released as fugitive emissions with no emission control technologies in operation.

EPA's EFAST was used to predict the ambient air concentrations. EFAST provides estimates of the concentrations of chemicals released to air, surface water, landfills, and consumer products. Estimates provided are potential inhalation, dermal, and ingestion dose rates resulting from releases of chemicals. Modeled estimates of concentrations and doses are designed to reasonably overestimate exposures for use in an exposure assessment in the absence of reliable monitoring data.

The point estimates of exposure derived from EFAST, as provided in Attachments 10, 11, and 12, are then used in the risk assessment. An RfC is an estimate (with uncertainty spanning up to an order of magnitude) of a continuous inhalation exposure to the human population (including sensitive subgroups) that is likely to be without an appreciable risk of deleterious effects during a lifetime (Crowl and Louvar, 2002). A HQ is the ratio of the potential exposure to the RfC. It is primarily used by EPA to assess the health risks of air toxics. A HQ less

[4] Available at https://www.epa.gov/tsca-screening-tools/e-fast-exposure-and-fate-assessment-screening-tool-2014-documentation-manual.

than or equal to 1 indicates that adverse effects are not likely to occur, and thus can be considered to have negligible risk. HQs greater than 1 cannot be interpreted as statistical probabilities of harm occurring. Instead, they are a simple statement of whether (and by how much) an exposure concentration exceeds the RfC.

The maximum annual 24-hr average concentration is 1.82E-02 µg/m^3 (1.82E-6 mg/m^3) whereas the maximum annual average concentration is 7.98E-05 µg/m^3 (4.16E-4 mg/m^3). Based on these predicted ambient air concentrations and a RfC of 3.0 mg/m^3, as shown in Section V, the HQs were calculated, as shown in Table 10:

Table 10. Ambient Air Concentrations from Manufacturing

	Air Concentration (µg/m^3)	Air Concentration (mg/m^3)	Reference Concentration (mg/m^3)	Hazard Quotient (HQ)
Max 24 hr avg	1.82E-02	1.82E-05	3	6.07E-06
Max annual avg	7.98E-05	7.98E-08		2.66E-08

2. Results from Air Dispersion Modeling for a Processing Facility

The maximum 24-hr average concentration is 3.98E-04 mg/m^3 and the maximum annual average concentration is 2.18E-05 mg/m^3.

Table 11. Ambient Air Concentrations from Processing

	Air Concentration (mg/m^3)	Reference Concentration (mg/m^3)	Hazard Quotient (HQ)
Max 24 hr avg	3.98E-04	3	1.33E-04
Max annual avg	2.18E-05		7.27E-06

3. Results from Air Dispersion Modeling for Contributions of 2-BEB into air from Releases into Water

The area of the water body (1E+10 m^2) from the EQC model was used to determine the length and width of the release opening. Assuming that the water body was approximately shaped like a square, both the length and width of the release opening are 1E+05 m. The release height was maintained at the default value of 3 m. The maximum 24-hr average concentration is 2.61E-06 mg/m^3 and the maximum annual average concentration is 2.08E-07 mg/m^3.

Table 12. Ambient Air Concentrations from Release of 2-BEB into Water

	Air Concentration (mg/m^3)	Reference Concentration (mg/m^3)	Hazard Quotient (HQ)
Max 24 hr avg	2.61E-06	3	8.70E-07
Max annual avg	2.08E-07		6.93E-08

The following table provides a summary of the total risk associated with the inhalation of 2-BEB arising from exposures to ambient air:

Table 13. Summary of HQs from Exposures to 2-BEB from Ambient Air

Source	HQ from Max 24 hr avg	HQ from max annual avg
Manufacturing	6.07E-06	2.66E-08
Processing	1.33E-04	7.27E-06
Release of 2-BEB into water	8.70E-07	6.93E-08
Total	1.40E-04	7.36E-06

G. Ingestion and Dermal Exposure to 2-BEB

1. Exposure to Drinking Water containing 2-BEB

Exposure to 2-BEB via ingestion was estimated using the concentration of 2-BEB in water and EPA's default exposure factors. Drinking water estimates were obtained as 95th percentile values from Chapter 3 - Ingestion of Water and Other Select Liquids.[5] HQs are presented to assess the risk. The RfD for both dermal and ingestion exposures has been derived in Section V.

Table 14. Hazards from Exposure to Drinking Water containing 2-BEB

Individual	Conc of 2-BEB in water (mg/L)	Ingestion Rate (L/day)	Exposure Frequency (days/yr)	Exposure Duration (yrs)	Oral Absorption Factor (unitless)	Body weight (kg)	Averaging time (days)	Average daily intake (mg/kg bw/day)	Reference Dose, RfD (mg/kg bw/day)	Hazard Quotient (HQ)
Adult (18+ years)	3.84E-11	2.976	350	20	1	70	7,300	1.56E-12	0.19	8.24E-12
Child (6-12 years)		1.395		6		30	2,190	1.71E-12		9.01E-12
Young child (1-5 years)		0.988		6		15	2,190	2.42E-12		1.28E-11

2. Exposure to 2-BEB during Bathing and Showering

Absorbed dermal dose rates can be calculated in user-defined scenarios, using a skin permeability coefficient K_p specific to the given chemical, which may be calculated by the

[5] Table 3-9. Two-Day Average per Capita Estimates of Combined Direct and Indirect Water Ingestion Based on National Health and Nutrition Examination Survey (NHANES) 2005−2010: Community Water (mL/day).

program from the octanol/water partition coefficient (K_{ow}). In the program, K_p is calculated from the following equation (US EPA, 1992e):

$\log K_p = 0.71 * \log K_{ow} - 0.0061 * MW - 2.72$ where:

K_p = permeability coefficient (cm/h)

K_{ow} = octanol/water partition coefficient

MW = molecular weight (g/mol)

The log K_{ow} as predicted by EPISuite is 3.03 and using a molecular weight of 222.28 g/mol, the K_p is 0.012 cm/hr. The skin exposure surface areas were obtained as 95th percentile values from EPA's Exposure Factors Handbook, Chapter 7 – Dermal Exposure Factors.[6]

Table 15. Hazards from Exposure to 2-BEB during Bathing and Showering

Individual	Conc of 2-BEB in water (mg/L)	Skin Surface Area Exposed (cm^2)	Permeability Coefficient (cm/hr)	Exposure Time (hrs/day)	Exposure Frequency (days/yr)	Exposure Duration (yrs)	Volumetric Conversion Factor (L/cm^3)	Body weight (kg)	Averaging time (days)	Average daily intake (mg/kg bw/day)	Reference Dose, RfD (mg/kg bw/day)	Hazard Quotient (HQ)
Adult (18+ years)	3.84E-11	25,600	0.012	0.2	350	20	0.001	70	7,300	3.20E-14	0.19	1.69E-13
Child (6-12 years)		20,600				6		30	2,190	6.01E-14		3.16E-13
Young child (1-5 years)		9,500				6		15	2,190	5.55E-14		2.92E-13

6 Table 7-9. Mean and Percentile Skin Surface Area (m2) Derived From U.S. EPA Analysis of NHANES 1999−2006 Males and Females Combined for Children <21 Years and NHANES 2005–2006 for Adults >21 Years.

3. Incidental Ingestion of Water Containing 2-BEB While Swimming in a Body of Water

A scenario was constructed to assess incidental ingestion of water during swimming in a body of water that contains 2-BEB. These values are obtained from EPA.[7]

Table 16. Hazards from Incidental Ingestion of Drinking Water containing 2-BEB while Swimming

Individual	Conc of 2-BEB in water (mg/L)	Ingestion Rate (L/day)	Exposure Frequency (days/yr)	Exposure Duration (yrs)	Oral Absorption Factor (unitless)	Body weight (kg)	Averaging time (days)	Average daily intake (mg/kg bw/day)	Reference Dose, RfD (mg/kg bw/day)	Hazard Quotient (HQ)
Adult (18+ years)	3.84E-11	0.13	36	20	1	70	7,300	7.03E-15	0.19	3.70E-14
Child (6-12 years)			108	6		30	2,190	4.92E-14		2.59E-13
Young child (1-5 years)			36	6		15	2,190	3.28E-14		1.73E-13

The following table provides a summary of the HQs arising from ingestion and dermal exposures to 2-BEB in drinking and surface water:

Table 17. Summary of HQs from Ingestion and Dermal Exposures to 2-BEB in Drinking and Surface Water

Individual	Exposure Pathway	Scenario	HQ - Dermal	HQ - Ingestion
Adult	Ingestion	Drinking Water containing 2-BEB		8.24E-12
	Ingestion	Incidental Ingestion of Drinking Water containing 2-BEB while Swimming		3.70E-14
	Dermal	Bathing and Showering	3.70E-14	
	Total		3.70E-14	8.27E-12
Child (6-12 years)	Ingestion	Drinking Water containing 2-BEB		9.01E-12
	Ingestion	Incidental Ingestion of Drinking Water containing 2-BEB while Swimming		2.59E-13
	Dermal	Bathing and Showering	3.16E-13	
	Total		3.16E-13	9.27E-12
Young child (1-5 years)	Ingestion	Drinking Water containing 2-BEB		1.28E-11
	Ingestion	Incidental Ingestion of Drinking Water containing 2-BEB while Swimming		1.73E-13
	Dermal	Bathing and Showering	2.92E-13	
	Total		2.92E-13	1.29E-11

[7] EPA. 1989a. Exposure Factors Handbook U.S. Environmental Protection Agency, Office of Health and Environmental Assessment, Washington, DC. EPA/600/8-89/043. July.

H. Summary of Risk Assessment

The risk assessments for exposures via inhalation, ingestion, and dermal pathways both for workers and consumers result in HQs that are substantially below 1. These low HQs reflect low to minimal risk associated with the manufacture and processing of 2-BEB. There is a high level of conservatism built into deriving these exposure estimates and subsequent HQ values. In summary the conservative assumptions include:

- Assume release of wash out from equipment and unit operations using default parameters.
- Assume open top mixing and processing of 2-BEB while incorporation into water-based paints. Traditionally this is a closed unit operation but for this worst-case assumption, the process is assumed to be an open process.
- Assume release of 2-BEB into water does not undergo any treatment at POTWs (Publicly Owned Treatment Works).
- During both manufacturing and processing, all emissions are assumed to be fugitive and not controlled such as when a thermal oxidizer is utilized.
- Emissions are assumed to be fugitive emissions and not point or stack sources. Stack or point results usually result in lower ambient ground-level concentrations compared with fugitive emissions modeling.
- It is also assumed that a person exposed to 2-BEB lives in the vicinity where the chemical is both manufactured and processed.

These conservative assumptions with a theoretical maximum production value of 2-BEB were used for emissions calculations and modeling. Despite the conservative assumptions and large production volumes, all HQs are substantially below 1, indicating low to minimal risk for human exposures.

VII. DELISTING 2-BEB SHOULD NOT RESULT IN AN INCREASE IN AMBIENT CONCENTRATIONS OF 2-BEB

HAP delisting will not result in increased exposure to 2-BEB. The most significant limitation on 2-BEB emissions and exposures is 2-BEB itself: its physical characteristics make it unlikely to result in exposures above the RfC even if 2-BEB use increases. The manner in which 2-BEB is manufactured, handled, and stored due to its low vapor pressure and evaporation rate will also limit emissions.

2-BEB is targeted to be used in a limited number of applications (the majority going into water-based coatings). Water-based coatings are considered by industry as more environmentally friendly and have a much lower VOC content than oil-based coatings. 2-BEB would be a preferred replacement for more volatile solvents and, thus, more environmentally friendly with a preferential toxicity profile.

Based on the above, delisting 2-BEB would not be expected to result in a significant increase in its emissions or an increase in exposure risks to the compound.

CONCLUSION

Pursuant to CAA Section 112(b)(3) (42 U.S.C. § 7412(b)(3)), The Dow Chemical Company is submitting this petition to EPA to delete 2-BEB from the glycol ethers category in the list of HAPs. 2-BEB is produced through the esterification of EGBE and benzoic acid. 2-BEB is

rapidly metabolized to EGBE and benzoic acid in mammals. Neither of those two substances is a listed HAP.

2-BEB has many environmental and sustainability benefits compared to the existing substances it is targeted to replace and as described in Section II, many of 2-BEB's physical and chemical properties provide many advantages over the targeted replacement products for the intended uses (*e.g.*, targeted to replace phthalates that are under increasing regulatory scrutiny). Dow expects that delisting of 2-BEB as a HAP will encourage product substitution, which will yield practical benefits for product formulators as well as potential net health and environmental benefits.

The proposed RfC/RfD (3 mg/m^3 and 0.19 mg/kg bw/day) for 2-BEB are conservative for reasons discussed in Section V, and there is no scientific reason to believe that 2-BEB exposures below the proposed RfC/RfD will pose any health hazard. Thus, it is appropriate to use the RfC/RfD as a health benchmark below which exposures to 2-BEB will not likely cause adverse health effects.

2-BEB is not expected to persist in the environment or bioaccumulate in the food chain and has a favorable hazard profile. An ecological risk assessment using a high level of conservatism to develop the exposure estimates and hazard values (*i.e.*, PNEC values) estimated RQ values for the aquatic and soil compartments substantially below 1 (*i.e.*, 3.07E-10 and 4.75E-11, respectively). Thus, it can be concluded that potential ecological risk from exposure to 2-BEB resulting from air emissions under manufacturing and use scenarios will be negligible.

The risk assessments for exposures via inhalation, ingestion, and dermal pathways both for workers and consumers result in HQs that are substantially below 1. These low HQs reflect low to minimal risk associated with the manufacture and processing of 2-BEB. As noted in Section VI, there is a high level of conservatism built into deriving these exposure estimates and the corresponding HQ values. In summary, even with the conservative assumptions and large production volumes, the HQs are substantially below 1, indicating low to minimal risk for human exposures.

Based on the scientific information summarized above, EPA can readily conclude that "there is adequate data on the health and environmental effects of the substance to determine that emissions, ambient concentrations, bioaccumulation or deposition of the substance may not reasonably be anticipated to cause any adverse effects to human health or adverse environmental effects." Accordingly, EPA should commence a rulemaking to delete 2-BEB from the glycol ethers category in the list of HAP.

LIST OF ATTACHMENTS

1. 2-Butoxyethyl benzoate (2-BEB): Technical Data Sheet of The Dow Chemical Company

2. 2-BEB: Ecological Risk Assessment in Support of HAP Delisting Petition

3. Justification for the Use of Information on 2-butoxyethanol (EGBE) for 2-BEB: Key Points

4. 2-BEB: Mammalian Toxicology Summary

5. 2-BEB: 2-Butoxyethyl Benzoate and Hematotoxicity

6. EPA, IRIS Summary - Ethylene Glycol Monobutyl Ether (EGBE) (2-Butoxyethanol); CAS RN 111-76-2, 2010

7. 2-BEB: Estimation of Vapor Pressure Using MpBp from EPA's EPISuite

8. 2-BEB: Emissions from Manufacturing

9. 2-BEB: Emissions from Processing

10. 2-BEB: E-FAST Report for Manufacturing

11. 2-BEB: E-FAST Report for Processing

12. 2-BEB: E-FAST Report for Water to Air Releases

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BEFORE THE
U.S. ENVIRONMENTAL PROTECTION AGENCY

ATTACHMENTS 1 – 12

PETITION OF THE DOW CHEMICAL COMPANY UNDER CLEAN AIR ACT SECTION 112(b)(3) TO REMOVE 2-BUTOXYETHYL BENZOATE FROM THE GLYCOL ETHERS CATEGORY IN THE LIST OF HAZARDOUS AIR POLLUTANTS

September 30, 2019

The Dow Chemical Company
Global Dow Center
2211 H.H. Dow Way
Midland, MI 48674
(989) 636-1000

Attachment 1
Technical Data Sheet

Product Name

XUS40782.00 Coalescing Agent

Synonyms

2-Butoxyethylbenzoate

Chemical Formula

$C_4H_9OCH_2CH_2OOCC_6H_5$

Product Description

XUS40782.00 is a low odor, high-boiling glycol ether ester with excellent coalescing properties for latex binders and zero VOC content as defined by either the EU Solvents Directive Deco Paints 2004/42/EC or NORM ISO 16000-6.

Applications

- Coalescing Agent for Low VOC coatings
- General Solvent Applications

Typical Physical Properties*

Property	Value
Molecular Weight (g/mol)	222.28
Boiling Point @ 760 mmHg	292°C
Flash Point (Setaflash Closed Cup)	146.2 °C (295.2° F)
Freezing Point	< -80°C
Vapor Pressure @ 20 °C	0.00029 mm Hg
Specific Gravity @ 25 °C /25 °C	1.02323
Liquid Density @ 25 °C	8.51 lb/gal
Viscosity, cP at 25 °C	4.32
Specific heat (J/g/°C @ 25 °C)	1.23
Heat of vaporization (J/g/°C @ 25°C)	400.1
Net heat of combustion (kJ/g predicted @ 25 °C)	29.8
Surface Tension @ 25 °C	23.608 dynes/cm
Evaporation Rate (n-butyl acetate = 1)	0.000146
Solubility, wt% at 25 °C	
Solvent in Water	<1.0 wt%
Water in Solvent	<1.0 wt%
Hansen Solubility Parameters (joules/cm^3)$^{1/2}$	
_d (Dispersion)	17.5
_p (Polar)	6.6
_h (Hydrogen Bonding)	4.6
Dielectric Constant @ 25°C	6.06
Refractive Index	
@ 20°C	1.4923
@ 25°C	1.4905

*These are typical properties, not to be construed as specifications.

Classification/ Registry Numbers/ Country Inventory

CAS #	5451-76-3
TSCA (U.S.)	5451-76-3
EINECS (EU)	226-685-8
REACH (EU)	Notified
ENCS (Japan)	3-4167
DSL (Canada)	5451-76-3
PICCS (Philippines)	5451-76-3

Product Stewardship

Dow has a fundamental concern for all who make, distribute, and use its products, and for the environment in which we live. This concern is the basis for our product stewardship philosophy by which we assess the safety, health, and environmental information on our products and then take appropriate steps to protect employee and public health and our environment. The success of our product stewardship program rests with each and every individual involved with Dow products - from the initial concept and research, to manufacture, use, sale, disposal, and recycle of each product.

Customer Notice

Dow strongly encourages its customers to review both their manufacturing processes and their applications of Dow products from the standpoint of human health and environmental quality to ensure that Dow products are not used in ways for which they are not intended or tested. Dow personnel are available to answer your questions and to provide reasonable technical support. Dow product literature, including safety data sheets, should be consulted prior to use of Dow products. Current safety data sheets are available from Dow.

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Attachment 2
2-BEB: Ecological Risk Assessment in Support of HAP Delisting Petition

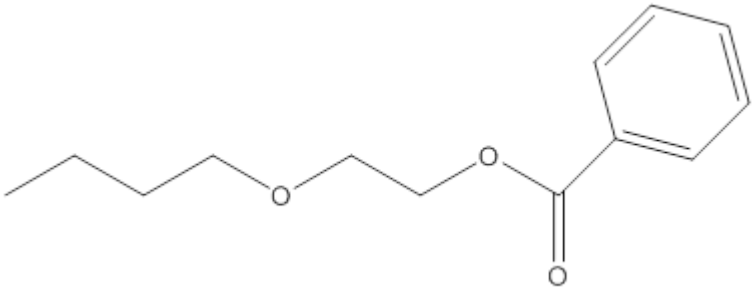
2-BUTOXYETHYL BENZOATE (2-BEB) ECOLOGICAL RISK ASSESSMENT IN SUPPORT OF HAP DELISTING PETITION

BACKGROUND/INTRODUCTION

The Dow Chemical Company is submitting a petition to the U.S. Environmental Protection Agency (EPA) to remove 2-butoxyethyl benzoate (2-BEB), CAS # 5451-76-3, from the category of glycol ethers listed as hazardous air pollutants (HAPs) under Section 112(b)(3) of the Clean Air Act (CAA) (42 U.S.C. § 7612(b)(3)). Under Section 112 of the CAA, EPA is mandated with evaluating and controlling emission of HAPs. Based on this mandate, 2-BEB was originally placed on the HAPs list as part of a category listing of glycol ether chemicals. Section 112 of the CAA contains a mandate for EPA to evaluate and control emissions of hazardous air pollutants. As part of this delisting petition, a screening level ecological risk assessment (ERA) was conducted to evaluate the potential for environmental effects as a result of future releases of 2-BEB to the air. The ecological risk assessment process is designed to evaluate the likelihood that adverse effects may occur as a result of exposure to one or more stressors via various pathways (1). The risk characterization process is designed to be an iterative process that typically starts with simplified, worst-case exposure scenarios and conservative toxicity estimates to help identify areas where potential risk might exist. If the potential for risk is identified (*i.e.*, exceedance of a level of concern), further risk characterization can be focused on these areas to further define the potential for risk. Risk characterization guidance documents developed by the USEPA served as the basis for the screening level approach of this risk characterization of 2-BEB from air releases at manufacturing and use sites[1, 2].

CHEMICAL IDENTITY

Chemical Name:	2-butoxyethyl benzoate
Common Name(s):	Ethylene glycol butyl ether benzoate; Ethanol, 2-butoxy-, benzoate
CAS Number:	5451-76-3
EC Number (EINECS):	226-685-8
Smiles:	O=C(OCCOCCCC)c(cccc1)c1

Structure:	

PHYSICAL AND CHEMICAL PROPERTIES

Physical and chemical properties are useful to predict and understand the potential behavior of a chemical in the environment, which can influence exposure to non-target organisms. Physical and chemical properties for 2-BEB are presented in Table 1. The low vapor pressure of 2-BEB suggests a minimal potential to volatilize at environmental temperatures (ECHA: https://echa.europa.eu/registration-dossier/-/registered-dossier/23065). 2-BEB is miscible in water, with an experimental water solubility of 106 mg/L at 20°C. Depending on the classification scheme considered, a log Kow of 3.37 has a moderate (log Kow between 3.0 and 5.0) or low (low Kow <4, GHS Purple Book) potential to bioconcentrate in the ecological food chain. There are additional estimations of log KOW: 3.77 at 30 °C by HPLC method[3] and 3.03 from KOWWIN v1.68[4]. The log Koc of 3.1 indicates that 2-BEB will have a potential to bind to organic materials in soil particles and would be considered slightly mobile in soil.

Table 1. Summary of Physical-Chemical Properties of 2-butoxyethyl benzoate (2-BEB)

Property	**Value**	**Footnote**
Molecular Formula:	$C_{13}H_{18}O_3$	a
Chemical Formula:	$C_4H_9OCH_2CH_2OOCC_6H_5$	b
Molecular Weight:	222.284 g/mol	b
Physical State:	Colorless liquid	a
Relative Density	1.025 at 20°C	a
Melting Point	-95°C at 101.3 kPa	a
Boiling Point	289.5°C at 101.3 kPa	a
Vapor Pressure	2.09E-04 mmHg at 20°C	a
Henry's Law Constant	0.128 Pa m^3/mol	c
Water Solubility	106 mg/L at 20°C	a
Log Kow	3.37	c
Log Koc:	3.10	c

[a] ECHA: https://echa.europa.eu/registration-dossier/-/registered-dossier/23065
[b] EPA Dashboard: https://comptox.epa.gov/dashboard
[c]Appendix B

PROBLEM FORMULATION

A problem formulation step helps to identify any points of concern for an ecological risk assessment by reviewing the proposed evaluation activity and summarizing physical, chemical, environmental fate, and ecotoxicological properties of the chemical of concern. This phase also includes consideration of the potential sources of introduction of the target chemical into the environment. Based on this information, the potential for exposure, estimates of exposure and relevant assessment endpoints (*i.e.*, ecological entities to be protected) are determined for evaluation. The problem formulation helps to define the conceptual model in order to gather all the information together to set up the risk characterization.

The CAA compels the U.S. EPA to establish national ambient air quality standards for specific common and widespread pollutants. In addition, CAA Section 112(b)(3) directed U.S. EPA to regulate the emissions of HAPs, which are those chemicals that are deemed to pose potential health risks or potential adverse effects to the environment. As a result, the U.S. EPA assembled an initial list of 189 HAPs. On this original list, the glycol ethers chemistry was added to this list as a whole category. Since the original creation of this list, there have been modifications resulting in a current list of 187 chemicals. One of these modifications was the removal of ethylene glycol monobutyl ether (EGBE) from this list in November of 2004 (Federal Register - November 29, 2004 (69 FR 69320)). 2-BEB is closely related to EGBE in that EGBE reacts with benzoic acid to synthesize 2-BEB. 2-BEB has more favorable phys-chem profile that make it less likely to be an air pollutant (see main HAP delisting document for 2-BEB). Thus, removal of 2-BEB from the HAP list, especially considering it has a more favorable environmental profile overall, would be a logical decision.

As previously mentioned, the Dow Chemical Company is preparing and submitting a petition to request that 2-BEB be removed from the category of glycol ethers listed as HAPs under Section 112(b)(3) of the Clean Air Act (CAA) (42 U.S.C. § 7612(b)(3)). This ecological evaluation and risk characterization was conducted to support this petition and demonstrate that 2-BEB should not be listed as a HAP based on ecological hazard and risk.

A risk characterization is needed because chemicals released to the air and subsequently deposited in other environmental compartments (*e.g.*, water, soil) have the potential to cause unintended impacts on the environment based on the magnitude of exposure to ecological receptors. The magnitude of exposure to these receptors in any environmental compartment is driven by a number of factors, including the quantity of the chemical in the compartment, the movement and potential transformation of the chemical in the environment, the duration of the exposure to the receptors and the inherent toxicity of the chemical to the receptors. Information and data on the manufacture and environmental fate of the chemical help to determine the potential for, and magnitude of, exposure to

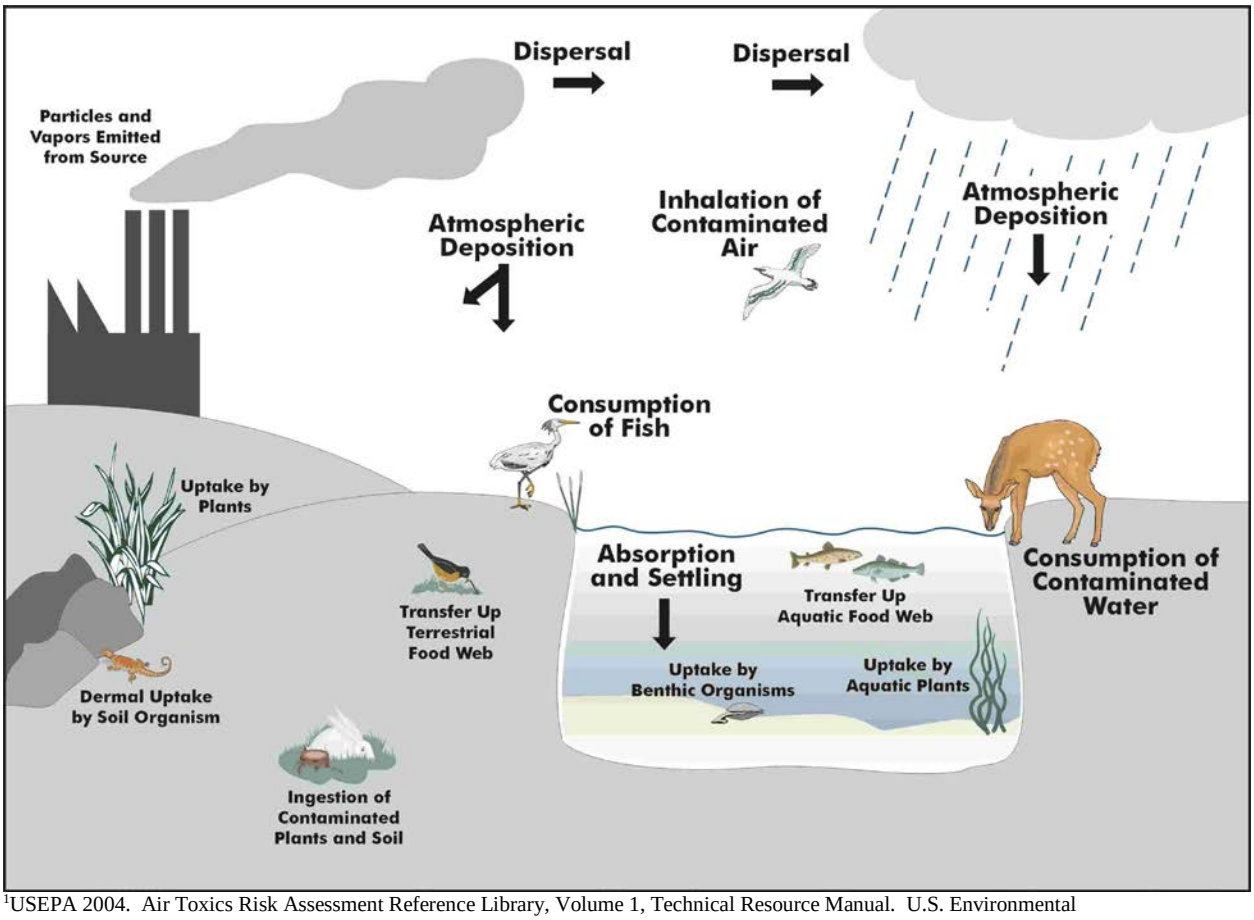
ecological receptors. Toxicity data generated using surrogate organisms according to internationally recognized test methods, as well as additional toxicity data from other sources, aid in developing a hazard profile to estimate toxicity potential for ecological receptors exposed to a target chemical. When the exposure and hazard data are synthesized in a risk characterization, the potential for harm to ecological receptors can be identified. As indicated earlier, risk characterization guidance documents developed by the USEPA served as the basis for the screening level approach of this risk characterization of 2-BEB from air releases at manufacturing and use sites[1, 2].

CONCEPTUAL MODEL

Figure 1 presents a conceptual model for risk characterization of air toxics developed by the USEPA that outlines the potential exposure pathways from the release of a chemical to air from a manufacturing site[5]. This conceptual model will serve as the basis for this screening level risk assessment of 2-BEB. Based on deposition patterns associated with release of particles and vapors of the chemical from the source (*e.g.*, at the manufacturing site and use sites), there is potential for exposure to biota to occur in both aquatic (via deposition to water and sediments) and terrestrial (via introduction to air and subsequent deposition to soil) compartments. Based on the low vapor pressure, short atmospheric half-life of 2-BEB in the air compartment (discussed later), as well as low volumes released during manufacturing (discussed later), exposure to terrestrial animals via inhalation was considered minimal and not addressed in this assessment. Risk in the sediment compartment was also not evaluated due to the low potential for partitioning to the sediment layer from deposition to water, as well as the minimal mass of 2-BEB deposited to the water phase (discussed later). Thus, the two main environmental compartments evaluated for potential exposure and subsequent risk were the surface water and soil compartments. As will be noted later, the resulting exposure concentrations determined for 2-BEB from the conservative manufacturing scenario emission estimates are so low that even a visual comparison of the exposure values with the Predicted No-Effect Concentration (PNEC) values will demonstrate that the level of potential for risk is many orders of magnitude below any level of concern. Based on this, the aquatic evaluation will determine a risk quotient based on the estimated worst-case surface water concentration and a PNEC determined by application of the appropriate safety factors to the most sensitive aquatic endpoint. The terrestrial assessment will focus on the risk to terrestrial plants and soil macroorganisms (*i.e.*, earthworms) determined by comparison of a worst-case soil concentration with the respective PNECs for these two receptors. These both represent direct exposure pathways. A direct exposure pathway not considered was for sediment dwelling organisms exposed to 2-BEB in the sediments due to the minimal predicted concentrations in sediment. Indirect exposure pathways were not considered for this assessment due to the extremely low potential for exposure. In addition, 2-BEB is not expected to bioaccumulate in the food chain so cumulative exposure via this indirect route is not considered as a potential risk. Thus, effects on

birds and mammals were not considered and risk is assumed to be equivalent to or less than for the evaluated ecological receptors.

Figure 1: Air Toxics Exposure Pathways of Potential Concern for Ecological Receptors[1]



[1]USEPA 2004. Air Toxics Risk Assessment Reference Library, Volume 1, Technical Resource Manual. U.S. Environmental Protection Agency, Office of Air Quality Planning and Standards Research Triangle Park, NC, EPA-453-K-04-001A, www.epa.gov/air/oaqps, April 2004.

ENVIRONMENTAL FATE PROFILE

The distribution of a chemical (*e.g.*, 2-BEB) in the environment depends on several factors, including its initial release mechanisms from production and uses, as well as its phys-chem and environmental fate properties which will contribute to determining how the chemical partitions and moves in the environment once released. Consistent with the emission modeling presented in the human risk assessment and EQP modeling (Appendix B), this assessment will consider releases to the air from manufacture, as well as use of the material, consistent with the USEPA Air Toxic Risk Assessment Library[5], as outlined in Figure 1 above.

Several phys-chem properties inform the fate and transport of 2-BEB are outlined in the Physical and Chemical Properties section (*e.g.*, octanol/water partition coefficient, Koc, vapor pressure). In addition to this information, two ready biodegradation tests demonstrate that 2-BEB is readily biodegradable and is not expected to persist in the environment. Both tests were conducted according to the "OECD, Guidelines for the Testing of Chemicals. Ready Biodegradability 301 F: Manometric Respirometry Test, 1992." Summaries of both tests are presented in Appendix A. The first test[6] evaluated a test substance concentration of 23.9 mg/L and reached 132% of ThOD by day 28 based on BOD. Biodegradation of the test material started approximately one day after inoculation and reached >60% within 3.5 days, meeting the 10-day window for consideration as readily biodegradable. A second test[7] was conducted and reached the same conclusion. This test evaluated a test substance concentration of 22.00 mg/L and reached 101% of ThOD by day 28 based on BOD. Biodegradation of the test material started attained an average of 91% by day 12 and met the 10-day window for consideration as readily biodegradable. Therefore, 2-BEB can be classified as "readily biodegradable" and is not expected to persist in the environment.

ECOLOGICAL EFFECTS PROFILE

The primary objective of the ecological effects assessment is to describe the available aquatic and terrestrial toxicity data for 2-BEB that will serve as surrogates for the ecological receptors of concern based on potential for exposure. Based on this data, appropriate PNEC values will be determined for the various groups of ecological receptors as measures of effect that will then be compared to predicted exposure concentrations.

Aquatic toxicity data summary

Table 2 presents the critical endpoints from the aquatic toxicity tests that have been performed with 2-BEB. Appendix A provides robust summaries of these studies. All studies were performed under relevant OECD and EPA GLP standards and conducted according to validated OECD toxicity testing protocols.

The acute and chronic fish testing was conducted with *Gobiocypris rarus* (Chinese Rare Minnow). Based on the existing data, fish are the most sensitive species type, both from an acute and chronic standpoint. The acute 96-h LC_{50} was determined to be 1.09 mg/L. The most sensitive endpoint was from the fish 28-day juvenile growth study, with a No-Observed-Effect Concentration (NOEC) based on growth rate of 0.0659 mg/L. A previous subchronic 14-day fish prolonged toxicity test yielded a NOEC of 0.147 mg/L based on mortality. Endpoints derived from an acute and a chronic study with the aquatic invertebrate *Daphnia magna* resulted in an acute 48-h EC_{50} of 15.5 mg/L and a chronic 21-d NOEC of 3.55 mg/L, respectively. Toxicity to aquatic plants was based on the result of a 72-h exposure to the freshwater green alga *Pseudokirchneriella subcapitata*. Based on the most sensitive measurement endpoint, inhibition of growth rate, the 72-h E_rC_{50} and NOE_rC were calculated to be 6.98 and 0.982 mg/L, respectively.

For the purposes of this assessment, the most sensitive aquatic endpoint was used as the basis for the toxicity value for the risk quotient calculation (*i.e.*, exposure/toxicity). The approach developed by ECHA for the chemical safety assessment of chemicals under REACH was used to calculated a sufficiently conservative PNEC for the aquatic compartment[8]. The PNEC is derived based on the quality and quantity of the data available. The data have been derived under relevant GLP standards and validated OECD protocols so are determined to be high quality studies. The $PNEC_{aquatic}$ is then based on the amount of data available. According to the assessment factor table R.10-4 in the ECHA (8) document, an assessment factor of 10 is applied to the lowest endpoint (*e.g.*, NOEC) from long-term studies representing at least three species (*i.e.*, fish, D. magna, algae). Based on the availability of these data, the lowest chronic result is the NOEC from the fish (*Gobiocypris rarus*) chronic study at 0.0659 mg/L. Application of the assessment factor of 10 to this value yields a $PNEC_{aquatic}$ of 0.00659 mg/L (or 6.59 µg/L), for use in the aquatic compartment risk assessment.

Terrestrial toxicity data summary

Table 2 presents the critical endpoints from the terrestrial toxicity tests that have been performed with 2-BEB. Appendix A provides robust summaries of these studies. All studies were performed under relevant OECD and EPA GLP standards and conducted according to validated OECD toxicity testing protocols.

Two terrestrial toxicity studies were conducted, an acute toxicity study with the soil macroinvertebrate earthworm (*Eisenia fetida*) and a seedling emergence and growth test with two plant species, one monocot (corn, *Zea mays*) and one dicot (soybean, *Glycine max*). The earthworm study indicated no effects at the highest dose, with a 14-d LC_{50} of >1,000 mg/L and a NOEC of 1,000 mg/L. In the plant study, no effects on seedling emergence or survival were noted for either species up to the maximum soil concentration of 1,000 mg/kg dw. Adverse effects on height and dry weight were noted for both species at the highest soil concentration (1,000 mg/kg dw) and for *G. max* at 500 mg/kg dw. The resulting NOEC values for *Z. mays* and *G. max* were 250 and 500 mg/kg dw, respectively, based on dry weight/height.

As with the aquatic compartment, for the purposes of this assessment, the most sensitive terrestrial endpoint was used as the basis for the toxicity value for the terrestrial risk quotient calculation (*i.e.*, exposure/toxicity). The approach developed by ECHA for the chemical safety assessment of chemicals under REACH was used to calculated a sufficiently conservative PNEC for the terrestrial soil compartment[8]. The PNEC is derived based on the quality and quantity of the data available. The data have been derived under relevant GLP standards and validated OECD protocols so are determined to be high quality studies. The $PNEC_{soil}$ is then based on the amount of data available. According to the assessment factor table R.10-10 in the ECHA[8] document, an assessment factor of 100 is applied to the lowest endpoint (*e.g.*, NOEC) from one long-term study (*i.e.*, plants in this case). Based on the availability of these data, the lowest long-term result is the NOEC for soybean (*G. max*) of 250 mg/kg dw. Application of the assessment factor of 100 to this value yields a $PNEC_{soil}$ of 2.5 mg/kg dw, for use in the terrestrial soil compartment risk assessment.

Activated sludge toxicity data summary

Table 2 presents the critical endpoint from the activated sludge toxicity test that was conducted with 2-BEB. Appendix A provides a robust summary of this study. This study was performed under relevant OECD and EPA GLP standards and conducted according to a validated OECD toxicity testing protocol. As the IC_{50} (50% inhibition concentration) and NOEC concentrations were well above the measured water solubility limit of the test material (i.e., 106 mg/L at 20 °C), 2-BEB is expected to have very low potential for adversely affecting biological wastewater treatment operations.

Table 2. Aquatic and Terrestrial Toxicity Data and derived $PNEC_{aquatic}$ and $PNEC_{soil}$ values for 2-BEB

Organism	Endpoint	Value	Units	Reference Number
Aquatic Toxicity Data				
Acute fish	96-h LC50	1.09	mg/L	9
Acute aquatic invertebrate	48-h EC50	15.5	mg/L	10
Aquatic plants algae	72-h ErC50	6.98	mg/L	11
	72-h EyC50	3.79	mg/L	11
	72-h NOEC	0.982	mg/L	11
Chronic aquatic invertebrate toxicity	NOEC	3.55	mg/L	12
Chronic fish toxicity	14-d NOEC	0.147	mg/L	13
	28-d NOEC	**0.0659**	**mg/L**	14
	$PNEC_{aquatic}$	***0.00659***	***mg/L***	Derived, 10-fold assessment factor to fish chronic 28-d NOEC
Terrestrial Toxicity Data				
Earthworm toxicity	LC50	>1000	mg/kg dw soil	15
Seedling emergence	LC50, dry weight/height/ emergence/ survival	>1000	mg/kg dwt	16
	NOEC, emergence/ survival	500	mg/kg dwt	16
	NOEC, dry weight/height	**250**	**mg/kg dwt**	16
	$PNEC_{soil}$	***2.5***	***mg/kg dwt***	Derived, 100-fold assessment factor to seedling emergence dry weight/height NOEC
Activated sludge toxicity data summary				
Activate sludge	EC50	>1,000	mg/L	17
	NOEC	**1,000**	**mg/L**	17

Note: Highlighted (i.e., bold) endpoints are the most sensitive endpoints for each ecological group evaluated.

EXPOSURE ASSESSMENT

Section 112 of the Clean Air Act requires EPA evaluation and subsequent control of emissions of HAPs. As previously discussed, 2-BEB is currently listed as a HAP based on its inclusion in the glycol ethers category. As indicated, the risk characterization process typically begins with a conservative, worst-case screening level assessment. A key component of this screening level risk assessment is to determine worst case estimates of potential exposure in relevant environmental media (*e.g.*, surface water, soil) from 2-BEB resulting from air deposition to the aquatic and terrestrial landscape. Based on the lack of existing emission data, in order to estimate potential worst case exposure concentrations in environmental media, a Mackay Level III fugacity model was used to estimate the steady state equilibrium concentrations of 2-BEB released to the atmosphere in each of four environmental media: air, soil, sediment, and water (Appendix B). The Equilibrium Criterion (EQC) multimedia fugacity model[18] has been developed and widely used to assess and/or predict the environmental fate, distribution, and transport of a chemical of interest released into the following environmental media: air, soil, and water. The model requires partitioning properties such as Henry's Law constant (or KAW, air-water partition coefficient), KOC (organic carbon-water partition coefficient) and KFW (fish-water partition coefficient), and reactive properties such as half-life in each environmental compartment in addition to environmental properties such as landscape and advection residence times. The model has been improved to use all the input variables properly and the new spreadsheet platform (instead of stand-alone program) was employed in the New EQC v.1.01[19, 20].

The EQC model run was conducted to evaluate the resulting steady state equilibrium concentration of 2-BEB in the four environmental media components (*i.e.*, air, soil, water and sediment) resulting from a release of a 2-BEB into the air, water and soil, respectively. The estimates generated were the result of emission of a typical volume (*i.e.*, 1000 kg/hr) into each of the three compartments. For the purposes of this particular assessment, only the emission scenario to air was considered, consistent with the mandate to evaluate the impacts of hazardous air pollutants. See Appendix B for a full description of the multimedia fugacity evaluation. Briefly, all simulations of the EQC multimedia fugacity model were conducted at 25 °C as a reference temperature, without evaluating temperature dependency of partitioning and transport processes. Default values of environmental compartment properties and advection residence times were used as presented in Appendix B, Table 1.

As indicated, the respective worst-case exposure concentrations in each compartment were derived based on an assumed emission rate of 1,000 kg/hour. However, the predicted maximum emission rate is much lower than this standard model assumption. Based on the human assessment for 2-BEB (see main HAP delisting document for 2-BEB), the modeled value for environmental emission to air from manufacturing and

processing was 3.88E-04 kg/hr, approximately six orders of magnitude lower than the model assumption. The manufacturing air emission rate was based on the following assumptions: 1) 20 days of operation a year, 2) 500 hours of operation (assume 48-50 hours per batch, 10 batches), and 3) a release of 2.74E-03 kg 2-BEB/year. The processing air emission rate was based on the following assumptions: 1) 250 days of operation a year, 2) 2000 hours of operation in the 250 days, and 3) a release of 7.65E-01 kg 2-BEB/year. The releases (in kg/hr) from manufacturing and processing were added together to calculate a total worst case air emission rate for 2-BEB. Thus, the EQC predicted concentrations for the soil and water compartments from the emission to air (Appendix B, Table 4) can be adjusted accordingly (*i.e.*, lowered by approximately six orders of magnitude). Table 3 presents the original predicted worst-case environmental media exposure values and the 2-BEB-specific manufacturing emission adjusted exposure values in the same environmental media.

Table 3. Predicted worst-case environmental exposure concentrations for 2-BEB from manufacturing emissions.

Environmental Compartment	Estimated Environmental Concentrations	
	1000 kg/hr[a]	3.88E-04 kg/hr[b]
Water (mg/L)	5.21E-06	2.02E-12
Soil (mg/kg dw)	3.06E-04	1.19E-10
Sediment (mg/kg dw)	5.96E-05	2.31E-11
Air (g/m^3)	1.40E-07	5.43E-14

[a]These values can be found in Appendix B, Table 5 in the attached graphic, except for the water value has been adjusted to µg/L from g/m^3 (*i.e.*, mg/L)
[b]These EEC values were the modeled values at a standard 1000 kg/hr emission rate corrected for the worst-case 2-BEB emission rate of 5.74E-06 kg/hr (*i.e.*, divided by 1.83E+08).

As indicated earlier, only the water and soil values will be considered for assessing the potential for risk to aquatic and terrestrial organisms, respectively. These exposure values were estimated based on what we consider to be a very conservative emission rate for BEB, which has been determined based on the absence of actual emission data. These values do not consider the abiotic and biotic factors that may further impact actual concentrations over time (*e.g.*, flow, biodegradation, etc.) that will likely result in even lower concentrations. Also, these exposure levels are exceptionally low due to the low production volume and limited production time over the course of a year.

RISK CHARACTERIZATION

The risk characterization phase brings together information on the chemical stressors, potential effects and ecological receptors to clarify these relationships and identify the potential areas of risk concern, i.e., reach conclusions regarding the occurrence of

exposure and the adversity of anticipated effects[1]. Thus, the results of the analysis phase (exposure and effect) are integrated to yield an estimate of potential risk resulting from exposure to 2-BEB from manufacturing emissions.

For this screening level risk characterization, risks to aquatic and terrestrial receptors were calculated by comparing the estimated environmental concentrations with derived PNEC values (ratio of exposure/toxicity). The resulting risk quotients (RQs) describe the potential for ecological risks. Using PNECs, which incorporate sufficient safety factors based on the available data set, a level of concern of one is set. Where RQs are less than one, it can be concluded that ecological risks are unlikely to occur. RQs greater than one suggest the potential for adverse effects to individual organisms. As indicated earlier, the purpose of a screening level risk assessment is to identify areas of potential for risk for further consideration. An RQ that exceeds one cannot be inferred to indicate that harm will occur to individual, populations, or communities but helps to focus resources for further focused evaluation (e.g., higher tier assessment, additional data needs, etc.).

As stated in the Conceptual Model section, the predicted environmental concentrations in air, soil, water, and sediment based on conservative manufacturing and processing assumptions will be very low. A visual comparison of the predicted environmental concentrations and the available PNEC values clearly demonstrates that no risk would be concluded. However, the water and soil compartments were evaluated using the risk quotient method to make this point clear. The results of the risk calculations for both aquatic and terrestrial receptors are presented in Table 4.

Table 4. Risk quotients for the aquatic surface water and terrestrial soil evaluation.

Compartment	Exposure Concentration	PNEC	Risk Quotient[a]
Water (mg/L)	2.02E-12	6.59E-03	3.07E-10
Soil (mg/kg dw)	1.19E-10	2.50E+00	4.75E-11

[a]RQ = Exposure concentration/PNEC (unitless)

The derived risk quotients for both aquatic surface water and terrestrial soil are at least 10 orders of magnitude lower than 1, the identified level of concern. No assessment was made for aquatic sediment dwelling invertebrates but toxicity to aquatic invertebrates was less than both fish and algae, indicating that the surface water assessment will be sufficiently protective of these organisms, especially given the exceptionally low exposure values. Thus, it can be concluded that risk from exposure to 2-BEB resulting from air emission under manufacturing and use scenarios will be negligible.

While no terrestrial vertebrates were covered in this assessment, the potential exposure levels would be so low that risk to mammals from direct consumption of vegetation and ingestion of soil contaminated with 2-BEB is precluded. The key mammalian toxicity endpoint is a RfC of 100 mg/kg dw per day, derived from two key mammalian toxicity studies (OECD 422 and 90-day). In short, the NOAEL values for both the OECD 422 and 90-day studies are 1500ppm 2-BEB in diet. The average mg/kg body weight/day over the study calculation from the full OECD 422 and 90-day studies for females were 117 and 94.9 mg/kg-day, respectively. Therefore, the NOAEL value being used as the point of departure to derive the RfC will be 100 mg/kg-day. During the 90-day study, the 1500ppm NOAEL females had body weight gains either similar to or higher than the control animals whether the mg/kg-day dose was above or below 100, therefore, 100 mg/kg-day is being used. Mammals may be exposed directly from consumption of vegetation where 2-BEB has been deposited or via soil ingestion and soil invertebrate ingestion. No surrogate dose from vegetation was calculated and soil invertebrates would not be expected to bioconcentrate 2-BEB (see next section). Thus, if any soil macroinvertebrates or vegetation were assumed to contain concentrations equivalent to the soil concentration and a conservative 1000-fold safety factor was assigned to the rat RfC (i.e., 0.1 mg/kg dw), the resulting risk quotient would be approximately nine orders of magnitude lower than 1.

There are, of course, many uncertainties in a screening level risk assessment. Where possible, conservative assumptions were used to approach a worst case. The exposure assessment is based on modeling as no monitoring data is available. This is one area that may provide the largest amount of uncertainty. However, with the effort to incorporate as much conservatism into this assessment as possible, and the magnitude at which the RQs passed the level of concern, it is assumed that these uncertainties would be captured within that range. To add additional conservatism to this evaluation, if the original soil and water compartment concentrations from the EQC model run assuming 1000 kg/hr emission to air were compared to the corresponding PNEC values, the risk quotient would still be approximately four orders of magnitude below the level of concern.

Bioconcentration/Bioaccumulation Potential

Under various federal laws, EPA and other federal agencies are tasked with making a broad range of decisions relative to the manufacture and use of chemicals that have the potential to cause unintended harm to the environment and public health. To aid in the evaluation and assessment of these substances, EPA researchers have created the Comptox Dashboard as a tool that integrates available information on chemistry, toxicity and exposure for over 875,000 chemicals. This data includes experimental and predicted data. This tool was employed to evaluate the bioconcentration and subsequent bioaccumulation potential of 2-BEB. As indicated in Appendix B, a log Kow value of 3.37 was estimated by ACD/Labs. An experimental log Kow of 3.77 was determined by HPLC method but due to lack of temperature dependence data on Kow, calculation of a value at 20 °C was not possible. The EPA Comptox Dashboard predicted an average log Kow of 3.09 with a range of 2.59 to 3.37. The Dashboard tool also predicted a bioconcentration factor (BCF) and a fish biotransformation half-life for 2-BEB. The predicted BCF value was 11.9, with a range of 10.7 to 13.6. The BCF value predicted in Appendix B was 46.2 L/kg (BCFBAF v3.01). In addition, the Dashboard tool estimated a fish biotransformation half-life of 0.778 days. The predicted log Kow values indicate 2-BEB would be of low to moderate bioconcentration potential. Estimated air, water, soil and sediment half-lives of 11.8, 82.8, 166, and 745 hours, respectively, are presented in Appendix B, indicating fairly rapid dissipation of 2-BEB in the environment. The EPA Comptox Dashboard calculated a similar aqueous half-life of 112 hours (4.67 days). Considering the predicted BCF values (11.9 – 46.2) and fish biotransformation half-life, in conjunction with a lack of persistence in the environment (i.e., ready biodegradability, short predicted half-lives in environmental media), 2-BEB would not be expected to bioaccumulate in the aquatic or terrestrial food chain and therefore would not constitute chronic hazard to ecological receptors.

Secondary Effects

Secondary effects are a concern when a direct primary exposure/effect leads to a cascade of additional effects in the ecosystem[1]. In an ecosystem, the potential exists where direct effects on some organisms can potentially lead to indirect or secondary effects on other organisms in the ecosystem by becoming a stressor to another entity[1]. Thus, secondary effects can cascade through the system and harm organisms not directly affected by the first stressor (i.e., severe reduction of a food source for a predator). Based on the exceptionally low estimated potential for exposure and predicted risk from 2-BEB in the environment from air deposition resulting from manufacturing operations, no potential concern for secondary effects is triggered. Thus, secondary effects were not assessed in this risk characterization.

CONCLUSIONS

CAA Section 112(b)(3) directed U.S. EPA to regulate the emissions of HAPs, which are those chemicals that are deemed to pose potential health risks or potential adverse effects to the environment. As a result, the U.S. EPA assembled an initial list of 189 HAPs. On this original list, the glycol ethers chemistry was added to this list as a whole category. Since the original creation of this list, there have been modifications resulting in a current list of 187 chemicals. One of these modifications was the removal of ethylene glycol monobutyl ether (EGBE) from this list in November of 2004 (Federal Register - November 29, 2004 (69 FR 69320)). As a follow up to the petition and subsequent removal of EGBE from the list, the Dow Chemical Company is submitting a petition to the U.S. Environmental Protection Agency (EPA) to remove 2-butoxyethyl benzoate (2-BEB), CAS # 5451-76-3, from the category of glycol ethers listed as hazardous air pollutants (HAPs) under Section 112(b)(3) of the Clean Air Act (CAA) (42 U.S.C. § 7612(b)(3)).

As part of this delisting petition, a screening level ecological risk assessment (ERA) was conducted to evaluate the potential for environmental effects as a result of future releases of 2-BEB to the air. 2-BEB is closely related to EGBE in that EGBE reacts with benzoic acid to synthesize 2-BEB. 2-BEB has a more favorable phys-chem profile that makes it less likely to be an air pollutant of concern. The existing environmental data for 2-BEB was reviewed and evaluated. 2-BEB is readily biodegradable and is not expected to persist in the environment. Modeled data (e.g., log Kow, fish biotransformation half-life, BCF) indicate that 2-BEB would not be expected to bioaccumulate in the aquatic or terrestrial food chain and constitute chronic hazard to ecological receptors. In addition, fugacity modeling concludes most 2-BEB released to air will be removed via reaction (82.3% of the total emission rate, E_T) and advection (14.0% of E_T) with only 2.8% and 1.0% deposited to soil and water, respectively. A screening level risk characterization was conducted for 2-BEB considering deposition in the environment from air released resulting from manufacturing and use based on worst case production and use assumptions. According to EQP modeling estimates adjusted for manufacturing and use air emissions, limited amounts of 2-BEB will enter environmental compartments from air deposition, thus the potential for exposure is very low. The screening level risk quotients for both aquatic surface water and terrestrial soil are at least 10 orders of magnitude lower than 1, the identified level of concern. Based on this assessment, it can be concluded that 2-BEB presents negligible risk to the environment from residues resulting from air deposition as a result of manufacture and use at projected volumes, with many orders of magnitude clearance of the level of concern.

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APPENDIX A (2-BUTOXYETHYL BENZOATE (2-BEB) ECOLOGICAL RISK ASSESSMENT IN SUPPORT OF HAP DELISTING PETITION): 2-BUTOXYETHYL BENZOATE ENVIRONMENTAL DATA SUMMARY

Ready Biodegradation

Title: 2-Butoxyethyl Benzoate: Ready Biodegradability by the Manometric Respirometry Test of 2-Butoxyethyl Benzoate; Dow Chemical; 25 December 2015; DR-0176-1951-016

Summary: The ready biodegradability of 2-butoxyethyl benzoate (DOWM20140410-0882) was determined in a 28-day dissolved oxygen depletion test using activated sludge from a domestic waste water treatment plant according to the guidelines of "OECD, Guidelines for the Testing of Chemicals. Ready Biodegradability 301 F: Manometric Respirometry Test, 1992."

The tested concentration of test substance was 22.00 mg/L (i.e., 50.60 mg ThOD/L). The concentration of sludge inoculum in the test system was 30mg/L, and the tested concentration of sodium benzoate used as reference substance was 100mg/L (Le.167.00 mg ThOD/L). Biodegradation of the reference substance (sodium benzoate) reached the pass level of the ready biodegradation test (>60% within 14 days), achieving 97% biodegradation by Day 14. The difference of extremes between replicate values of the removal of the test substance during the 28d test period was less than 20%. The results of the toxicity control showed that the test substance met the criteria for not being inhibitory to the microbial inoculum. Thus, the test is valid.

Results showed that under the experimental conditions, biodegradation of the test substance attained an average of 91% at Day 12 (10-d window) and 101% at Day 28, exceeding the readily biodegradable criterion of >60% in 10 day window. Therefore, the test substance can be considered to be readily biodegradable under the experimental conditions according to this test method.

Title: Butyl CELLOSOLVE™ Benzoate: Determination of Ready Biodegradability According To OECD Guideline 301F - Manometric Respirometry Test; S. J. Gonsior, M.S. and C. A. Hales, A.A.S.; 3 June 2013; DR-0176-1951-007

Summary: The ready biodegradability of 2-butoxyethyl benzoate was determined using the OECD Guideline No. 301F: Manometric Respirometry Test. Biodegradation of 2-butoxyethyl benzoate (23.9 mg/L equivalent to 54.9 mg/L as theoretical oxygen demand [ThOD]) reached 132% based on biological oxygen demand (BOD) at the end of this 28-day test. Biodegradation of the test material started approximately one day after the addition of the test material into the reaction mixture and exceeded 60% within 3.5 days of the initiation of the test, which indicates that the 10-day window criteria described in

the OECD 301F guideline was met. Therefore, 2-butoxyethyl benzoate can be classified as “readily biodegradable.” These BOD results are obtained from a single Test Suspension reaction mixture due to unexplainable high CO2 levels in one of the replicate test vessels during the test.

Aquatic Toxicity

Acute

Fish

Title: 2-Butoxyethyl Benzoate: Acute Toxicity test of 2-Butoxyethyl Benzoate to Chinese Rare Minnow (*Gobiocypris rarus*); Dow Chemical; 25 December 2015; DR-0176-1951-017

Summary: According to "OECD, Guidelines for the Testing of Chemicals. 203 Fish, Acute Toxicity Test, 1992", the acute toxicity of the test substance, 2-butoxyethyl benzoate, to *Gobiocypris rarus* was determined by a semi-static test. Based on the information from the sponsor, the stability of the test substance would be influenced by microorganisms in test water and with the presence of fish. A nominal concentration of 100 mg/L of the test substance was prepared and stirred (via magnetic stirrer) in the dark for 24h at 500 rpm in sterile test water, which was treated by autoclaving (121°C for 20 min) as the stock solution. The test solutions were prepared by dilution of the stock solution with test water. Based on the results of the range-finding test, five treatment groups, a control group of the test water and the control group of the sterile test water were included in the definitive test. The nominal concentrations of the treatment groups were 0.38, 0.65, 1.1, 1.9 and 3.0 mg/L (time-weighted mean measured concentrations were 0.247, 0.426, 0.847, 1.41 and 2.47 mg/L, respectively). The test duration was 96h and the frequency of test solution renewal was every 24h.

No mortality occurred in either control group during the test and the dissolved oxygen concentration was greater than 60.0% of the air saturation value (ASV) throughout the test duration. Hence, the test was considered to be valid. During the test, though measures were taken to prevent degradation of the test substance in the test solutions (*e.g.* 24-h renewals, stock solutions prepared in sterile water), the measured concentrations of the test substance still declined over each renewal period and thus concentrations varied more than 20%; therefore, the results were expressed using the time-weighted mean (TWM) measured concentrations. The 96-h LC50 value for the test substance to *Gobiocypris rarus* was 1.09 mg/L and its 95% confidence limits ranged from 0.766 to 1.48 mg/L. The maximum TWM mean measured concentration causing no mortality and the minimum TWM mean measured concentration causing 100 percent mortality within the period of the test were 0.426 mg/L and 2.47 mg/L, respectively.

Daphnia

Title: 2-Butoxyethyl Benzoate: An Acute Toxicity Study with the Freshwater Cladoceran, *Daphnia magna*; R. J. Currie, Ph.D., K. L. Hutchinson, B.S., and W. B. Holzheuer, B.S.; 28 July 2014; DR-0176-1951-008

Summary: The purpose of this study was to assess the effects of 2-butoxyethyl benzoate to the freshwater cladoceran, *Daphnia magna* semi-static according to OECD Guideline 202 (Daphnia sp. Acute Immobilisation Test). The study was performed for 48 hours with a renewal of the exposure solutions at 24 hours. Target concentrations were 0 (water control), 6.25, 12.5, 25.0, 50.0, and 100 mg 2-butoxyethyl benzoate/L. Test solutions were analyzed at test initiation and termination by high performance liquid chromatography with diode array detection (HPLC/DAD). None of the analyses of the water control exhibited a concentration exceeding the lowest level quantitated (LLQ) equivalent to 0.25 mg 2-butoxyethyl benzoate/L. Mean measured concentrations were <LLQ, 5.53, 10.8, 22.1, 45.4, and 91.9 mg 2-butoxyethyl benzoate/L. The data collected were used to calculate the 24- and 48-hour EC50 values (the concentrations estimated to result in 50% immobility of the test population after 24- and 48-hours of exposure, respectively) and a 48-hour no observed-effect concentration (NOEC).

The acute toxicity values for the daphnid (*D. magna*) exposed to 2-butoxyethyl benzoate over a 48-hour static-renewal exposure period and based on mean measured concentrations were as follows:

- 24-hour EC50 = 26.5 mg/L
- 48-hour EC50 = 15.5 mg/L
- 48-hour NOEC = 10.8 mg/L (Based on the highest concentration exhibiting no significant immobility or sublethal effects)

Algae

Title: 2-Butoxyethyl Benzoate: Growth Inhibition Test with the Freshwater Green Alga, *Pseudokirchneriella subcapitata*; R. J. Currie, Ph.D., K. L. Hutchinson, B.S., and W. B. Holzheuer, B.S.; 28 July 2014; DR-0176-1951-009

The purpose of this study was to assess the effects of 2-butoxyethyl benzoate to the freshwater green alga, *Pseudokirchneriella subcapitata*, according to OECD Guideline 201 (Alga, Growth Inhibition Test). The study was performed for 72 hours with target concentrations of 0 (AAP control), 0.625, 1.25, 2.50, 5.00, and 10.0 mg 2- butoxyethyl benzoate/L. Test solutions were analyzed at test initiation and termination by HPLC/DAD. None of the analyses of the media control exhibited a concentration exceeding the lowest level quantitated (LLQ) equivalent to 0.25 mg 2-butoxyethyl benzoate/L. Mean measured concentrations were <LLQ, 0.480, 0.982, 2.01, 4.16, and 8.62 mg 2-butoxyethyl benzoate/L. The data collected were used to determine EC50 (the concentration causing 50% inhibition) values for 72-hour cell density, 0-72-hour cell

yield, and 0-72-hour average specific growth rate. No-observable-effect concentrations (NOEC) were determined for each endpoint based on the highest concentration with algal growth not significantly different from the control.

The acute toxicity values for *Pseudokirchneriella subcapitata* exposed to 2-butoxyethyl benzoate over a 72-hour exposure period and based on mean measured concentrations were as follows:

- 0-72-hour cell yield
  EyC50 = 3.79 mg/L
  NOEC = 0.982 mg/L
- 0-72 hour growth inhibition
  ErC50 = 6.98 mg/L
  NOEC = 0.982 mg/L

Chronic toxicity

Fish

Title: 2-Butoxyethyl Benzoate: Fish, Juvenile Growth test of 2-Butoxyethyl Benzoate to Chinese Rare Minnow (*Gobiocypris rarus*); Yang Jing; 27 November 2015; DR-0176-1951-033

Summary: According to "OECD Guidelines for the Testing of Chemicals 215 Fish, Juvenile Growth test, 2000," the effect on growth of juvenile fish from exposure of the test substance 2-butoxyethyl benzoate to the Chinese Rare Minnow (*Gobiocypris rarus*) was determined by a semi-static test.

The test substance was added in sterilized test water and stirred in the dark for 24 h to prepare a stock solution with a nominal concentration of 100 mg/L. the test solutions were prepared by dilution of the stock solution with test water. Five treatment groups, a test water control group and a sterilized test water control group were used in the test. The nominal concentrations were 0.048, 0.086, 0.15, 0.28 and 0.50 mg/L, which equaled time-weighted measured concentrations of 0.0238, 0.0407, 0.659, 0.113 and 0.190 mg/L. Renewal frequency was 24 hour and the test duration was 28 days.

The mortality in both the test water and sterilized test water controls groups was zero at the end of the exposure, and the dissolved oxygen concentration was >60% of air saturation throughout the test and test temperatures were maintained within acceptable limits.

The EC10 value for the growth rate was 0.0868 mg/L. The no observable effect concentration (NOEC) was 0.0659 mg/L and the lowest observable effect concentration (LOEC) was 0.113 mg/L.

Title: 2-Butoxyethyl Benzoate: Prolonged Toxicity Test (14-day Study) of 2-Butoxyethyl Benzoate to Chinese Rare Minnow (*Gobiocypris rarus*); Yang Jing; 25 December 2015; DR-0176-1951-018

Summary: According to "OECD Guidelines for the Testing of Chemicals 204 Fish Prolonged Toxicity Test: 14-day Study", the prolonged toxicity of the test substance, 2-butoxyethyl benzoate (DOWM2014041 0-0882), to *Gobiocypris rarus* was determined by a semi-static test.

The test substance was added in sterilized test water (test water autoclaved at 121°C for 20 min) and stirred (via magnetic stirrer) in the dark for 24h at 500 rpm to prepare a stock solution with a nominal concentration of 100 mg/L. The test solutions were prepared by dilution of the stock solution with test water. Based on the results of fish acute toxicity test with the same test substance, five treatment groups, a sterilized test water control group and a control group were included in the test. The nominal concentrations of the treatment groups were 0.3, 0.5, 0.9, 1.7 and 3.0 mg/L, and the time-weighted mean measured concentrations were 0.147, 0.240, 0.409, 1.41 and 2.54 mg/L, respectively. All treatment groups, sterilized test water control group and control group had 3 replicates each containing 5 fish. The frequency of the test solution renewal was 24h and the test duration was 14 days.

The mortality in the control group and sterilized test water control group were both zero at the end of the test and the dissolved oxygen concentration was greater than 60.0% of the air saturation value (ASV) throughout the test. So the test was considered to be valid.

Results from the UPLC analysis of the test solutions showed that the measured concentrations of the newly prepared (renewal) test solutions varied less than ± 20% of their geometric mean measured concentrations during the test. However, though measures were taken to prevent degradation of the test substance in the test solutions (e.g. 24-h renewals in clean vessels, stock solutions prepared in sterile water), the measured concentrations of the test substance declined and varied more than 20% over the renewal periods (old test solutions). Thus, results were expressed as the time-weighted mean measured concentrations. Under the tested conditions, the LC50 of *Gobiocypris rarus* exposed to the test substance for 14 days was 0.338 mg/L with 95% confidence interval (CI) of 0.287-0.416 mg/L; the no observed effect concentration (NOEC) was 0.147 mg/L; the threshold level of the lethal effect was 0.240 mg/L.

Daphnia

Title: 2-Butoxyethyl Benzoate: A 21-Day Chronic Toxicity Study with the Daphnid, *Daphnia magna*; K. Coady, Ph.D., D. W. Louch, B.S., LATG, W. B. Holzheuer, B.S., E. J. Nelson, B.S., and L. G. McFadden, M.S.; 08 October 2015; DR-0176-1951-015

The purpose of this study was to assess the chronic toxicity of 2-butoxyethyl benzoate to the freshwater daphnid, *Daphnia magna*. A 21-day static-renewal (daily) exposure was conducted and endpoints included adult daphnid survival, reproduction (total young produced per surviving adult female), and growth (length and weight of surviving adults).

The study was conducted with daphnids (one individual per replicate with ten replicates per treatment level) exposed to nominal concentrations of 0 (water control), 0.75, 1.5, 3.0, 6.0, and 12 mg 2-butoxyethyl benzoate/L. Test solutions were renewed daily throughout the 21- day exposure. Daily observations were made and the number of surviving daphnids recorded. Reproduction was evaluated by counting and removing neonates during renewals. Lengths and dry weights of all surviving adult daphnids were measured and recorded following termination of exposure.

Freshly-prepared bulk test solutions were sampled at test initiation and on days 1, 7, 14, and 19 of the study for analytical verification of 2-butoxyethyl benzoate concentrations. Spent test solutions (10 replicates per dose level when applicable) were pooled and analyzed on days 1, 7, 14, and at the end of exposure (day 21). The samples were analyzed for 2- butoxyethyl benzoate by high-performance liquid chromatography with photodiode array detection (HPLC/DAD). The resulting mean measured test concentrations were 0.578, 1.00, 1.90, 3.55, and 10.6 mg/L. No 2-butoxyethyl benzoate was detected in the water control above the lowest level quantitated (LLQ) of 0.250 mg/L.

The chronic toxicity values for *Daphnia magna* exposed to 2-butoxyethyl benzoate over a 21-day static-renewal (daily) exposure period were statistically and/or empirically determined using mean measured test concentrations. The resulting endpoint values are presented below:

- The LOEC and MATC for reproduction, length and weight (at study termination) were > 3.55 mg/L.
- The LOEC and MATC for survival (at study termination) were 10.6 and 6.13 mg/L, respectively.
- The NOEC for survival, reproduction, and length and weight (at study termination) was 3.55 mg/L.

Activated Sludge Inhibition

Title: 2-Butoxyethyl Benzoate: Determination of Activated Sludge Respiration Inhibition According to OECD Guideline 209; R. J. West, B.S. and W. B. Holzheuer, B.S.; 09 March 2016; DR-0176-1951-032

Summary: The potential for 2-butoxyethyl benzoate to inhibit the respiration of municipal activated sludge was evaluated using the OECD Guideline 209 “Activated Sludge, Respiration Inhibition Test.” This test method assesses the potential effect of a

range of test chemical concentrations on measured activated sludge respiration rates following a three-hour contact period. In this study, the potential impact on respiration rates was also evaluated after a 30 min. contact period, in consideration of the ready biodegradability and volatile properties of the test material. The 2-butoxyethyl benzoate substance, at nominal concentrations of 100, 300, and 1000 mg/L did not show > 50% inhibition of the respiration rate of the activated sludge after either 30 min. or three hours contact time. Therefore, the 30 min and three hour EC50 values were determined empirically to be EC50 > 1,000 mg/L. A statistical comparison (ANOVA) of respiration rates at each test material concentration and contact time resulted in determination of no observed effect concentrations (NOEC) for 30 min. and three hours contact times of 300 mg/L and 1,000 mg/L, respectively. Further testing of potential impact of the test material on nitrifying activity of activated sludge was deemed to be unnecessary, because respiration of nitrifying bacteria represents a relatively small proportion of total activated sludge respiration, and very high concentrations of test material (above solubility limit) were necessary to impact total respiration. Considering that these EC50 and NOEC concentrations are well above the measured water solubility limit of the test material (*i.e.*, 106 mg/L at 20 °C), the 2-butoxyethyl benzoate substance is expected to have very low potential for adversely affecting biological wastewater treatment operations.

Terrestrial Toxicity

Earthworm

Title: 2-Butoxyethyl Benzoate: An Acute Toxicity Study with the Earthworm in an Artificial Soil Substrate; Terry Lee Sloman, B.S., John R. Porch, M.S; 23 March 2016; DR-0176-1951-034

Summary: The toxicity of 2-butoxyethyl benzoate to earthworms was evaluated according to OECD Guideline 207 "Earthworm, Acute Toxicity Tests." Adult earthworms (*Eisenia fetida*) were exposed to a geometric series of five concentrations of 2-butoxyethyl benzoate in artificial soil. Nominal concentrations of 62.5, 125, 250, 500, and 1000 mg/kg dry soil were selected by the sponsor. A negative control group was maintained concurrently in soil prepared without the addition of the test material. This route of administration was selected because it was representative of the natural exposure of earthworms to chemicals. Four replicate chambers were maintained for each test treatment and negative control group with ten earthworms in each replicate chamber. The sources organisms was an in-house culture started with earthworms obtained from the University of Maryland Wye Research & Education Center Queenstown, MD 21658 The earthworms were exposed to 2-butoxyethyl benzoate for 14 days. Observations of mortality and clinical signs were conducted on Days 7 and 14. The mean weight of the live test organisms in each test chamber was determined at the beginning and end of the test. Based on the observations done at the conclusion of exposure (i.e., after 14 days of exposure), the results are as follows:

- 14-Day LC50: >1000 mg/kg dry soil.
- No Observed Effect Concentration (NOEC): 1000 mg/kg dry soil

Seedling emergence

Title: 2-Butoxyethyl Benzoate: A Toxicity Test to Determine the Effects on Seedling Emergence and Growth of Two Species of Terrestrial Plants; Andrea R. Orvos, M.S., John R. Porch, M.S., Leslie A. Danos, B.S.; 11 May 2016; DR-0176-1951-036

Summary: One monocot and one dicot species of terrestrial non-target plants (*Z. mays* or *G. max)* were exposed to a series of five geometrically spaced test concentrations of the test substance incorporated in soil, as well as a negative control (containing water purified by reverse osmosis) and a solvent control (acetonitrile). Nominal concentrations were 0 (Negative Control), Solvent Control (acetonitrile), 63, 125, 250, 500 and 1000 mg/kg dry soil (milligrams per kilogram of dry soil). Each test and control group consisted of eight replicate test pots containing five planted seeds of one species. After planting, test pots were placed on a greenhouse bench top according to a randomized

block design. The test duration was 21 days following planting, which was at least 14 days after 50% emergence of control plants for both species. The number of emerged seedlings was observed weekly and the percentage of surviving seedlings, seeding height and dry weight were determined at test termination.

Test soil concentrations of up to 1000 mg/kg dry soil resulted in no adverse effects on the seedling emergence or survival of either *Z. mays* or *G. max*. There were adverse effects on height and dry weight of both *Z. mays* and *G. max* at the highest treatment levels. The NOEC and LOEC for *Z. mays* (corn) were 500 and 1000 mg/kg dry soil, respectively, for both dry weight and height. The NOEC and LOEC for *G. max* (soybean) were 250 and 500 mg/kg dry soil, respectively, for both dry weight and height.

APPENDIX B (2-BUTOXYETHYL BENZOATE (2-BEB) ECOLOGICAL RISK ASSESSMENT IN SUPPORT OF HAP DELISTING PETITION): FATE, DISTRIBUTION, AND TRANSPORT OF 2-BUTOXYETHYL BENZOATE REPORT

STUDY TITLE
Petition -- Attachment 2 (00281719).DOCX

Test Guidelines
No Test Guidelines

Author(s)

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Study Completion Date

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Petition -- Attachment 2 (00281719).DOCX

Jaeshin Kim

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ABSTRACT

The fate, distribution and transport of 2-butoxyethyl benzoate (2-BEB; CASRN 5451-76-3) in the environment were evaluated using the Equilibrium Criterion (EQC) multimedia fugacity model. Property values, measured and/or estimated, for partitioning and degradation of 2-BEB in the environment were critically evaluated and the best available property values were used for the model simulations. In addition, sensitivity analyses were performed to identify the property values and input parameters having the most influence on the model results using calculated sensitivity ratios (SR).

When it is released to air only, 2-BEB is removed by reaction (82.3% of the total emission rate, ET) and advection (14.0% of ET) whereas 2.8% and 1.0% of ET are deposited to soil and water, respectively. At steady-state, mass fractions in air, soil, water and sediment are 64.7%, 30.4%, 4.9%, and <0.1%, respectively. The overall persistence is 21.6 hours, which is half-life in air (SR=0.96), Henry's Law constant (SR= – 0.28) and half-life in soil (t½,S, SR=0.30).

When it is released to water only, 2-BEB is removed by reaction and advection (89.2% and 10.7% of ET, respectively) whereas transports to other compartments are limited. At steady state, mass distributions in water and sediment are 99.4% and 0.6%, respectively. The overall persistence is 107 hours, which is sensitive exclusively to half-life in water (SR=0.89).

When it is released to soil only, 2-BEB is removed by reaction (99.1% of ET) whereas transports to other compartments are limited. At steady state, mass distributions in soil and water are 99.7% and 0.3%, respectively. The overall persistence is 238 hours, which is sensitive exclusively to half-life in soil (SR=0.99).

I. INTRODUCTION

The Equilibrium Criterion (EQC) multimedia fugacity model (Mackay, 2001) has been developed and widely used to assess and/or predict the environmental fate, distribution, and transport of a chemical of interest. The model requires partitioning properties such as Henry's Law constant (or KAW, air-water partition coefficient), KOC (organic carbon-water partition coefficient) and KFW (fish-water partition coefficient), and reactive properties such as half-life in each environmental compartment in addition to environmental properties such as landscape and advection residence times. The model has been improved to use all the input variables properly and the new spreadsheet platform (instead of stand-alone program) was employed in the New EQC v.1.01 (Hughes et al., 2012; Kim et al., 2013).

The current study performed the EQC Level III (i.e., non-equilibrium steady state) modeling of 2-butoxyethyl benzoate (2-BEB; CASRN 5451-76-3) under various emission scenarios. The model output is discussed in terms of mass distribution, fugacity values, removal by reaction and advective transport, persistence times, and intermedia transport. This study further analyzed the EQC model with sensitivity analyses in order to determine which chemical properties influence the model's results significantly. Note that throughout this study the environmental properties were fixed as an evaluative physical setting.

II. METHODS

A. Physico-chemical properties

All simulations of the EQC model were conducted at 25 °C as a reference temperature without evaluating temperature dependency of partitioning and transport processes. Default values of environmental compartment properties and advection residence times were used as shown in Table 1. The intermedia mass transport velocities were same as used in the EQC Model v.2.02 (Table 2, CEMC (2003)).

Measured values of physico-chemical inputs were preferably selected over estimated ones. When a measured value for 2-BEB were not available, the property were estimated by QSAR (Quantitative Structure-Activity Relationship) models (Table 3).

- A Log K_{OW} value of 3.37 was estimated by ACD/Labs (2019). There are additional estimations of Log K_{OW} such as 3.77 at 30 °C by HPLC method (European Chemicals Agency, 2019), 3.03 from KOWWIN v1.68 (US EPA, 2019). Since there is no data for temperature dependence on K_{OW}, it was not possible to predict a value at 25 °C with HPLC method.
- A Henry's Law constant (HL_C) of 0.128 Pa m^3 mol^{-1} was estimated by HENRYWIN v.3.20 (US EPA, 2019). The dimensionless Log K_{AW} is equivalent to –4.29.
- A Log K_{OC} value of 3.10 at 20 °C was estimated by a HPLC method (European Chemicals Agency, 2019).

- A BCF (bioconcentration factor) value of 46.2 L/kg was estimated by BCFBAF v3.01 (US EPA, 2019).
- A degradation half-life ($t_{½,A}$) of 11.8 hours in air was estimated by AOPWIN v1.92 (US EPA, 2019).
- A degradation of half-life ($t_{½,W}$) of 82.8 hours in water was calculated based on 91% biodegradation of 2-BEB in 12 days with an assumption of an exponential decay (European Chemicals Agency, 2019).
- A degradation of half-life ($t_{½,S}$) of 166 hours in soil was estimated based on an assumption of 1:2 ratio (water:soil), which is typically used in EPI Suite™ (US EPA, 2019).
- A degradation of half-life ($t_{½,Sed}$) of 745 hours in sediment was estimated based on an assumption of 1:9 ratio (water:sediment), which is typically used in EPI Suite™ (US EPA, 2019).

B. Emission scenarios

Three 'evaluative' emission scenarios (or modes of entry, MoEs) were tested for EQC modeling at a total emission rate (E_T) of 1,000 kg/hr: (1) to air only, (2) to water only, and (3) to soil only. Although these emission scenarios are not necessarily realistic, each emission mode would produce straightforward outcomes so that users may better understand the fate and transport of target chemicals. Since the emission rate is arbitrary, the mass (and thus concentration, fugacity, transport flux, etc.) of 2-BEB in each compartment is proportional to the emission rate and is not necessarily relevant information. However, mass fractions and persistence times are independent of the emission rate and are still meaningful for the evaluation of fate and distribution of 2-BEB in the environment.

C. Sensitivity Analysis

A conventional sensitivity analysis was conducted to quantify the effect of changing one input variable (I_i) at a time by a fixed amount (ΔI_i) on the output of interest (O_j). Seven input parameters were examined, including HL_C, K_{OC}, BCF and half-lives in air, water, soil and sediment with $\Delta I/I = 0.001$, a typical value for the local sensitivity analysis (MacLeod et al., 2002). An Excel macro code was created to calculate fractional changes of model outcome ($\Delta O/O$) from the New EQC platform and generate sensitivity responses (SR as defined in Equation 1):

$$SR_{i,j} = \frac{\Delta O_j / O_j}{\Delta I_i / I_i} \qquad \text{Equation 1}$$

where *i* represents an input variable (partitioning and reactive properties of 2-BEB) and *j* a model outcome such as 2-BEB mass distribution, persistence and intermedia transport rates normalized to emission rate.

III. RESULTS AND DISCUSSION

A. Assessment of Fate, Distribution, and Transport

The results of the EQC model are provided for the assessment of fate (i.e., reaction and reaction rates), distribution (i.e., mass fraction in each compartment) and transport (i.e., rates of advection and intermedia transport). Since the terms of mass and concentration in the output were proportionally dependent on the emission rate, the values of output were converted into values normalized to the total mass remaining, which are independent of mass in the evaluative system. The normalized values are expressed in a percentage of total mass remaining if they are larger than 0.1%. On the contrary, if the percentage values are smaller than 0.1%, they are expressed in a scientific notation with two decimal places. It should be noted that realistic presence of a chemical is typically considered when a mass fraction is 5% or more of the total mass, although the criterion may range from 1% to 10% (Woodfine and Mackay, 2001). Since reaction, advection and overall persistence times were calculated with mass terms being canceled out (i.e., mass divided by mass/time), these values are informative and independent of total emission rate. For consistency, the total emission rate (E_T) in each of the five emission scenarios was fixed at 1,000 kg/hr while individual emissions to air, water and soil compartments were varied. Thus, the ratios of emissions to each compartment were important input variables of the EQC model.

1. Level II (Steady-state, equilibrium) modeling

Prior to Level III (i.e., non-equilibrium, steady-state) modeling, Level II (i.e., equilibrium, steady-state) analysis was performed to determine the ultimate equilibrium mass distribution in the environment. In this case, there are no net intermedia transport rates because fugacity values are same in the entire environment system. As shown in Table 4, when 2-BEB was released to the environment at 1,000 kg/hr, the equilibrium fugacity was 1.27×10^{-7} Pa. Note that fugacity is a criterion of equilibrium and a surrogate for concentration and that the fugacity value is also proportional to the total emission rate. Fugacity was used in the present study only for comparison with different scenarios in a relative sense. Essentially almost all 2-BEB was expected to be present either in soil (71.6%) or in water (26.1%). 2-BEB was lost by reaction at rates of 50.6%, 36.9%, and 6.7% of the total release rate (E_T or 1,000 kg/hr) in soil, water, and air, respectively. Advection loss was relatively smaller: 4.4% and 1.1% of E_T from air and water, respectively. Advection, reaction and overall persistence times were 3041, 179 and 169 hours, respectively.

2. Level III (Steady-state, non-equilibrium) modeling

In Level III model runs, intermedia transport processes between the compartments were also explored. The rate of intermedia transport is the product of fugacity and a mass transfer coefficient (Table 2), which is similar to 1st-order reaction kinetics. For

this reason, Level III model was expected to produce different fugacity values in different environmental compartments. Thus, Level III EQC model was tested to understand behaviors of 2-BEB under simple emission scenarios, such as emissions to a single compartment. Since the evaluative emission scenarios are not necessarily realistic, a plausible emission scenario would be useful in the future to best predict the fate, distribution and transport of 2-BEB in the evaluative environment. For each emission scenario, a table of major model outcomes with the most significant values shown in bold is provided, along with complete graphical representation. The table includes emission rates, mass distribution, fugacity values, losses via reaction and advection, normalized net intermedia transport rates, and residence times (reaction, advection and overall persistence). It is noted that intermedia transport rates are normalized to the total emission rate (E_T or 1,000 kg/hr), and only the net values of the normalized rates from one compartment to another are shown in the table.

Emission to Air

When 2-BEB is released to the air compartment only at an E_T of 1,000 kg/hr, 85.9% and 14.1% of E_T are removed by reaction and advection (Table 5a). Only 2.8% and 1.0% of E_T deposit to soil and water, respectively. As a result, 2-BEB is distributed to air (64.6% of total mass), soil (30.6%), water (4.8%), and sediment (<0.1%) at steady-state. Predicted concentrations of 2-BEB in air, soil, water, and sediment are 1.40×10^{-7}, 5.21×10^{-6}, 3.67×10^{-4}, and 2.86×10^{-5} g/m³, respectively. The fugacity value in air (1.55×10^{-6} Pa) is 2-3 orders-of-magnitude greater than those in other compartments (6.59×10^{-10} – 6.93×10^{-9} Pa). The advection, reaction and overall persistence times are 154, 25.2 and 21.6 hours, respectively, for this emission scenario.

Emission to Water

In the scenario where 2-BEB is emitted to the water compartment only at an E_T of 1,000 kg/hr, 89.3% and 10.7% of E_T are removed by reaction (more specifically biodegradation) and advection, respectively (Table 5b). Intermedia transports of 2-BEB to other compartments are insignificant: only 0.1% or less of E_T transport to the other compartments. At steady state, 2-BEB mass is distributed predominantly to water (98.6%) whereas insignificant mass fractions are predicted in other compartments. The large mass fraction in water is because transport to air and sediment was limited due to low K_{AW} and K_{OC} values. The mass in other compartments is insignificant (<0.1% in soil – 1.4% in sediment). Predicted concentrations of 2-BEB in water, sediment, air, and soil are 5.32×10^{-4}, 2.92×10^{-3}, 1.90×10^{-10}, and 5.01×10^{-7} g/m³, respectively. Fugacity values in water (3.06×10^{-7} Pa) and sediment (6.74×10^{-8} Pa) are 2-4 orders-of-magnitude greater than those in air (2.12×10^{-9} Pa) and soil (9.45×10^{-12} Pa). The advection, reaction and overall persistence times are 1012, 121 and 108 hours, respectively.

Emission to Soil

When it is released to soil, virtually all (i.e., 100%) of E_T is removed by reaction (Table 5c). Intermedia transports of 2-BEB to other compartments are insignificant:

only 0.1% and 0.2% of E_T transport to air and water, respectively. At steady state, 2-BEB mass is distributed predominantly to soil (99.9%) whereas insignificant mass fractions are predicted in other compartments. The large mass fraction in soil is because transport to sediment was limited due to low K_{AW} and K_{OC} value. The mass in other compartments is insignificant (<0.1% in air & sediment - 0.1% in water). Predicted concentrations of 2-BEB in soil, water, air, and sediment are 1.32×10^{-2}, 1.05×10^{-6}, 5.81×10^{-11}, and 5.79×10^{-6} g/m³, respectively. Fugacity values in soil (2.50×10^{-7} Pa) is 2-3 orders-of-magnitude greater than those in other compartments (1.33×10^{-10} – 6.46×10^{-10} Pa). The advection, reaction and overall persistence times are 8.87×10^{5}, 239 and 239 hours, respectively.

Summary for the Release to Air, Water, and Soil Only Scenarios

The model results with the three simple emission scenarios above show that a major fraction of the emission rate of 2-BEB is retained in or transported to water and/or soil compartments due to the small HL_C (or K_{AW}) value when 2-BEB is released to air. In the case, the removal of 2-BEB takes place predominantly in air where the rates of degradation and advection are relatively fast. On the other hand, volatilization to air is limited when 2-BEB is released to water or soil only. In the emission scenarios, a major fraction of E_T is removed by reaction and still remains in the compartment that receives 2-BEB.

B. Sensitivity Analysis

The sensitivity ratio (SR), which is calculated from Equation 1, represents the sensitivity of model outcome (O) to a small change in an input variable ($\Delta I/I$ = 0.001). For the change of each input variable, the effect on outcome is shown as SR and tabulated in Table 6. For persistence, absolute values of the SRs ≥ 0.1 are considered significant. For the mass distribution and intermedia transport SRs, the outcome values also must be significant (≥5%). Since the change of input is small, the SR results indicate the sensitivity of the model at the 'local' point of the input data set rather than in a wide range for the uncertainty analysis.

When 2-BEB is released to air (Table 6a), the mass fraction in air (i.e., the major compartment for the emission scenario) is HL_C (SR=0.31) and half-life in soil ($t_{½,S}$, SR=–0.30) whereas mass fraction in soil is more sensitive to HL_C (SR=–0.65) and half-life in soil ($t_{½,S}$, SR=0.69). The overall persistence is sensitive to half-life in air ($t_{½,A}$, SR=0.82), HL_C (SR=–0.28) and half-life in soil ($t_{½,S}$, SR=0.31). Intermedia transport processes from air to soil and water are sensitive to both HL_C (SR=–0.93) and half-life in air ($t_{½,A}$, SR=0.82), respectively.

When 2-BEB is released to water (Table 6b), mass distribution in water (i.e., the major compartment for the emission scenario) is not sensitive to any input variables whereas concentration in water is sensitive to only half-life in water ($t_{½,W}$, SR=0.89). Since all the intermedia transport processes are negligible, their sensitivity ratios are not meaningful. The overall persistence is influenced exclusively by $t_{½,W}$ (SR=0.89).

When 2-BEB is emitted to soil (Table 6c), mass distribution in soil (i.e., the major compartment for the emission scenario) is not sensitive to any input variables whereas

concentration in soil is sensitive to only $t_{½,S}$ (SR=1.00). Since all the intermedia transport processes are negligible, their sensitivity ratios are not meaningful. The overall persistence is also influenced exclusively by $t_{½,S}$ (SR=1.00).

IV. SUMMARY AND CONCLUSIONS

This study evaluated the fate, distribution and transport of 2-butoxyethyl benzoate (2-BEB) using the New EQC multimedia fugacity model. The EQC modeling was performed with the best selection of chemical property values as input data, and three standard emission scenarios. Sensitivity analyses were also performed to discover the most influential chemical properties of 2-BEB relevant to the fate, distribution and transport of the chemical. The main findings from the study are summarized as follows.

1. When it is released to air only, 2-BEB is removed by reaction (85.9% of the total emission rate, E_T) and advection (14.1% of E_T) whereas 2.8% and 1.0% of E_T are deposited to soil and water, respectively. At steady-state, mass fractions in air, soil, water and sediment are 64.6%, 30.6%, 4.8%, and <0.1%, respectively. The overall persistence is 21.6 hours, which is half-life in air (SR=0.82), Henry's Law constant (SR=–0.28) and half-life in soil ($t_{½,S}$, SR=0.31).
2. When it is released to water only, 2-BEB is removed by reaction and advection (89.3% and 10.7% of E_T, respectively) whereas transports to other compartments are limited. At steady state, mass distributions in water and sediment are 98.6% and 1.4%, respectively. The overall persistence is 108 hours, which is sensitive exclusively to half-life in water (SR=0.89).
3. When it is released to soil only, 2-BEB is removed by reaction (100% of E_T) whereas transports to other compartments are limited. At steady state, mass distributions in soil and water are 99.9% and 0.1%, respectively. The overall persistence is 239 hours, which is sensitive exclusively to half-life in soil (SR=1.00).

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TABLES

Table 1. Default values of landscape parameters and advection residence time in the EQC model

	Area (m^2)	**Depth (m)**	**Volume Fractions**	**Volume (m^3)**	**Density (kg/m^3)**	**Advection residence time (hr)**
Air (bulk)	**1×10^{11}**	**1,000**	**1**	**1×10^{14}**	**1.19**	**100**
Pure Air			1	1×10^{14}	1.19	
Aerosol			2×10^{-11}	2×10^{3}	2000	
Water (bulk)	**1×10^{10}**	**20**	**1**	**2×10^{11}**	**1000**	**1000**
Liquid			1	2×10^{11}	1000	
Susp. Particles			5×10^{-6}	1×10^{6}	1500	
Fish			1×10^{-6}	2×10^{5}	1000	
Soil (bulk)	**9×10^{10}**	**0.2**	**1**	**1.8×10^{10}**	**1500**	**N/A**
Air			0.2	3.6×10^{9}	1.19	
Liquid			0.3	5.4×10^{9}	1000	
Solid			0.5	9×10^{9}	2400	
Sediment (bulk)	**1×10^{10}**	**0.05**	**1**	**5×10^{8}**	**1280**	**50,000**
Liquid			0.8	4×10^{8}	1000	
Solid			0.2	1×10^{8}	2400	

Table 2. The intermedia transport velocities as mass transfer coefficients (MTC) used in the EQC model (same values were used from the EQC Model version 2.02)

Transport parameter	m/hr	m/year
Air side air-water MTC	5	43830
Water side air-water MTC	0.05	438.3
Rain rate	1×10^{-4}	0.877
Aerosol deposition velocity	6×10^{-10}	5.26×10^{-6}
Soil air phase diffusion MTC	0.02	175
Soil water phase diffusion MTC	1×10^{-5}	0.0877
Soil air boundary layer MTC	5	43830
Sediment-water MTC	1×10^{-4}	0.877
Sediment deposition velocity	5×10^{-7}	4.38×10^{-3}
Sediment resuspension velocity	2×10^{-7}	1.75×10^{-3}
Soil water runoff rate	5×10^{-5}	0.438
Soil solids runoff rate	1×10^{-8}	8.77×10^{-5}

Table 3. Input parameters used in EQC level III modeling of 2-butoxyethyl benzoate (2-BEB)

Compound	2-butoxyethyl benzoate (2-BEB)	
CASRN	5451-76-3	
EC Number	226-685-8	
Molecular weight (g/mol)	222.29	
Data temperature (°C)	25	
Melting point (°C)	–95	European Chemicals Agency (2019)
Vapor pressure (Pa)	0.052	European Chemicals Agency (2019)
Water solubility (mg/L)	106	at 20 °C, European Chemicals Agency (2019)
Log K_{OW} (-)	3.37	Estimated by ACD/Labs (2019) (Note 1)
Log K_{AW} (-)	–4.29	HENRYWIN v.3.20 (US EPA, 2019) HL_C: 0.128 Pa m^3 mol^{-1}
Log K_{OC} (-)	3.10	European Chemicals Agency (2019)
BCF (L/kg)	46.2	BCFBAF (v3.01) (US EPA, 2019)
Half-life (hr)		
Air	11.8	AOPWIN v1.92 (US EPA, 2019)
Water	82.8	Biodegradation (European Chemicals Agency, 2019)
Soil	166	Estimated: 2 × Half-life in water
Sediment	745	Estimated: 9 × Half-life in water

Note 1: There are additional estimations of log K_{OW}: 3.77 at 30 °C by HPLC method (European Chemicals Agency, 2019), 3.03 from KOWWIN v1.68 (US EPA, 2019)

Table 4. Output of preliminary EQC level II equilibrium modeling of 2-butoxyethyl benzoate (2-BEB) at a total emission rate of 1,000 kg/hr, followed by complete graphic interpretation

Emission to the environment

	Air	Water	Soil	Sediment	All
Emission rate (kg/hr)	-	-	-	-	1000
Mass fraction	0.67%	**26.1%**	**71.6%**	1.6%	100%
Fugacity (Pa)	7.50×10^{-8}	7.50×10^{-8}	7.50×10^{-8}	7.50×10^{-8}	7.50×10^{-8}
Reaction loss	**6.7%**	**36.9%**	**50.6%**	0.1%	94.4%
Advection loss	1.1%	4.4%	0%	5.50×10^{-5}	5.6%
Overall persistence (hr)			**169**		
Reaction time (hr)			179		
Advective time (hr)			3,041		

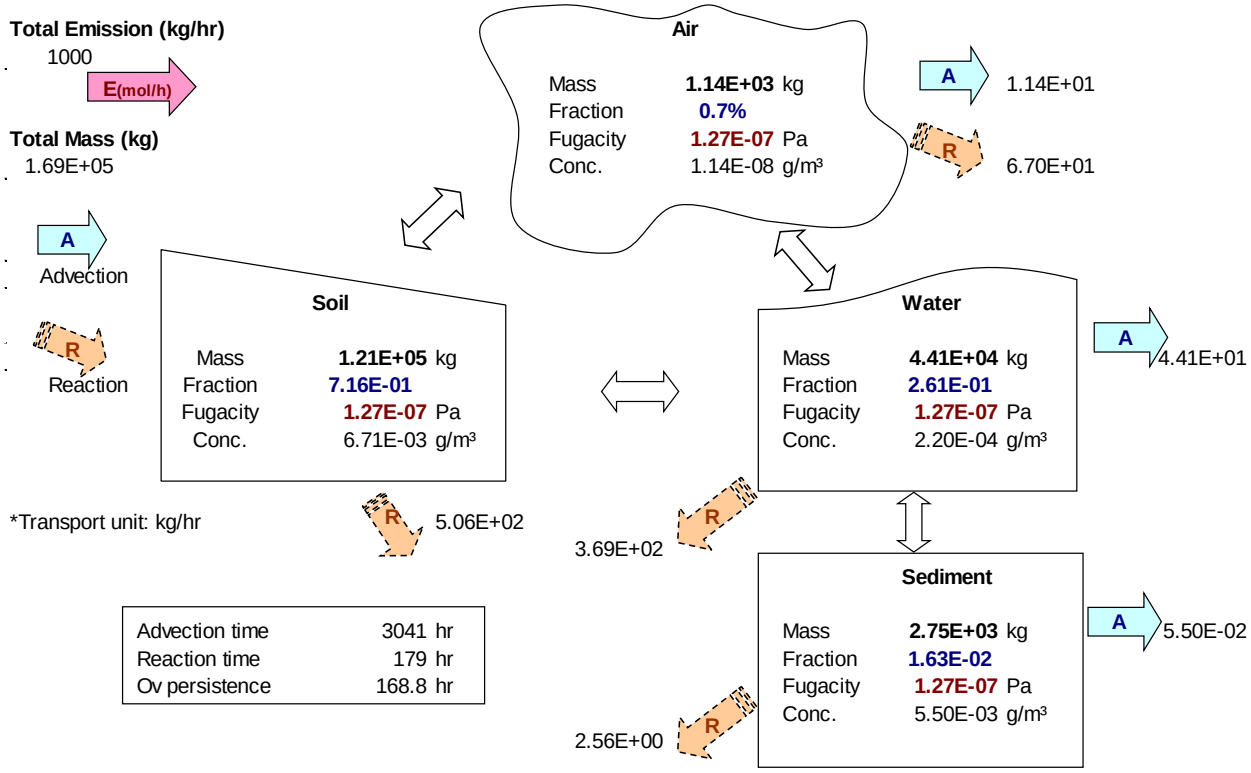
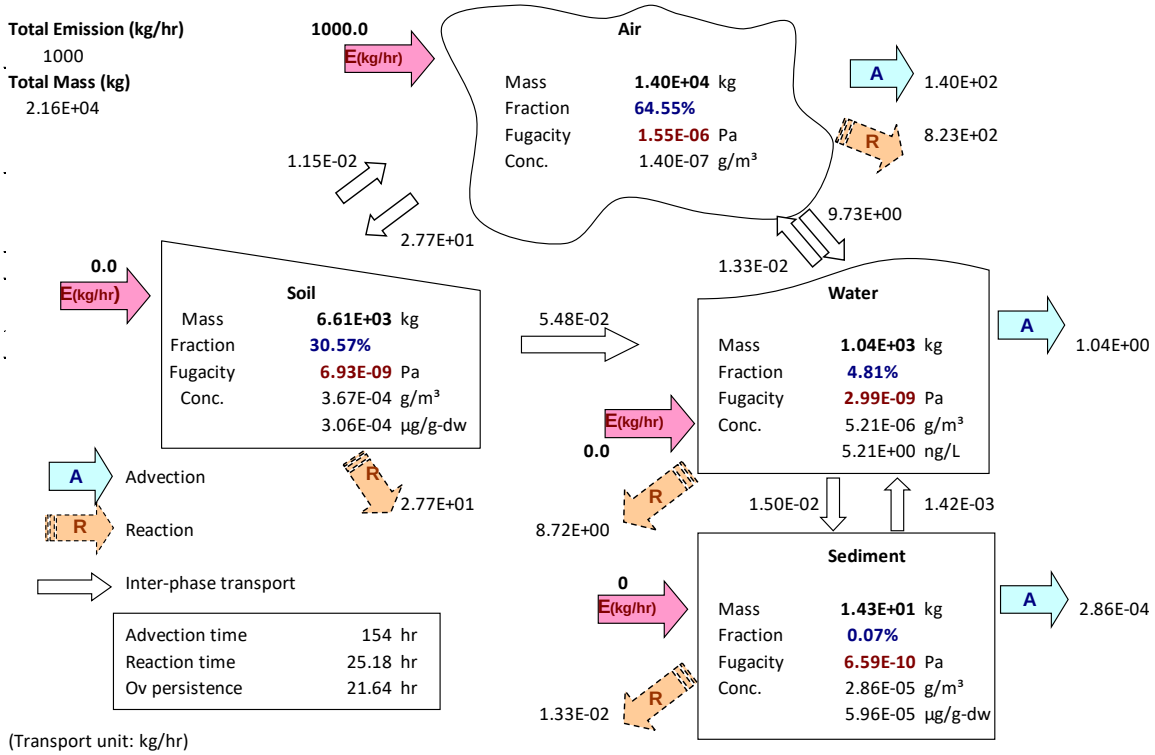


Table 5. Output of EQC level III modeling of 2-butoxyethyl benzoate (2-BEB), followed by graphic interpretation. The most significant values are shown in bold.

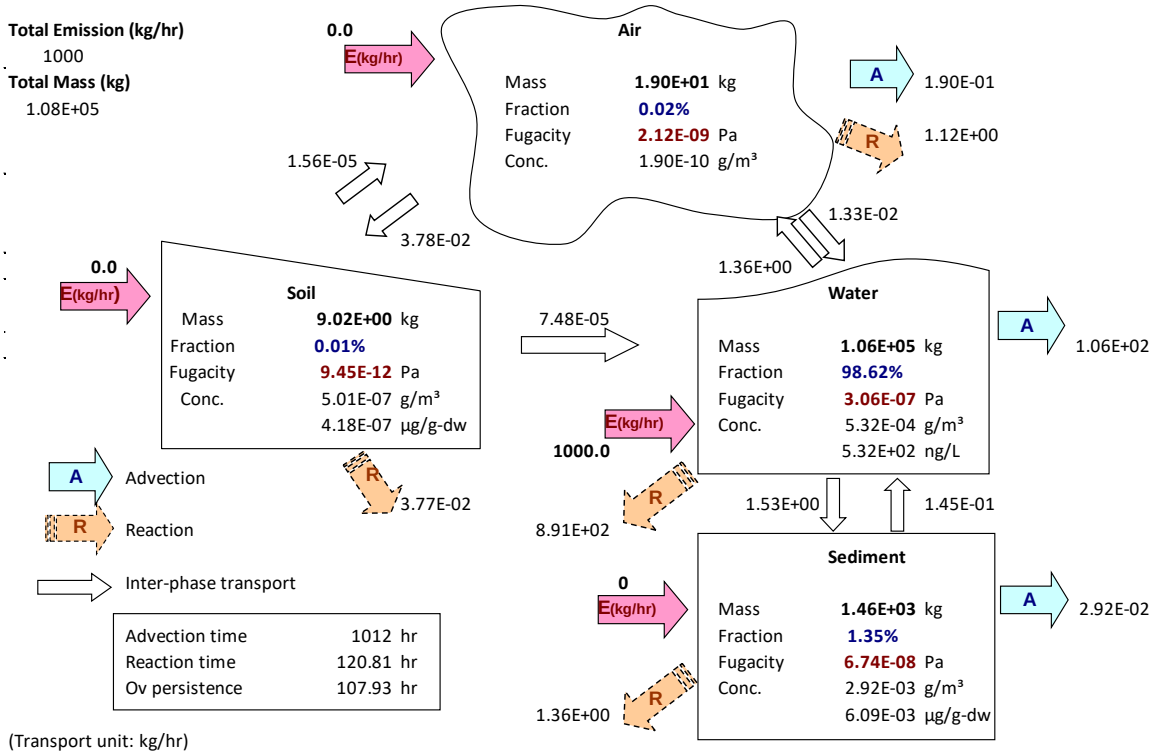
(a) Emission to Air scenario

	Air	Water	Soil	Sediment	All
Emission rate (kg/hr)	1000	0	0	0	1000
Mass fraction	**64.6%**	4.8%	**30.6%**	6.61×10^{-4}	100%
Fugacity (Pa)	1.55×10^{-6}	2.99×10^{-9}	6.93×10^{-9}	6.59×10^{-10}	-
Reaction loss	**82.3%**	0.9%	2.8%	1.33×10^{-5}	85.9%
Advection loss	**14.0%**	0.1%	0%	2.86×10^{-7}	14.1%
Net intermedia transport rate (fraction to the total emission rate)	A→W	1.0%		W→Sed	1.36×10^{-5}
	A→S	2.8%		S→W	5.48×10^{-5}
Overall persistence (hr)			**21.6**		
Reaction time (hr)			25.1		
Advective time (hr)			154		



(b) Emission to Water scenario

	Air	Water	Soil	Sediment	All
Emission rate (kg/hr)	0	1000	0	0	1000
Mass fraction	1.76×10^{-4}	**98.6%**	8.36×10^{-5}	1.4%	100%
Fugacity (Pa)	2.12×10^{-9}	3.06×10^{-7}	9.45×10^{-12}	6.74×10^{-8}	-
Reaction loss	0.1%	**89.1%**	3.77×10^{-5}	0.1%	89.3%
Advection loss	1.90×10^{-4}	**10.6%**	0%	2.92×10^{-5}	10.7%
Net intermedia transport rate (fraction to the total emission rate)	W→A	0.1%		W→Sed	0.1%
	A→S	3.78×10^{-5}		S→W	7.48×10^{-8}
Overall persistence (hr)			**108**		
Reaction time (hr)			121		
Advective time (hr)			1,012		



(c) Emission to Soil scenario

	Air	Water	Soil	Sediment	All
Emission rate (kg/hr)	0	0	1000	0	1000
Mass fraction	2.44×10^{-5}	0.1%	**99.9%**	1.21×10^{-5}	100%
Fugacity (Pa)	6.46×10^{-10}	6.05×10^{-10}	2.50×10^{-7}	1.33×10^{-10}	
Reaction loss	3.42×10^{-4}	0.2%	**99.8%**	2.69×10^{-6}	100%
Advection loss	5.81×10^{-5}	2.11×10^{-4}	0%	5.79×10^{-8}	2.69×10^{-4}
Net intermedia transport rate (fraction to the total emission rate)	W→A	1.36×10^{-6}		W→Sed	2.75×10^{-6}
	S→A	4.02×10^{-4}		S→W	0.2%
Overall persistence (hr)			**239**		
Reaction time (hr)			239		
Advective time (hr)			887,085		

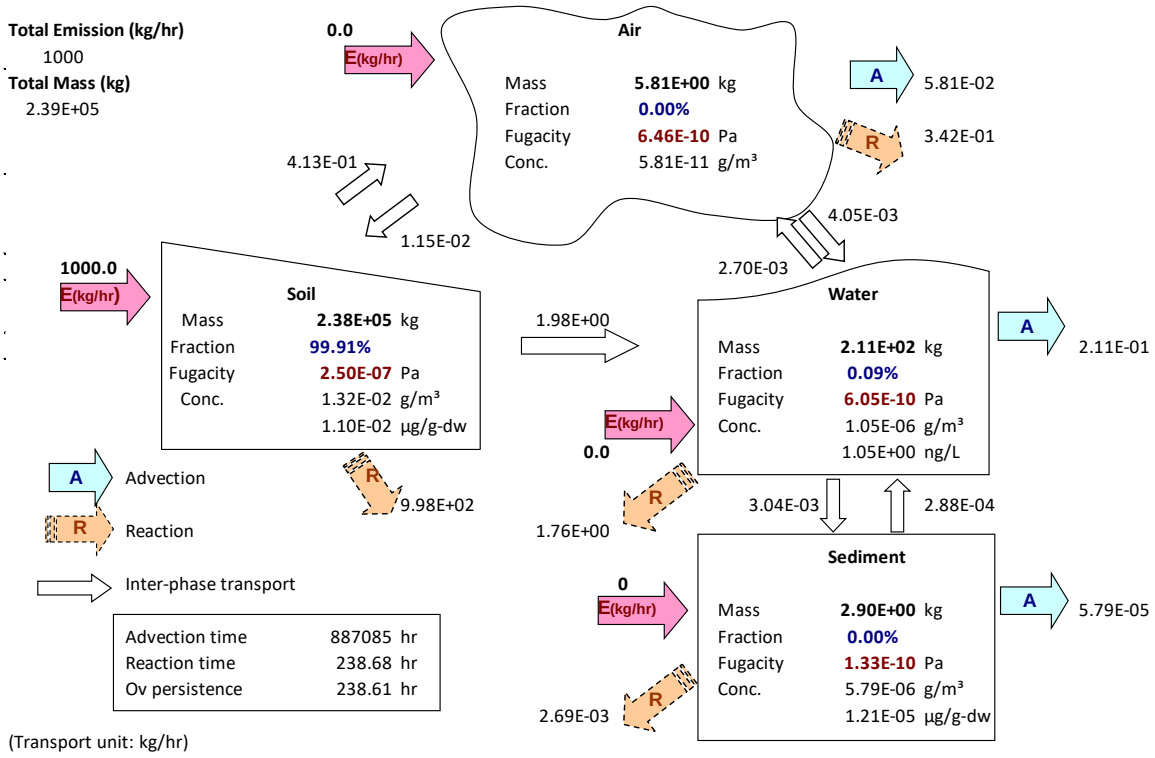


Table 6. The sensitivity analysis of 2-BEB mass distribution, persistence and intermedia transport (normalized to the total emission rate) to input parameters. Sensitivity ratio, SR = (ΔO/O)/(ΔI/I), where (ΔI/I) = 0.001. The most significant values are shown in bold.

(a) Emission to Air scenario

Sensitivity Ratio	Mass distribution				Persistence		
	Air	Water	Soil	Sediment	Advection Time (h)	Reaction Time (h)	Overall Persistence (h)
Base Value	**64.6%**	4.8%	**30.6%**	6.61E-04	154	25.2	**21.6**
Henry's LC	**0.3062**	0.0200	**-0.6498**	0.0200	**-0.3040**	**-0.2724**	**-0.2769**
K_{OC}	-0.0009	-0.0073	0.0015	**0.7178**	0.0009	0.0009	0.0009
BCF	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000
Half-life in air	0.0000	0.0000	0.0000	0.0000	0.0000	**0.9576**	**0.8227**
Half-life in water	-0.0435	**0.8472**	-0.0435	**0.8472**	0.0369	0.0446	0.0435
Half-life in soil	**-0.3051**	**-0.2995**	**0.6922**	**-0.2995**	**0.3052**	**0.3052**	**0.3052**
Half-life in sediment	-0.0006	-0.0005	-0.0006	**0.8856**	0.0006	0.0006	0.0006

Sensitivity Ratio	Concentrations and net intermedia transport normalized to total emission rate						
	C_A (g/m^3)	C_W (g/m^3)	C_S (g/m^3)	C_Sed (g/m^3)	A←→W	A←→S	W←→Sed
Base Value	1.40E-07	5.21E-06	3.67E-04	2.86E-05	1.0%	2.8%	1.36E-05
Henry's LC	0.0293	**-0.2569**	**-0.9265**	**-0.2569**	**-0.2531**	**-0.9265**	**-0.2569**
K_{OC}	0.0000	-0.0065	0.0023	**0.7187**	0.0000	0.0004	**0.7187**
BCF	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000
Half-life in air	**0.8227**	**0.8227**	**0.8227**	**0.8227**	**0.8227**	**0.8227**	**0.8227**
Half-life in water	0.0000	**0.8907**	0.0000	**0.8907**	-0.0012	0.0000	**0.8907**
Half-life in soil	0.0000	0.0056	**0.9976**	0.0056	0.0000	-0.0004	0.0056
Half-life in sediment	0.0000	0.0001	0.0000	**0.8862**	0.0000	0.0000	-0.0926

(b) Emission to Water scenario

Sensitivity Ratio	Mass distribution				Persistence		
	Air	Water	Soil	Sediment	Advection Time (h)	Reaction Time (h)	Overall Persistence (h)
Base Value	1.76E-4	**98.6%**	8.36E-05	1.4%	1012	121	**108**
Henry's LC	**1.0239**	-0.0002	0.0673	-0.0002	-0.0016	-0.0011	-0.0012
K_{OC}	-0.0117	-0.0098	-0.0094	**0.7153**	0.0096	0.0087	0.0088
BCF	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000
Half-life in air	**0.8225**	-0.0002	**0.8225**	-0.0002	-0.0013	0.0004	0.0002
Half-life in water	0.0000	0.0000	0.0000	0.0000	0.0000	**0.9972**	**0.8907**
Half-life in soil	-0.0001	-0.0001	**0.9975**	-0.0001	0.0001	0.0001	0.0001
Half-life in sediment	-0.0120	-0.0120	-0.0120	0.8741	0.0118	0.0122	0.0121

Sensitivity Ratio	Concentrations and net intermedia transport normalized to total emission rate						
	C_A (g/m^3)	C_W (g/m^3)	C_S (g/m^3)	C_Sed (g/m^3)	A←→W	A←→S	W←→Sed
Base Value	1.90E-10	**5.32E-4**	5.01E-07	**2.92E-3**	-0.1%	3.78E-05	1.39E-03
Henry's LC	**1.0228**	-0.0013	0.0661	-0.0013	**0.9960**	0.0661	-0.0013
K_{OC}	-0.0029	-0.0010	-0.0006	**0.7242**	-0.0029	-0.0025	**0.7242**
BCF	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000
Half-life in air	**0.8227**	0.0000	**0.8227**	0.0000	-0.0081	**0.8227**	0.0000
Half-life in water	**0.8907**	0.8907	**0.8907**	**0.8907**	**0.8907**	**0.8907**	**0.8907**
Half-life in soil	0.0000	0.0000	**0.9976**	0.0000	0.0000	-0.0004	0.0000
Half-life in sediment	0.0001	0.0001	0.0001	0.8862	0.0001	0.0001	-0.0926

(c) Emission to Soil scenario

Sensitivity Ratio	Mass distribution				Persistence		
	Air	Water	Soil	Sediment	Advection Time (h)	Reaction Time (h)	Overall Persistence (h)
Base Value	2.44E-05	0.1%	**99.9%**	1.21E-05	887085	239	**239**
Henry's LC	**0.1655**	-0.0016	0.0000	-0.0016	-0.0345	-0.0001	-0.0001
K_{OC}	**-0.9882**	**-0.9774**	0.0009	**-0.2529**	**0.9805**	0.0012	0.0014
BCF	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000
Half-life in air	**0.8227**	0.0017	0.0000	0.0017	**-0.1790**	0.0001	0.0000
Half-life in water	0.0050	**0.8899**	-0.0008	**0.8899**	**-0.6983**	0.0010	0.0008
Half-life in soil	0.0000	0.0000	0.0000	0.0000	0.0000	**0.9979**	**0.9976**
Half-life in sediment	0.0000	0.0001	0.0000	**0.8862**	-0.0003	0.0000	0.0000

Sensitivity Ratio	Concentrations and net intermedia transport normalized to total emission rate						
	C_A (g/m^3)	C_W (g/m^3)	C_S (g/m^3)	C_Sed (g/m^3)	A←→W	A←→S	W←→Sed
Base Value	5.81E-11	1.05E-06	**1.32E-02**	5.79E-06	1.35E-06	-4.02E-4	2.75E-06
Henry's LC	**0.1655**	-0.0017	-0.0001	-0.0017	**-2.3389**	**0.1571**	-0.0017
K_{OC}	**-0.9868**	**-0.9760**	0.0023	**-0.2515**	**-1.0048**	**-0.9869**	**-0.2515**
BCF	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000
Half-life in air	**0.8227**	0.0017	0.0000	0.0017	**2.4691**	-0.0236	0.0017
Half-life in water	0.0058	**0.8907**	0.0000	0.8907	**-1.7688**	-0.0002	**0.8907**
Half-life in soil	**0.9976**	**0.9976**	**0.9976**	**0.9976**	**0.9976**	**0.9976**	**0.9976**
Half-life in sediment	0.0000	0.0001	0.0000	**0.8862**	-0.0003	0.0000	-0.0926

Attachment 3
Justification for the use of information on 2-Butoxyethanol (EGBE) for 2-Butoxyethylbenzoate (2-BEB) – Key Points

Summary

There are several key aspects to justify the use of EGBE information for BEB based on metabolic/biotransformation to common compounds (or for this case, biotransformation of the target compound to two source compounds). The key aspects of this justification are: 1) rapid metabolism of the target compound to the source compounds; 2) lack of formation of non-common compounds and 3) no impact of parent compound.

Introduction

2-Butoxyethylbenzoate (BEB) is an ester of 2-butoxyethanol (EGBE) and benzoic acid (BA). In the body, it is rapidly hydrolyzed by the numerous esterases present in mammalian systems (such as intestinal esterases, liver esterases, and/or blood esterases) to BA and EGBE. BA and EGBE are subsequently metabolized to their corresponding metabolites. Consequently, systemic exposure is to the metabolites (EGBE and BA) rather than BEB and therefore, the toxicity of BEB can be evaluated using the available data on EGBE and BA.

Evidences for supporting the quick hydrolysis metabolic pathways of BEB

1) No BEB was detected in C_{max} rat blood samples from oral gavage studies at dose levels of 25 mg/kg or 250mg/kg

   Radio-labeled BEB (where the radio-labeled position was on the glycol ether portion of BEB) was used to evaluate its absorption, distribution, metabolism and elimination (Dow, 2016a). Animals were dosed by oral gavage either once (25 and 250 mg/kg bw) or daily for 14 days (25 mg/kg bw). C_{max} blood samples were collected from the study and analyzed by high performance liquid chromatography (HPLC) separation with in-line radiochemical detection (RAM) or fraction collection with liquid scintillation spectrometry (LSS) assay of the fractions followed by HPLC with electrospray ionization and accurate mass/time-of-flight mass spectrometry detection (LC/ESI/TOF-MS) (for metabolite identification). This analysis showed no detectable parent (BEB) in any of the C_{max} blood samples. The most abundant C_{max} blood metabolite was identified as 2-butoxyacetic acid (BAA) which was formed from the EGBE metabolite of BEB.

   The absence of BEB and the presence of BAA as the most abundant metabolite in C_{max} blood samples clearly indicated that BEB was quickly hydrolyzed to BA and EGBE after

absorption. Once formed, EGBE was then subsequently metabolized to BAA and other metabolites.

2) Similar dose recoveries were observed in excreta and CO_2 from both ADME studies of ^{14}C-BEB (radio-labeled position was on the 2-butoxyethanol portion) and ^{14}C-EGBE (radiolabeled position was the same as in ^{14}C-BEB) at equal molar dose levels in rats

The percentages (based on the radioactivity) of the dose recovered in excreta and CO_2 from the Dow ADME study on BEB {dose level 250 mg/kg (1.1 mmole/kg), Dow, 2016a} and a previous ADME study on 2-butoxyethanol (EGBE) {dose level 125 mg/kg (1.1 mmole/kg), Ghanayem, 1987} are summarized in **Table 1**.

Table 1 Percentages of dose recoveries in excreta and CO_2

Test material	Dose level		Percentage of dose recoveries in excreta and CO_2				Minimal absorption
	mg/kg	mmole/kg	In 24 hr urine	In 24 hr CO_2	In 48 hr CO_2	In 48 hr Feces	% of the dose
BEB [a]	250 mg/kg	1.1 mmole/kg	61-62	11-14	13-15	2	88-95
EGBE[b]	125mg/kg	1.1 mmole/kg	64	14	18	2	>88

[a]: Dow Chemical (2016a), both excreta and CO2 were collected through 168 hrs after dosing;
[b]: Ghanayem (1987), both excreta and CO2 were collected through 48 hrs after dosing;

As shown in **Table 1**, very similar percentages of dose recoveries in excreta and CO_2 were observed for BEB and EGBE at the same mmole/kg dose levels and the same corresponding collection time points after dosing. Since the same ^{14}C-radiolabeled positions were labeled in both test substances, the results in **Table 1** clearly indicate again that BEB was very quickly hydrolyzed to EGBE and BA after dosing and subsequently the formed EGBE exhibited similar toxicokinetics to the singularly administered EGBE in rats.

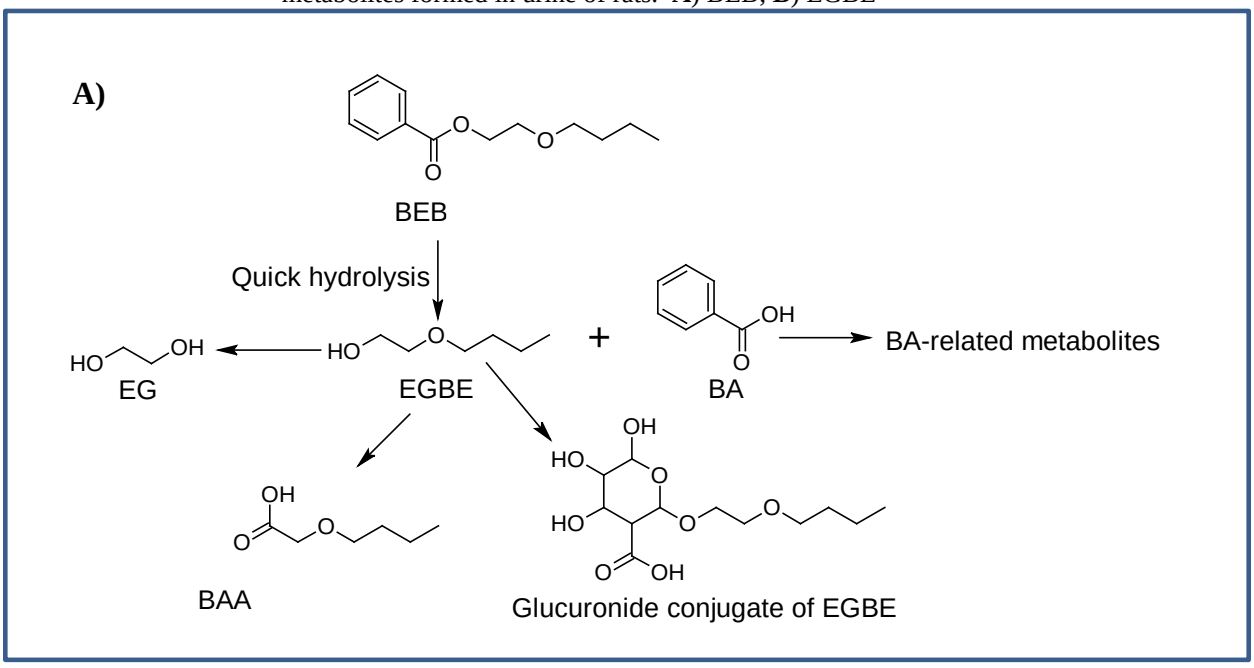
3) Similar major metabolite profiles were observed in urine from both ADME studies of ^{14}C-BEB (radio-labeled position was on the 2-butoxyethanol portion) and ^{14}C-EGBE (radio-labeled position was the same as in ^{14}C-BEB) at equal molar dose levels in rats

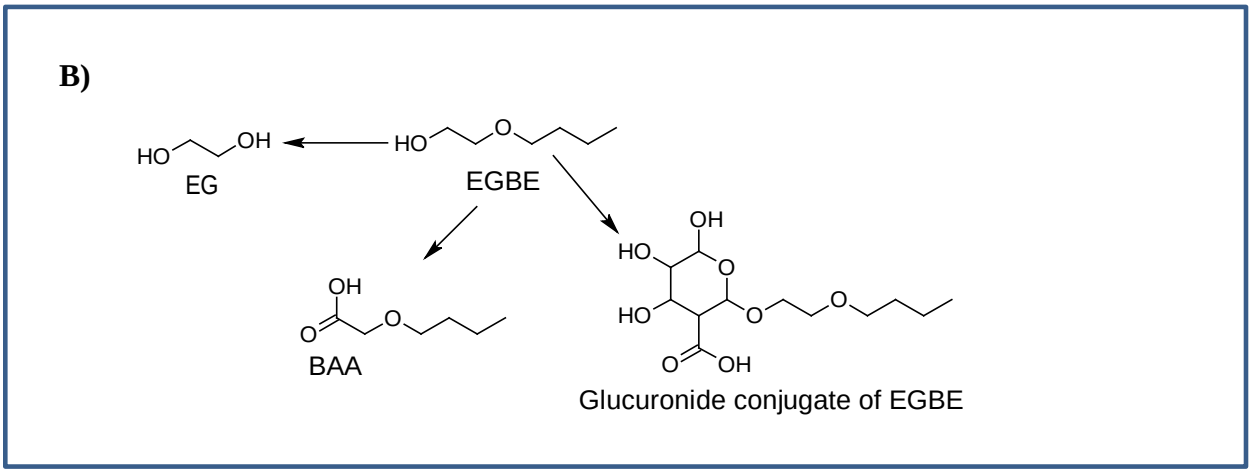
According to the urinary metabolite profiling results from the Dow BEB ADME study in rats at the dose level of 250 mg/kg (1.1 mmole/kg, Dow, 2016a), no parent BEB was detected in the urine samples and three major metabolites were detected and identified as 2-butoxyacetic acid (BAA, most abundant), 2-butoxyethanol glucuronide (the second most abundant), and ethylene glycol (EG, the third most abundant peak, this peak was eluted in solvent front and had the same retention time as radiolabeled ^{14}C-EG). In a similar way, three major metabolites were detected in the urinary samples of the Bhanayem's 2-butoxyethanol (EGBE) ADME study in rats at a molar equivalent dose level of 125 mg/kg

{(1.1 mmole/kg), Ghanayem (1987)}. These three metabolites were identified as 2-butoxyacetic acid (BAA, most abundant), 2-butoxyethanol glucuronide (the second most abundant), and a third peak (the third most abundant peak) which was eluted in the solvent front and was not identified in the Bhanayem study possibly due to the lack of appropriate analytical methods at the time of this study. However, based on the early retention time of this peak, it is most likely to be EG as identified in the Dow study on BEB.

Based on the major urinary metabolite profiling results, the metabolic pathways of both BEB and EGBE can be proposed (**Figure 1)**.

Figure 1. Proposed metabolic pathways of BEB and EGBE based on the major metabolites formed in urine of rats: **A**) BEB; **B**) EGBE





As shown in **Figure 1**, the similar major urinary metabolite formation pattern between BEB and EGBE further indicated that BEB was quickly hydrolyzed to EGBE and benzoic acid (BA) after oral administration in rats. The resulting EGBE was subsequently further metabolized to the same major metabolites as direct oral administered EGBE in rats.

Similar toxicology effects supporting the use of EGBE data

An evaluation of BEB and its two metabolites, EGBE and BA, show a similar pattern of toxicity between BEB and EGBE. Comparing oral repeat dose studies with BEB and EGBE, dietary and drinking water respectively (US NTP, 1993; Dow, 2016b), show the same toxicity profile with effects on body weight, hematology (decreased hemoglobin, erythrocytes and MCHC; increased reticulocytes, MCV and MCH), and liver histopathology (increased cytoplasmic eosinophilia), along with females being more sensitive for both substances. When the data is evaluated on a molar basis, noting that the LOEL for hematology effects for EGBE in males was ~280 mg/kg/day and females ~150 mg/kg/day, the molar equivalent dose of BEB would be ~525 mg/kg/day and ~280 mg/kg/day for males and females, respectively. This correlates well with the study results from the OECD 422 performed with BEB, showing hematology effects in the high dose females (BEB dose through gestation of ~380 and during lactation of ~565 mg/kg/day) and no effect in males (BEB dose in high dose males of ~380 mg/kg/day) (**Table 2**).

Table 2: Hemolytic effect compared to EGBE dose

Study	**Gender**	**EGBE[a] dose (mg/kg/day)**						
		~20	~70	~140	~200	~300	~365	~460
EGBE 90-day	male		69	129		281[b]	367[b]	452[b]
	female		82	151[c]		304[c]	363[c]	470[c]
BEB OECD 422	male	21	61		201			
	female (gestation)	20	60		202[c]			
	female (lactation)	28	90			300[c]		

a: for BEB, molar equivalent EGBE dose

b: hemolytic effect in males

c: hemolytic effect in females

BA, with its low toxicity, especially at the molar equivalents in the BEB studies, showed no clear trend in toxicity across studies and therefore does not contribute toxicity to BEB.

Conclusions

Based on the Cmax blood profiling results on BEB, similar dose recovery results in excreta and CO_2, and the same major urinary metabolite formation from both BEB and EGBE ADME studies at equal mole dose level (mmole/kg), BEB was clearly quickly hydrolyzed to EGBE and BA in rats after oral administration. This rapid enzyme hydrolysis shows that the parent (target) compound will not impact toxicity. This along with the formation of the same major urinary metabolites means there would be no non-common compounds formed. The rapid metabolism to EGBE is also supported by both EGBE and BEB having similar toxicological findings at similar molar dose levels. Since BA is considered safe for use as a food preservative and thus can be considered as having a low order of toxicity, it can be expected that the toxicity of BEB is driven solely by the metabolite product EGBE. Therefore, the toxicity of BEB can be evaluated using the available data on EGBE and BA.

Reference:

1. The Dow Chemical Company (2016a). 2-Butoxyethyl benzoate: Pharmacokinetics and metabolism in F344/DuCrl Rats. Testing laboratory: Dow Toxicology and Environmental Research and Consulting, Midland MI. Report no.: DR-0176-1951-027. Owner Company: The Dow Chemical Company. Study number: 151042. Report date: 2016-08-02.
2. The Dow Chemical Company (2016b). 2-Butoxyethyl benzoate: A combined dietary toxicity study with the reproduction/developmental toxicity screening test in Crl:CD(SD) rats. Testing laboratory: Dow Toxicology and Environmental Research and Consulting, Midland MI. Report no.: DR-0176-1951-028. Owner Company: The Dow Chemical Company. Study number: 151056. Report date: 2016-02-24.
3. Ghanayem BI, Burka LT, Sanders JM, Mathews HB (1987) Metabolism and disposition of ethylene glycol monobutyl ether (2-butoxyethanol) in rats. *Drug Metab. Dispos*. 15, 478-490.
4. US NTP (1993). NTP Technical Report 26 on Toxicity Studies of Ethylene Glycol Ethers 2-Methoxyethanol, 2-Ethoxyethanol, 2-Butoxyethanol Administered in Drinking Water to F344/N Rats and B6C3FX Mice. NIH Publication 93-3349.

Attachment 4

2-Butoxyethyl Benzoate Mammalian Toxicology Summary

Below are summaries of the full toxicity data set for 2-butoxyethyl benzoate. More extensive study summaries were included in the REACh dossier submission and can be viewed at the following link for more details: https://echa.europa.eu/registration-dossier/-/registered-dossier/23065

Acute Oral

Title: Butyl CELLOSOLVE™ Benzoate: Acute Oral toxicity Study (Up and Down Procedure) in Wistar rats; The Dow Chemical Company; 27 February 2013; DR-0176-1951-002[4]

Summary: An acute oral toxicity study performed in female Wistar rats using the 'Up-Down' procedure identified an LD50 value of approximately 940 mg/kg bw after a dose range of 550 and 2000 mg/kg bw) was tested. All animals dosed with 2000 mg/kg bw via oral gavage died within 6 days of dosing. All animals dosed with 550 mg/kg bw survived to the end of the study, gained weight and showed no abnormal clinical signs during the observation period. The necropsy of the animals dosed with 2000 mg/kg showed clear evidence of systemic toxicity. The observations of systemic toxicity in the animals dosed with 2000 mg/kg bw 2-butoxyethul benzoate included:

- kidney – discolored red, multifocal
- urinary bladder – distended with red color content
- stomach glandular mucosa - erosion, discolored red multifocal
- liver – pale

These findings are highly consistent with those observed in acute oral toxicity studies with 2-butoxyethanol (EGBE). The acute toxicity of 2-butoxyethanol in rodents is well understood. 2-Butoxyethanol is metabolized to butoxyacetic acid which causes hemolysis of red blood cells. The hemolysis is considered to be the main factor resulting in death of the animals in acute oral toxicity studies. The systemic toxicity observations in this study with 2-butoxyethyl benzoate are indicative of hemolysis as well and likely plays a key role in the acute oral toxicity. As such, it appears likely that the 2-butoxyethyl benzoate is metabolized to release benzoic acid and 2-butoxyethanol, with metabolite 2-butoxyethanol playing the major role in acute oral toxicity (Figure 1; Pharmacokinetics Study).

A significant body of work demonstrates human red blood cells are far more resistant to the hemolytic effects of 2-butoxyethanol than rodent species (Attachment 4). It is therefore likely that humans would be more resistant to the effects of 2-butoxyethyl benzoate on red blood cells. However, irrespective of the difference in sensitivity between rats and humans, 2-butoxyethanol still requires classification for acute toxicity (oral route). As such the potential species differences in sensitivity could not be used to argue that 2-butoxyethyl benzoate should not be classified for acute toxicity.

Based on the data from this study 2-butoxyethyl benzoate meets the criteria for classification as Acute Toxicity Category 4 according to GHS (and CLP), and Xn R22: Harmful if swallowed, according to DSD

Acute Dermal

Title: Butyl CELLOSOLVE™ Benzoate: Acute Dermal toxicity Study (Up and Down Procedure) in Wistar rats; The Dow Chemical Company: 29 December 2012; DR-0176-1951-003[1]

Summary: An acute dermal toxicity test was conducted with male and female Wistar rats to determine the potential for 2-butoxyethyl benzoate to produce toxicity from a short term exposure via the dermal (semi-occluded) route.

The test was initiated with five female rats at the dose of 2000 mg/kg body weight. As there were no clinical signs of toxicity, local skin reactions or mortality, the treatment was then conducted in 5 male rats at the same dose. All the rats were observed for clinical signs of toxicity and mortality for 14 days post application. There were no clinical signs of toxicity, local skin reactions or mortality. All animals had gained body weight during the 14- day observation period. At the end of the observation period, all animals were euthanized and subjected to necropsy. There were no gross pathological abnormalities detected at the necropsy.

Under the conditions of this study, the acute dermal LD50 of 2-butoxyethyl benzoate is greater than 2000 mg/kg body weight in male and female Wistar rats. Therefore there is no classification of acute dermal toxicity for 2-butoxyethyl benzoate

Acute Inhalation

Title: 2-Butoxyethyl Benzoate: Acute Liquid Aerosol Inhalation Toxicity Study in F344/DuCrl Rats; The Dow Chemical Company; 16 November 2015; DR-0176-1951-025[9]

Summary: An acute inhalation toxicity test was conducted with male and female F344/DuCrl rats to determine the potential for 2-butoxyethyl benzoate to produce toxicity from a short term exposure via the inhalation route.

Two groups of five F344/DuCrl rats/sex were exposed for four hours, using a nose-only inhalation exposure system, to time-weighted average (TWA) chamber concentrations of 3.71 or 5.39 mg 2-Butoxyethyl benzoate per liter of air. The mass median aerodynamic diameter (MMAD) of aerosolized 2-Butoxyethyl benzoate present in the exposure chamber test atmosphere averaged 4.15 microns with an average geometric standard deviation (GSD) of 2.17 microns for the 3.71 mg/L exposure and 2.90 microns with a GSD of 2.04 microns for the 5.39 mg/L exposure. All the rats were observed for clinical signs of toxicity and mortality for 14 days post exposure. All animals survived through the 14 day observation period. Clinical signs of toxicity were limited to soiling on various parts of the body which returned to normal by test day 7. Both treatment groups had mean body weight losses on test day 2 but body weights exceeded pre-exposure levels on test day 8. At the end of observation period, all animals were euthanized and subjected to necropsy. There were no gross pathological abnormalities detected at the necropsy.

Under the conditions of this study, the acute inhalation four-hour LD50 of 2-butoxyethyl benzoate is greater than 5.39 mg/L in male and female F344/DuCrl rats. 2-Butoxyethyl benzoate is therefore not classified for acute inhalation toxicity.

Skin Irritation

Title: Butyl CELLOSOLVE™ Benzoate: Acute Dermal Irritation/Corrosion study in rabbits; The Chemical Company; 30 January 2013; DR-0176-1951-004[2]

Summary: An acute dermal irritation/corrosion study was conducted in rabbits to evaluate the skin irritation potential of 2-butoxyethyl benzoate. Three rabbits were treated (simultaneously for 4 hours) as per sponsor's request. A volume of 0.5 mL of the undiluted test substance was applied to the 6 cm^2 test site of approximately (2 x 3 cm) and covered by a 6-ply gauze pad. The patch was secured to the body of the animal by a non-irritating semi-occlusive adhesive tape. The patch was removed after 4 hours of skin contact and test sites were evaluated for skin irritation according to the Draize (1944) evaluation method.

The degree of irritation was evaluated and scored by Draize (1944) evaluation method at 1, 24, 48, 72 hours and on Day 7 post removal of the test patch. There were no clinical signs of toxicity or mortality. The skin reactions observed are as follows:

Rabbit No.	Sex	Treatment period	Observation time (post removal of the 4-hr test patch)	Erythema score	Edema Score	Total score
RB9663	M	4 hours	1 hour	0	0	0
			24 hours	1	0	1
			48 hours	1	0	1
			72 hours	1	0	1
			7^{th} day	0	0	0
RB9664	M	4 hours	1 hour	0	0	0
			24 hours	1	0	1
			48 hours	1	0	1
			72 hours	1	0	1
			7^{th} day	0	0	0
RB9665	M	4 hours	1 hour	0	0	0
			24 hours	1	1	2
			48 hours	1	1	2
			72 hours	1	1	2
			7^{th} day	0	0	0

M : Male

The individually determined mean irritation scores for each animal for erythema and edema resulting from application of 2-butoxyethyl benzoate for the 24, 48 and 72-hour intervals are:

Animal No. (Sex)	Erythema	Edema
RB9663 (M)	1.00	0.00
RB9664 (M)	1.00	0.00
RB9665 (M)	1.00	1.00

Based on the very minimal observations of irritation in this study and the absence of any effects persisting to the 7th day post treatment, under the testing conditions of this study, 2-butoxyethyl benzoate is not irritating.

Eye irritation

Title: Butyl CELLOSOLVE™ Benzoate: Acute Eye Irritation study in rabbits; The Dow Chemical Company; 27 February 2013; DR-0176-1951-005[3]

Summary: An acute eye irritation / corrosion study in rabbits was conducted to evaluate the eye irritation potential of 2-butoxyethyl benzoate. The test was performed in a stepwise manner. A single rabbit was initially exposed to the test substance. Since the test substance was not corrosive or severely irritating, the study was completed using two additional rabbits.

A quantity of 0.1 mL of the test substance was placed in the everted lower lid (conjunctival sac) of the left eye of each of three rabbits. The lids were gently held together for about one second, in order to minimize loss of the test substance. The right eye of each rabbit remained untreated and served as the reference control. The eyes were evaluated at 1, 24, 48 and 72 hours post instillation according to the scale for scoring ocular lesions (DRAIZE, 1944). There were no clinical signs of toxicity or mortality. All rabbits appeared healthy and gained body weight throughout the observation period.

There was no eye irritation (*i.e.* iritis, conjunctival irritation or corneal opacity) observed in any treated eye during the study at 1, 24, 48 and 72 hours post instillation. Under the conditions of this study, the mean eye irritation scores were as follows:

Observations at post instillation	Mean score			
	Conjunctiva	Iris	Cornea	Total mean score
1 hour	0	0	0	0
24 hours	0	0	0	0
48 hours	0	0	0	0
72 hours	0	0	0	0

The individually determined mean irritation scores for each animal for corneal opacity, iris lesion, conjunctival redness and conjunctival chemosis for the 24-, 48- and 72-hour intervals are:

Animal No. (Sex)	Corneal Opacity	Iris Lesion	Conjunctival Redness	Conjunctival Chemosis
RB9666 (M)	0	0	0	0
RB9667 (M)	0	0	0	0
RB9668 (M)	0	0	0	0

Under the conditions of this study, 2-butoxyethyl benzoate did not cause any eye irritation.

Skin Sensitizing Potential

Title: Butyl CELLOSOLVE™ Benzoate: Local Lymph Node Assay (LLNA) in Mice; The Dow Chemical Company; 31 March 2013; DR-0176-1951-001[6]

Summary: 2-Butoxyethyl benzoate was assessed for skin sensitising potential using the mouse Local Lymph Node Assay (LLNA). Based on the absence of irritation in the irritation screen, 2-butoxyethyl benzoate was tested at concentrations of 5, 25 and 100%. The vehicle used to make the dilutions was Methyl Ethyl Ketone. 2-butoxyethyl benzoate did not produce a stimulation index of >3 at any concentration. As such, this substance is not a skin sensitizer.

Pharmacokinetics

Title: 2-Butoxyethyl Benzoate: Pharmacokinetics and Metabolism in F344/DuCrl Rats; The Dow Chemical Company; 2 August 2016; DR-0176-1951-027[14]

Summary: Animals were dosed by oral gavage either once (25 and 250 mg/kg bw) or for 14 days (25 mg/kg bw) with radio-labelled 2-butoxyethyl benzoate. It should be noted that the radio-label was located on the glycol ether portion of 2-butoxyethyl benzoate so the metabolically derived benzoic acid (unlabeled) could not be evaluated.

Absorption and distribution: Orally administered 2-butoxyethyl benzoate was absorbed rapidly without any apparent lag time. The percent absorption in the low and high dose groups was at least 88-95% based on total radioactivity recovered from urine, expired CO_2, non-GI tissues, and cage rinse. Similar pharmacokinetic parameters were observed it rats for either dose level. The plasma time-course of ^{14}C-2-butoxyethyl benzoate derived radioactivity exhibited a biphasic decline after reaching C_{max} (on average at 3hr.) and was thus fitted to a two compartment model. Plasma radioactivity declined rapidly during the early phase ($t_{½}$ = 3-6hrs), followed by a slower decline during the terminal phase ($t_{½}$ = 47-52hrs). Based on the amount of 2-butoxyethyl benzoate remaining in the animal after 7 days indicates that it has low bioaccumulation potential.

Elimination: The majority (52-68%) of the administered ^{14}C-2-butoxyethyl benzoate derived radioactivity was rapidly excreted in urine without any significant difference between the dose levels. Also, the majority of the urinary elimination (91-95%) occurred within the first 24 hours post-

dosing. Most of the remaining oral dose (16-26%) was eliminated as expired CO_2, with the majority of the expired CO_2 elimination (83-87%) occurring within the first 48 hours post-dosing.

Metabolism: A total of nineteen radiochemical peaks were detected in the urine and/or fecal samples across the profiles of all treatment groups (single and repeat dose). A total of eight radiochemical peaks were detected in C_{max} blood samples. Only three major peaks of nineteen radiochemical peaks in the urine and/or fecal samples accounted for more than 5% of the administered dose. No parent 2-butoxyethyl benzoate was detected in the urine or C_{max} blood samples. 2-Butoxyethyl benzoate was detected in the fecal samples at a level of less than 0.5% of administered dose. Among the three major peaks detected in urine and/or fecal samples, the most abundant metabolite, 2-butoxyacetic acid, accounted for ~14 % to ~32 % of the administered dose in all 3 groups, the second most abundant metabolite, glucuronide conjugate of 2-butoxyethanol, accounted for ~3.4 % to ~7.6 % of the administered dose in all 3 groups, and the third most abundant metabolite, ethylene glycol, accounted for ~3.3 % to ~6.2 % of the administered dose in all 3 groups. Both ethylene glycol and 2-butoxyacetic acid were also present in C_{max} blood samples. Across both sexes, 2-butoxyacetic acid was the most abundant metabolite in C_{max} blood samples, although females had approximately equal amounts of ethylene glycol present as well. Other identified urine and/or fecal minor metabolites, which accounted for less than 5% of administered dose, included (3-oxobutoxy)acetic acid, glucuronide conjugate of 4-(2-hydroxyethoxy)butan-2-ol and glycine conjugate of 2-butoxyacetic acid. None of these minor metabolites were present in C_{max} blood samples. Figure 1 shows the proposed metabolism pathway for 2-butoxyethyl benzoate.

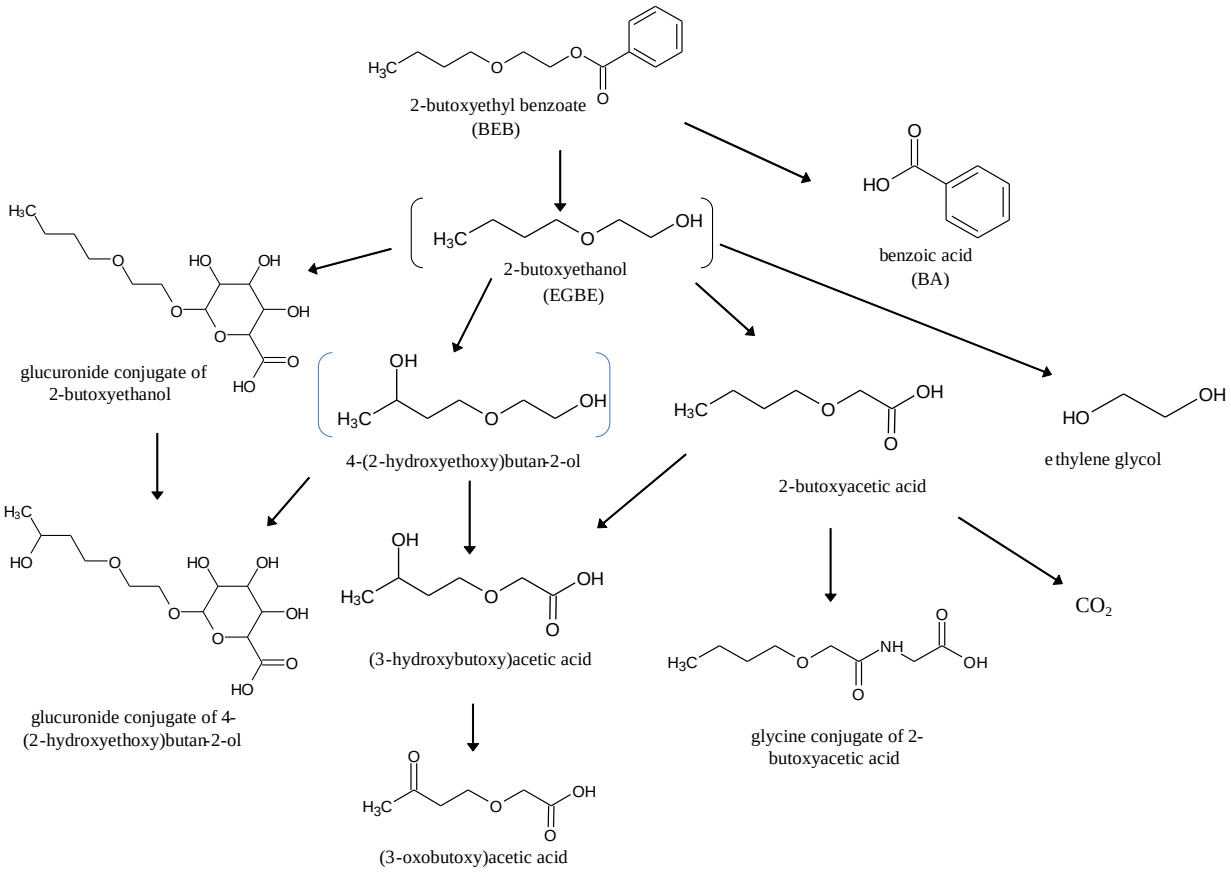


Figure 1. Likely metabolic pathway following oral treatment of rats with 2-butoxyethyl benzoate.

Toxicokinetics

As part of three oral dietary repeat dose studies, toxicokinetic evaluation was performed assessing for parent and the 2 major metabolites in blood in all studies and urine in one. In the OECD 422, OECD 414 (dams and fetuses) and 90-day (blood and urine) studies 2-butoxyethyl benzoate, EGBE and 2-butoxyacetic acid were analyzed for in non-fasted animals. In general, parent was either not detected or only at very low levels in blood and urine (in urine it was likely a contaminant from the diet) with 2-butoxyacetic acid being detected in all samples and 2-butoxyethanol was found in many blood samples in a dose-dependent manner.

Repeated Dose: 14-Day Dietary

Title: 2-Butoxyethyl Benzoate: Dietary Range-Finding Study in Crl:CD(SD) Rats; The Dow Chemical Company; 23 July 2015; DR-0176-1951-010[7]

Summary: The purpose of this range-finding study was to evaluate the palatability in feed and potential toxicity of 2-butoxyethyl benzoate in Crl:CD(SD) rats following dietary administration for up to 13 days. Three groups of five female rats were fed test diets formulated to supply 3500, 7000, or 10500 ppm of 2-butoxyethyl benzoate, which corresponded to time-weighted average dose levels of 286, 548, and 727 mg/kg bw/day. The 7000 ppm group was exposed for 13 days, and the 3500 and 10500 ppm groups were exposed for seven days. An additional group of five females was given control feed for 13 days. Parameters evaluated were daily cage-side observations, clinical observations, body weights, and feed consumption, as well as hematology, liver, kidney and spleen weights, and gross examinations.

All animals survived the treatment period. The 7000 and 10500 ppm groups had treatment-related decreased feed consumption in the first three days of exposure, which was attributed to decreased palatability of the test diets. The 7000 and 10500 ppm groups had decreased body weight and body weight gains at the beginning of treatment which improved during the thirteen or seven day exposure period, respectively. There were no treatment-related effects on feed consumption, body weight or body weight gain at 3500 ppm.

The hematologic evaluation revealed anemia at 7000 and 10500 ppm as indicated by dose-related decreases in red blood cell counts, 7aemoglobin and 7aemoglobin concentrations. The relationship of treatment to changes in anemia-related parameters at 3500 ppm was considered equivocal. Treatment-related organ weight changes were limited to marginally higher absolute and relative spleen weights in the 10500 ppm group. There were no treatment-related gross pathologic changes at any dose level tested.

Based upon the treatment-related decrease in body weight gain and anemia observed at 7000 ppm in this study, 2-butoxyethyl benzoate dietary dose levels $\leq$ 7000 ppm may be considered for a subsequent developmental/reproduction toxicity study in Crl:CD(SD) rats.

Repeated Dose: 28-Day Dietary (OECD 422)

Title: 2-Butoxyethyl Benzoate: A Combined Dietary Toxicity Study with the Reproduction/Developmental Toxicity Screening Test in Crl:CD(SD) Rats; The Dow Chemical Company; 24 February 2016; DR-0176-1951-028[12]

Summary: The purpose of this study was to evaluate the potential effects of 2-butoxyethyl benzoate following rat dietary administration on general toxicity, neurological and reproductive function, prenatal/early neonatal growth and offspring survival. This study evaluated 2-butoxyethyl benzoate in the OECD 422 design. Groups of 12 male and 12 female Crl:CD(SD) rats were administered 2-butoxyethyl benzoate via the diet at concentrations supplying 0, 500, 1500, and 5000 ppm. Females were dosed daily for two weeks prior to breeding, through breeding (up to two weeks), gestation (three weeks), and through postpartum day 4. Females were necropsied on post-partum day 5. The males were dosed for two weeks prior to breeding, through breeding and until test day 35. Effects on reproductive and neurological function as well as general toxicity were evaluated. In addition, post-mortem examinations included a gross necropsy of the adults with collection of organ weights and extensive histopathologic examination of tissues. Litter size, pup survival, sex, body weight, and the presence of gross external abnormalities were also assessed.

Dietary administration of 2-butoxyethyl benzoate to Crl:CD(SD) rats resulted in treatment-related decreases in female body weight only at the high dose level (5000 ppm). At the 5000 ppm dose level, treatment-related decreases in female body weights were observed on test days 4, 8 and 15 during pre-breeding, as well as gestation days 0, 7, 14, and 20, and lactation days 1 and 4. These decreases were statistically identified on treatment days (TD) 8 and 15, gestation days (GD) 0 and 7, and lactation days (LD) 1 and 4. No treatment-related differences in body weight gains were observed for females at any dose level tested throughout gestation or lactation. No treatment-related differences in body weights or body weight gains were observed for females at 500 or 1500 ppm or for males at any dose level throughout the duration of the study.

Similar to body weight effects, treatment-related decreases in feed consumption were only observed in females at the high dose level (5000 ppm). Females in the 5000 ppm group had treatment-related decreases in feed consumption during the intervals of TD 1-4, 4-8 and 8-15 during pre-breeding, and LD 1-4, which correlated to the observed body weight decreases. These feed consumption decreases were statistically identified on TD 1-4, 4-8 and 8-15. No treatment-related differences in feed consumption were observed for females in the 5000 ppm group throughout gestation. No treatment-related differences in feed consumption were observed for females at 500 or 1500 ppm or for males at any dose level throughout the duration of the study.

Treatment-related hematologic effects were observed only in females at the high dose level (5000 ppm). Females given 5000 ppm had treatment-related and statistically identified lower mean red blood cell count and hemoglobin concentration, higher mean MCV and MCH, lower mean MCHC, and higher mean reticulocyte count. These hematologic effects were representative of regenerative anemia in females given 5000 ppm, and were interpreted to be adverse. Females given 5000 ppm also had a treatment-related higher platelet count, which may have been caused by a generalized increase in platelet production within the bone marrow in association with the reticulocytosis. There were no treatment-related hematologic effects in females given 500 or 1500 ppm, or in males at any

dose level. There were no treatment-related changes in prothrombin times for males and females at any exposure level.

Treatment-related clinical chemistry effects were observed only in females at the high dose level (5000 ppm). Females given 5000 ppm had statistically identified higher mean urea nitrogen, triglyceride, creatinine and phosphorus concentrations. Higher phosphorus and creatinine concentrations were interpreted to be treatment-related effects. All of the treatment-related elevations in clinical chemistry parameters were interpreted to be non-adverse, because there were no corresponding alterations in organ weights, and no histopathologic correlates. There were no treatment-related clinical chemistry effects in females given 500 or 1500 ppm, or in males at any dose level.

There were no treatment-related changes in urinalysis parameters for males at any dose level.

Treatment-related effects on organ weight were observed only in the liver of females at the high dose level (5000 ppm). Females given 5000 ppm had a treatment-related lower mean final body weight (6.1%), relative to controls. Females given 5000 ppm had a treatment-related higher mean relative liver weight (5.1%), relative to controls. The higher relative liver weight corresponded to the histopathologic observation of very slight hypertrophy of centrilobular/midzonal hepatocytes, with increased cytoplasmic eosinophilia, in females given 5000 ppm. The lower mean final body weight and higher mean relative liver weight in females given 5000 ppm were interpreted to be non-adverse. There were no treatment-related alterations in final body weights or organ weights in females given 500 or 1500 ppm, or in males at any dose level.

There were no treatment-related gross pathologic observations.

A treatment-related liver histopathologic change was observed only in females at the high dose level (5000 ppm). Treatment-related very slight hypertrophy of centribolublar/midzonal hepatocytes, with increased cytoplasmic eosinophilia, was present in the liver of 11/12 females given 5000 ppm. The hepatocellular hypertrophy was interpreted to be a non-adverse and adaptive effect, based on the modest corresponding increase in liver weights, along with the absence of any treatment-related changes in liver enzyme activities (ALT, AST and GGT), and the absence of necrosis, increased apoptosis, inflammation, proliferative or degenerative changes in the liver of females at this dose level.

Based on these results, the no-observed-effect level (NOEL) for general toxicity was 1500 ppm in females and 5000 ppm in males.

Repeated Dose: 90-Day Dietary

Title: 2-Butoxyethyl Benzoate: 90-Day Dietary Toxicity Study in Crl:CD(SD) Rats; The Dow Chemical Company; 18 August 2016; DR-0176-1951-031[15]

Summary: Ten male and ten female Crl:CD(SD) rats per group were given test diets formulated to supply 0, 500, 1500, or 5000 ppm 2-butoxyethyl benzoate for at least 90 days. These values correspond to time-weighted average doses of 0, 28.9, 88.1, or 285 mg/kg/day for males and 0, 32.6, 94.9, or 310 mg/kg/day for females, respectively. Parameters evaluated were daily cage-side observations, weekly detailed clinical observations, ophthalmic examinations, body weights/body

weight gains, feed consumption, hematology, prothrombin time, clinical chemistry, urinalysis, selected organ weights, and gross and histopathologic examinations.

Dietary administration of 2-butoxyethyl benzoate to Crl:CD(SD) rats resulted in treatment-related decreases in female body weight gains and feed consumption only at the high dose level (5000 ppm). No treatment-related differences in body weights/body weight gains or feed consumption were observed for females at 500 or 1500 ppm or for males at any dose level throughout the duration of the study.

There were no treatment-related effects in clinical signs, ophthalmic, hematology, prothrombin time, or urinalysis parameters. There were no treatment-related effects on organ weight, gross or histopathologic observations. Male rats given 5000 ppm had a very slight and statistically-identified decrement in sodium that was interpreted to be associated with treatment but was considered non-adverse.

The no-observed-effect level (NOEL) for Crl:CD(SD) rats of either sex was 1500 ppm 2-butoxyethyl benzoate based on decreases in body weight gain and feed consumption in 5000 ppm females and decrements in serum sodium levels in 5000 ppm males. The no-observed- adverse effect level (NOAEL) was 1500 ppm in females and 5000 ppm in males.

Genotoxicity: Ames

Title: Butyl CELLOSOLVE™ Benzoate: Salmonella-Escherichia Coli / Mammalian-Microsome Reverse Mutation Assay Pre-Incubation Method with a Confirmatory Assay; The Dow Chemical Company; 11 March 2013; DR-0176-1951-006[5]

Summary: 2-Butoxyethyl benzoate, was tested for its mutagenic potential in the bacterial reverse mutation assay. The study was conducted using TA98, TA100, TA1535 and TA1537 strains of *Salmonella typhimurium* and WP2*uvr*A (pKM101) strain of *Escherichia coli* in two phases. In the first phase, an initial toxicity-mutation test was performed. The second phase was an independent confirmatory mutation test. The bacterial tester strains were exposed to the test substance in the presence and absence of a metabolic activation system (S-9 fraction prepared from Aroclor 1254 induced rat liver) using a pre-incubation procedure.

2-Butoxyethyl benzoate did not precipitate on the basal agar plates at any of the tested doses. No toxicity was observed in the tester strains TA98, TA100, TA1535 and TA1537 up to 320 μg/plate and up to 500 μg/plate in the strain WP2*uvr*A (pKM101), either in the presence or absence of metabolic activation when compared to the vehicle control. However, for TA98, TA100, TA1535 and TA1537, there was a slight reduction in the intensity of bacterial background lawn at 1013 and 3200 μg/plate. For WP2*uvr*A (pKM101), there was a slight reduction in the intensity of bacterial background lawn at 1580 as well as at 5000 μg/plate. There was no positive mutagenic response observed in any of the strains at any of the tested doses either in the presence or in the absence of metabolic activation.

In this study, there was a more than 3-fold increase in the mean numbers of revertant colonies in the positive controls, demonstrating the sensitivity of the assay.

All criteria for a valid study were met as described in the protocol. Under the conditions of the current study, the test substance, 2-butoxyethyl benzoate was negative (non-mutagenic) in this *Salmonella-Escherichia coli*/Mammalian-Microsome Reverse Mutation Assay.

Genotoxicity: RLCAT Gene Mutation

Title: Evaluation of 2-Butoxyethyl Benzoate In An In Vitro Chromosomal Aberration Assay Utilizing Rat Lymphocytes; The Dow Chemical Company; 12 November 2015; DR-0176-1951-022[8]

Summary: 2-Butoxyethyl benzoate was evaluated in an in vitro chromosomal aberration assay utilizing rat lymphocytes. Approximately 48 hours after the initiation of whole blood cultures, cells were treated either in the absence or presence of S9 activation with concentrations ranging from 0 (vehicle control) to 425.0 µg 2-Butoxyethyl benzoate per ml of culture medium. The highest concentration was based on the limit of solubility of the test material in the treatment medium. The duration of treatment was 4 or 24 hours without S9 and 4 hours with S9. The analytically determined concentrations of 2-Butoxyethyl benzoate in the dose preparations ranged from 97.7 to 101.1% of the targeted values. Selection of concentrations for the determination of the incidence of chromosomal aberrations was based upon solubility of the test material and the mitotic index values. In this study cultures treated for 4 hours with targeted concentrations of 0 (vehicle control), 26.6, 106.3, and 425.0 µg/ml in the presence of S9, 0 (vehicle control), 90.0, 130.0, and 190.0 µg/ml in the absence of S9, and cultures treated for 24 hours with 0 (vehicle control), 90.0, 130.0 and 170.0 µg/ml in the absence of S9 were analyzed for chromosomal aberrations.

There were no significant increases in the frequency of cells with aberrations administered 2-Butoxyethyl benzoate in either the absence or presence of S9 activation. In addition, the frequencies of aberrant cells observed in the test material treated cultures were within the laboratory historical background range. Cultures treated with the positive control chemicals (i.e., mitomycin C without S9 and cyclophosphamide with S9) had significantly higher incidences of aberrant cells in all assays. Based upon these results, 2-Butoxyethyl benzoate was considered to be negative in this in vitro chromosomal aberration assay utilizing rat lymphocytes.

Genotoxicity: CHO/HGPRT Cytogenetics

Title: Evaluation of 2-Butoxyethyl Benzoate in the Chinese Hamster Ovary Cell/Hypoxanthine-Guanine- Phosphoribosyl Transferase (CHO/HGPRT) Forward Mutation Assay; The Dow Chemical Company; 13 November 2015; DR-0176-1951-021[10]

Summary: 2-Butoxyethyl benzoate was evaluated in the in vitro Chinese Hamster Ovary cell/hypoxanthine-guanine-phosphoribosyl transferase (CHO/HGPRT) forward gene mutation assay. The genotoxic potential of the test material was assessed in two independent assays in the absence and presence of an externally supplied metabolic activation (S9) system. The concentrations ranged from 26.6 to 425 µg/ml in the absence of S9 and in the presence of S9. The highest concentration was based on limit of solubility of the test material in the treatment medium. The analytically determined concentrations of 2-Butoxyethyl benzoate in the dose preparations ranged from 97.7 to 101.3%. The adequacy of the experimental conditions for detection of induced mutation was confirmed by employing positive control chemicals, ethyl methanesulfonate for assays in the

absence of S9 and 20-methylcholanthrene for assays in the presence of S9. Vehicle control cultures were treated with the solvent used to dissolve the test material (i.e. dimethyl sulfoxide).

There were no statistically significant treatment-related increases in the mutant frequency in the test material-treated cultures compared to the vehicle control cultures in either the absence or presence of S9. The results of the CHO/HGPRT forward gene mutation assay with 2-Butoxyethyl benzoate indicate that under the conditions of this study, the test article was nonmutagenic when evaluated in the absence or presence of an externally supplied metabolic activation (S9) system.

Genotoxicity: In Vivo Micronucleus

Title: Evaluation of 2-Butoxyethyl Benzoate in the Mouse Peripheral Blood Micronucleus Test; The Dow Chemical Company; 3 December 2015; DR-0176-1951-023[11]

Summary: The in vivo genotoxic potential of 2-butoxyethyl benzoate was evaluated by examining the incidence of micronucleated reticulocytes (MN-RET) in the peripheral blood. The test material was administered to male Crl:CD1(ICR) mice by single oral gavage on two consecutive days at dose levels of 0 (negative control), 375, 750, and 1500 mg/kg body weight (bw). The highest dose level was based upon the results of a range-finding test where at higher doses treatment-related deaths were observed in male and female mice.

All animals were observed for clinical signs prior to dosing and at 2, 5, and 24 hours following each dosing. Groups of animals were euthanized 48 hours after the second treatment for the collection of peripheral blood and evaluation of RET (approximately 5,000/animal) for MN by flow cytometry. The proportion of RET was also determined based upon 5,000 RET per animal and the results expressed as a percentage. Mice treated with 40 mg/kg bw cyclophosphamide monohydrate by a single gavage dose and euthanized 48 hours later served as positive controls.

There were no treatment-related deaths or treatment-related clinical signs in the observation period of the definitive micronucleus test. There were no statistically significant increases in the frequencies of MN-RET or statistically significant effects on the percent RET in groups treated with the test material as compared to the negative controls. There was a significant increase in the frequency of MN-RET and a decrease in the percentage of RET in the positive control chemical group as compared to the negative control group. Based upon the results of the study reported herein, 2-butoxyethyl benzoate is considered negative in this test system under the experimental conditions used.

Reproductive

Title: 2-Butoxyethyl Benzoate: A Combined Dietary Toxicity Study with the Reproduction/Developmental Toxicity Screening Test in Crl:CD(SD) Rats; The Dow Chemical Company; 24 February 2016; DR-0176-1951-028[12]

Summary: This study evaluated 2-butoxyethyl benzoate in the OECD 422 design. Groups of 12 male and 12 female Crl:CD(SD) rats were administered 2-butoxyethyl benzoate via the diet at concentrations supplying 0, 500, 1500, and 5000 ppm. Females were dosed daily for two weeks prior to breeding, through breeding (up to two weeks), gestation (three weeks), and through postpartum day 4. Females were necropsied on post-partum day 5. The males were dosed for two weeks prior to breeding, through breeding and until test day 35. Effects on reproductive and neurological function

as well as general toxicity were evaluated. In addition, post-mortem examinations included a gross necropsy of the adults with collection of organ weights and extensive histopathologic examination of tissues. Litter size, pup survival, sex, body weight, and the presence of gross external abnormalities were also assessed. In this study there were no treatment-related effects on reproductive or fertility parameters at any dose level along with no histopathology findings in reproductive organs.

Developmental

Title: 2- Butoxyethyl Benzoate: Dietary Developmental Toxicity Study in Crl:CD(SD) Rats; The Dow Chemical Company; 27 July 2016; DR-0176-1951-029[13]

Summary: The purpose of this study was to evaluate the maternal and developmental toxicity of 2-butoxyethyl benzoate in Crl:CD(SD) rats following dietary administration. Groups of 24 time-mated female Crl:CD(SD) rats were administered 2-butoxyethyl benzoate in the diet at concentrations of 0, 500, 1500, or 5000 ppm on gestation day (GD) 6-21, which corresponded to time-weighted average doses of 0, 37.4, 109, or 352 mg/kg/day. In-life maternal study parameters included clinical observations, body weight, body weight gain and feed consumption. On GD 21, all surviving rats were bled for a hematological evaluation, euthanized and examined for gross pathologic alterations. Liver, kidneys, spleen, and gravid uterine weights were recorded, along with the number of corpora lutea, uterine implantations, resorptions, and live/dead fetuses. All fetuses were weighed, sexed and examined for external alterations. Approximately one half of the fetuses were examined for visceral alterations while skeletal examinations were conducted on the remaining fetuses. In addition, chemical analyses of terminal blood samples were conducted to determine parent compound, 2-butoxyethyl benzoate, and suspected major metabolites, 2- butoxyethanol and 2-butoxyacetic acid.

Maternal toxicity was limited to dams given 5000 ppm and consisted of the following treatment-related effects: decreases in body weight gain, feed consumption, increases in spleen weights, and hematological effects. Dams provided 5000 ppm had a statistically identified treatment-related 0.5% decrease in maternal body weight gain throughout the GD 6-21 treatment period and a 22.6% decrease during the GD 18-21 interval. These body weight gain effects correlated with decreases in feed consumption during the GD 18-21 interval. Treatment-related hematological effects consisted of statistically-identified lower mean red blood cell count and hemoglobin concentration, hematocrit, higher mean corpuscular volume (MCV), lower mean corpuscular hemoglobin concentration (MCHC), and a statistically identified higher mean reticulocyte count. These hematological effects were representative of regenerative anemia. At necropsy, there were treatment-related increases in absolute and relative spleen weights of 31.9% and 35.3%, respectively. Treatment-related gross pathological changes included dark spleens in four dams and an increased size of the spleen in two of the four dams. There was no treatment-related maternal toxicity in the 500 or 1500 ppm dose groups. Administration of 2-butoxyethyl benzoate in the diet at dose levels up to and including 5000 ppm produced no indications of embryo/fetal toxicity or teratogenicity.

Therefore, under the conditions of this study, the no-observed-effect level (NOEL) for maternal toxicity was 1500 ppm, and the embryo/fetal NOEL was 5000 ppm.

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Attachment 5

2-Butoxyethyl Benzoate (BEB) and Hematotoxicity

In studies performed on 2-butoxyethyl benzoate (BEB) *in vivo*, clinical observations during the acute oral study noted the presence of red discoloration of urine at dose levels that resulted in deaths and in a repeated dose study hematological changes indicate that BEB causes hemolysis. The similarity of these findings to those seen with 2-butoxyethanol (EGBE) and the fact that BEB has been shown to be metabolized to EGBE and butoxyacetic acid (BAA), indicates that the hematotoxic effects of BEB are due to the EGBE/BAA metabolites. *In vitro* studies have shown that BAA causes hematotoxicity at very low concentration. Mechanistic studies that blocked the metabolic pathways leading to the formation of BAA, resulted in no effects on red blood cells (RBCs). Based on these findings, it can be concluded that metabolism of BEB to EGBE and subsequently BAA is responsible for the hematotoxicity *in vivo* and not EGBE itself. *In vitro* studies have also shown that humans, including potentially sensitive sub-populations, show less sensitivity. Further evidence of humans being less sensitive to the hematotoxicity than rat (rodents) is from documented deliberate and accidental ingestion of EGBE by humans as well as inhalation exposure in human volunteers.

The data supporting differences in the sensitivity of species (humans being less sensitive than rats) to hemolysis after EGBE treatment is directly applicable to the toxicity of BEB given its rapid metabolism to EGBE (and benzoic acid). See Attachment 3) for details and supporting information.

The hemolytic effect of EGBE on red blood cells has been shown to be caused by BAA, the principle metabolite of EGBE (Carpenter, 1956; Ghanayem, 1987, 1989, 1993). The formation of BAA from EGBE is possible in rodents, rabbits and humans. It appears that BAA increases the fragility, in some species, of red blood cells which then leads to their rupture (Ghanayem, 1989). It has also been shown to cause more hemolysis in older animals which is due increased fragility of older red blood cells (which older animals have more of). This was supported by comparing the susceptibility to hemolysis of animals that were bled (increasing the production of new red blood cells) compared to animals that had not been bled. The bled animals had a higher LD50 for EGBE which indicated that the hemolytic effect was lessened due to the 'younger' red blood cells and that hemolysis was the critical cause of toxicity (Ghanayem, 1990, 1992; Sivarao, 1995).

Acute toxicology studies using EGBE shows evidence that hemolysis occurs in rats and rabbits, however, studies performed in guinea pigs showed no evidence of hemolysis. *In vitro* studies examining the red blood cells from numerous species (*i.e.* rodents, guinea pigs, rabbits, dogs, cats, pigs and primates, including human) for hemolysis demonstrated that red blood cells from rodents and rabbits were noticeably more sensitive to the hemolytic effects of BAA than the effect on guinea pigs and humans, which were considerably less sensitive (Ghanayem, 1993; Udden 1994a, 2000). Red blood cells of potentially sensitive sub-populations of humans, including the young and elderly, and individuals with diseases of the red blood cells (*i.e.* hereditary spherocytosis and sickle cell disease), were evaluated and none of them were susceptible to BAA induced hemolysis (Udden, 1994b).

Physiologically based pharmacokinetic modeling of EGBE has shown that humans cannot achieve a high enough level of BAA in plasma by either inhalation (up to the saturated vapor concentration) or dermal (assume 10% skin surface exposure, high permeability) exposure to cause even slight hemolysis (Corley, 1996; EU, 2006). This lack of hemolysis in humans is also reflected in the numerous cases reported of

acute intoxication with EGBE by humans where no evidence of hemolysis was present (Bauer, 1992; Butera, 1996; Burkhart, 1998; Dean, 1992; Gijsenbergh, 1989; Gualtieri, 1995, 2003; Hung, 2010; McKinney, 2000; Rambourg-Schepens, 1988). Finally, in an old study where two men and one woman voluntarily were exposed to 0.98mg/L EGBE for 2x4hr exposures, with a 30-minute break between, had no signs of hemolysis after hematology analysis (The Dow Chemical Co., 1955). A similar exposure to rodents or rabbits would have led to significant hemolysis.

Based on this information, the toxicity seen with BEB in rats is linked to its metabolism to EGBE and ultimately BAA which causes these hemolytic effects. The extensive research into the hemotoxicity of EGBE/BAA has shown that rodents are more sensitive to this hemotoxicity and therefore the hazard to human population is significantly lower. This same lower human sensitivity to hemolysis can be extrapolated to BEB based on its rapid metabolism the EGBE/BAA.

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Attachment 6

Ethylene glycol monobutyl ether (EGBE) (2-Butoxyethanol); CASRN 111-76-2

Human health assessment information on a chemical substance is included in the IRIS database only after a comprehensive review of toxicity data, as outlined in the IRIS assessment development process. Sections I (Health Hazard Assessments for Noncarcinogenic Effects) and II (Carcinogenicity Assessment for Lifetime Exposure) present the conclusions that were reached during the assessment development process. Supporting information and explanations of the methods used to derive the values given in IRIS are provided in the guidance documents located on the IRIS website.

STATUS OF DATA FOR Ethylene glycol monobutyl ether (EGBE)

Category (section)	Assessment Available?	Last Revised
Oral RfD (I.A.)	yes	03/31/2010
Inhalation RfC (I.B.)	yes	03/31/2010
Carcinogenicity Assessment (II.)	yes	03/31/2010

I. Health Hazard Assessments for Noncarcinogenic Effects

I.A. Reference Dose (RfD) for Chronic Oral Exposure

Substance Name — Ethylene glycol monobutyl ether (EGBE)
CASRN — 111-76-2
Last Revised — 3/31/2010

The RfD is an estimate (with uncertainty spanning perhaps an order of magnitude) of a daily oral exposure to the human population (including sensitive subgroups) that is likely to be without an appreciable risk of deleterious effects during a lifetime. The RfD is intended for use in risk assessments for health effects known or assumed to be produced through a nonlinear (presumed threshold) mode of action. It is expressed in units of mg/kg-day. Please refer to the guidance documents at http://www.epa.gov/iris/backgrd.html for an elaboration of

these concepts. Because RfDs can be derived for the noncarcinogenic health effects of substances that are also carcinogens, it is essential to refer to other sources of information concerning the carcinogenicity of this chemical substance. If the U.S. EPA has evaluated this substance for potential human carcinogenicity, a summary of that evaluation will be contained in Section II of this file.

The previous oral RfD for EGBE (posted on the IRIS database in 1999) was 0.5 mg/kg-day, based on a National Toxicology Program (NTP, 1993, 042063) subchronic drinking water study in rats and mice using changes in mean corpuscular volume as the critical effect. C_{max} (peak blood concentrations) for 2-butoxyacetic acid (BAA) in arterial blood of female rats following oral exposure was estimated using the physiologically based pharmacokinetic (PBPK) model of Corley et al. (1994, 041977) as modified by Corley et al. (1997, 041984). The benchmark dose $(BMD)_{05}$ was determined to be 64 µM, using the 95% lower confidence limit of the dose-response curve expressed in terms of the C_{max} for BAA in blood. The PBPK model of Corley was used to "back-calculate" to a human equivalent dose (HED) of 5.1 mg/kg day, assuming that rats and humans receive their entire dose of EGBE from drinking water over a 12 hour period each day. The RfD was calculated by applying an uncertainty factor (UF) of 10 for intrahuman variability to the benchmark dose, 95% lower bound (BMDL) HED of 5.1 mg/kg day.

I.A.1. Chronic Oral RfD Summary

Critical Effect	Point of Departure*	UF	Chronic RfD
Hemosiderin deposition in the liver **Chronic (rat and mouse) inhalation study** **NTP (2000, 196293)**	BMDL(HED): 1.4 mg/kg-day (PBPK and BMD_{10})	10	0.1 mg/kg-day

*Conversion Factors and Assumptions - Based on the limited oral database and because the critical endpoint, hemosiderin pigmentation, was more pronounced in the chronic inhalation study (NTP, 2000, 196293), versus the available subchronic oral study (NTP, 1993, 042063), EPA used a route to route extrapolation from the NTP, 2000 (196293) study for the derivation for the RfD. As with the animal-to-human extrapolation used in the development of the reference concentration (RfC), the dose metric used for animal-to-human and route-to-route (inhalation-to-oral) extrapolation for the derivation of the RfD is the area under the curve (AUC) of BAA at 12 months in arterial blood. This dose metric was used for dose-response

modeling of chronic inhalation data to derive the point of departure (POD) of 133 µmol-hour/L, expressed as a BMDL based on animal data. The corresponding human BMDL was then back-calculated using the human PBPK model (Corley et al., 1994, 041977; Corley et al., 1997, 041984) to obtain an equivalent human oral drinking water dose ($BMDL_{HED}$) of 1.4 mg/kg-day. A simplifying assumption was used that the entire dose of drinking water EGBE was consumed over a 12-hour period each day.

I.A.2. Principal and Supporting Studies (Oral RfD)

NTP (National Toxicology Program) (2000, 196293) NTP technical report on the toxicology and carcinogenesis studies of 2 butoxyethanol (CAS No. 111 76 2) in F344/N rats and B6C3F$_1$ mice (inhalation studies). http://ntp.niehs.nih.gov/?objectid=070AC403-B110-CA79-3A23AF79DE7B752A**;** http://ntp.niehs.nih.gov/ntp/htdocs/LTrpts/tr484.pdf

NTP (2000, 196293) completed a 2-year inhalation study on EGBE in both genders of rats and mice. In this chronic study, animals were exposed to EGBE 6 hours/day, 5 days/week at concentrations of 0, 31, 62.5, and 125 ppm (0, 150, 302, and 604 mg/m^3) for groups of 50 F344/N rats and 0, 62.5, 125, and 250 ppm (0, 302, 604, and 1,208 mg/m^3) for groups of 50 B6C3F$_1$ mice. The researchers stated that the highest exposure was selected to produce a 10-15% depression in hematologic indices. They reported that no effect on survival was observed in rats, but survival was statistically significantly decreased in male mice exposed to 125 or 250 ppm, compared with chamber controls (54, 52, and 78% respectively). Although statistics were not reported for mean body weights, the rats exposed to 31 and 62.5 ppm had similar mean body weights to the control rats. Mean body weights of the exposed mice were generally less than for controls, with females experiencing greater and earlier reductions. From week 17 to the end of the study, the mean body weights of 125 ppm female rats were generally less than those of controls. Non-neoplastic effects in rats included hyaline degeneration of the olfactory epithelium in males (13/48, 21/49, 23/49, 40/50) and females (13/50, 18/48, 28/50, 40/49) and Kupffer cell pigmentation in the livers of males (23/50, 30/50, 34/50, 42/50) and females (15/50, 19/50, 36/50, 47/50). The severity of the olfactory lesion was not affected by exposure. The Kupffer cell pigmentation is a result of hemosiderin accumulation and is a recognized secondary effect of the hemolytic activity of EGBE.

Statistically significant effects observed in mice included forestomach ulcers and epithelial hyperplasia, hematopoietic cell proliferation and hemosiderin pigmentation in the spleen, Kupffer cell pigmentation in the livers, and bone marrow hyperplasia (males only). Hyaline degeneration of the olfactory epithelium (females only) was increased relative to chamber controls but was not statistically significant. As in the rats, the Kupffer cell pigmentation was considered a secondary effect of the hemolytic activity of EGBE. Bone marrow hyperplasia, hematopoietic cell proliferation, and hemosiderin pigmentation in the spleen were also

attributed to the primary hemolytic effect; it was followed by regenerative hyperplasia of the hematopoietic tissue. The forestomach lesions did not appear to be related to the hemolytic effect of EGBE. Incidences of ulcer were significantly increased in all exposed female groups, as well as males exposed to 125 ppm. Incidences of epithelial hyperplasia, usually focal, were significantly increased in all exposed groups of males and females. The hyperplasia was often associated with ulceration, particularly in the females, and consisted of thickness of the stratified squamous epithelium and sometimes the keratinized layer of the forestomach. Ulceration consisted of a defect in the forestomach wall that penetrated the full thickness of the epithelium and frequently contained accumulations of inflammatory cells and debris.

Using the same exposure levels described above, additional groups of rats (27/gender/exposure group) and mice (30/gender/exposure group) in the 2-year study were examined at 3, 6, and 12 months (8-10 animals/time point) for hematologic effects. Nine male and nine female rats were exposed to 31 ppm EGBE, specifically to evaluate hematology at 3 months and to receive a total evaluation at 6 months. Animals were continuously exposed, as described above, until their sacrifice at 3, 6, or 12 months. As in the 14-week study, inhalation of EGBE by both species resulted in the development of exposure-related hemolytic effects, inducing a responsive anemia. In rats, the anemia was persistent and did not progress or ameliorate in severity from 3 months to the final blood collection at 12 months. Statistically significant ($p < 0.05$) decreases in automated and manual hematocrit (Hct) values, hemoglobin (Hb) concentrations, and red blood cell (RBC) counts occurred at 3, 6, and 12 months in the 125 ppm female mice and the 250 ppm male and female mice. Statistically significant decreases in these same endpoints were also observed in 62.5 ppm females at 6 months and in 125 ppm males at 6 and 12 months (decreases in Hct were observed only at 3 and 6 months). Mean cell volume (MCV) was increased in female mice at the highest duration (12 months) and exposure (250 ppm) levels. Reticulocyte counts were increased significantly in the 125 ppm females at 3 and 6 months and in the 125 ppm males at 6 months of exposure.

In the subchronic portion of the inhalation NTP (2000, 196293) study, F344 rats and $B6C3F_1$ mice (10/gender) were exposed to EGBE concentrations of 0, 31, 62.5, 125, 250, and 500 ppm (0, 150, 302, 604, 1,208, and 2,416 mg/m^3) 6 hours/day, 5 days/week for 14 weeks. Hematologic and hemosiderin staining results are indicative of the various degrees of hemolysis caused by exposure to increasing concentrations of EGBE. Both rat genders exhibited clinical signs at the three highest doses, consistent with the hemolytic effects of EGBE, including: (1) deficits in RBCs as a result of lysis manifestation through the clear dose-related decrease in Hct, a finding consistent with decreases noted for both RBC count and Hb concentrations; and (2) increases in both reticulocytes and nucleated erythrocytes at higher doses, homeostatic responses that would be anticipated to occur as the lysed blood cells are being replaced. Female rats may be somewhat more sensitive: several statistically significant effects occurred at the 31 ppm level in females, as opposed to a single parameter for males. In

addition, the degree to which these various measures are affected is somewhat greater in females than males, indicated as percent control, particularly at the three highest concentrations. Hematologic evaluation showed mild-to-moderate regenerative anemia at all concentrations in females and at the three highest concentrations in males. Exposure-related trends were noted for reticulocyte count, RBC count, MCV, Hb concentration, and Hct. Liver-to-body-weight ratios increased significantly in males at the two highest concentrations and in females at the highest concentration. Histopathologic effects at concentrations in excess of 62.5 ppm for male rats and 31 ppm for females consisted of excessive splenic congestion in the form of extramedullary hematopoiesis, hemosiderin accumulation in Kupffer cells, liver necrosis, centrilobular hepatocellular degeneration, renal tubular degeneration, intracytoplasmic Hb and hemosiderin deposition, and bone marrow hyperplasia. In addition, five moribund female rats were sacrificed from the highest concentrations, and one from the 250 ppm group. The lowest-observed-adverse-effect level (LOAEL) for hematological alterations was 31 ppm for female rats and 62.5 ppm for male rats. The 31 ppm exposure level was considered a no-observed-adverse-effect level (NOAEL) for male rats.

The mice exposed via the inhalation route exhibited clinical signs consistent with the hemolytic effects of EGBE at the two highest concentrations for both genders. Hematologic evaluation indicated a moderate regenerative anemia (marked by decreased RBC counts, increased reticulocyte counts, and increased MCV) with an increase in platelets at the three highest concentrations in both genders. Histopathological effects consisted of excessive extramedullary splenic hematopoiesis, renal tubular degeneration, hemosiderin deposition in the spleen and kidney and accumulation in Kupffer cells, and testicular degeneration. Forestomach necrosis, ulceration, inflammation, and epithelial hyperplasia were observed at concentrations >31 ppm for females and 62.5 ppm for males. In addition, four females and four males either died or were sacrificed moribund at the highest concentration. The NOAEL for male and female mice was 31 ppm and the LOAEL in mice was 62.5 ppm, based on histopathological changes in the forestomach.

I.A.3. Uncertainty Factors

$UF = 10$

$= 10\ (UF_H) \times 1(UF_A) \times 1(UF_D)$.

A UF of 10 was selected to account for the uncertainty associated with the variability of the human response (UF_H) to the effects of EGBE. Potentially susceptible subpopulations include individuals with enhanced metabolism or decreased excretion of BAA and individuals whose RBC membranes are more susceptible to the lysis caused by BAA, the precursor step to developing hemosiderin staining in the liver. Human in vitro studies suggest that the elderly and patients with fragile RBCs would not be more sensitive to the hemolytic effects of EGBE

than normal adults. Laboratory animal studies suggest that older animals are more sensitive than neonates and that females are more sensitive than males. While developmental studies do not reveal increased susceptibility in infants, none of the developmental studies examined fetal or infant blood for signs of effects from prenatal exposure to EGBE. Additionally, human responses to EGBE have not been observed under a broad range of exposure conditions (e.g., repeated or long-term exposures) and potentially sensitive subjects (e.g., individuals predisposed to hemolytic anemia or infants).

A UF of 1 was selected to account for the uncertainty associated with interspecies variability resulting from toxicodynamic and toxicokinetic differences between animals and humans (UF_A). Traditionally, these components (toxicodynamic and toxicokinetic) are individually represented by partial UFs of 3 for a total UF of 10 in the absence of chemical-specific information; thus, application of a full UF of 10 would depend on two areas of uncertainty (i.e., toxicokinetic and toxicodynamic uncertainties). In this assessment, the toxicokinetic uncertainty is addressed by the determination of an HED, using a combination of measured internal blood levels in the test animals and PBPK modeling. A value of 1 was selected for the toxicokinetic portion of the UF_A. Regarding toxicodynamics, in vivo (Carpenter et al., 1956) and in vitro (Ghanayem and Sullivan, 1993, 041609; Udden, 2002, 042111; Udden and Patton, 1994, 056374) studies indicate that humans may be significantly less sensitive than rats to the hematological effects of EGBE. A value of 1 was selected for the toxicodynamic portion of the UF_A.

A UF to account for extrapolation from subchronic to chronic exposure (UF_S) was not needed because the RfD was derived from a chronic inhalation study.

A UF for LOAEL to NOAEL (UF_L) was not applied because the current approach is to address this extrapolation as one of the considerations in selecting a benchmark response (BMR) for BMD modeling. In this case, EPA concluded a 10% increase in hemosiderin staining, indicating a precursor to an adverse effect, is appropriate for use in deriving the RfD under the assumption that it represents a minimal biologically significant change.

A UF of 1 was selected to account for deficiencies in the database (UF_D). While no chronic oral studies or adequate human data are available for EGBE, PBPK models allow for deriving a BMDL from the chronic inhalation study using measured internal dose metrics and then extrapolating it back to an equivalent human oral dose. The database for inhalation exposure includes chronic and subchronic studies in two species (rats and mice), and several reproductive and developmental studies, including a two-generation reproductive toxicity study.

I.A.4. Additional Studies/Comments

Carpenter et al. (1956, 066464) conducted three controlled inhalation studies. In the first study, a group of two men and six rats were exposed simultaneously for 4 hours to an EGBE concentration of 113 ppm in a 1,250 cubic foot room. Effects observed in humans included nasal and ocular irritation, a metallic taste, and belching. Erythrocyte osmotic fragility did not change for the men, yet rose appreciably for the rats. In a second study, a group of two men, one woman, and three rats were exposed to 195 ppm EGBE for two 4-hour periods, separated by a 30-minute recess, in a 6.5 cubic foot room. There was no change in the subjects' blood pressure, erythrocyte fragility, or pulse rate. They experienced nose and throat irritation, followed by ocular irritation and disturbed taste; one subject reported a headache. In the rats, an increase in erythrocyte fragility values was noted. In the third study, two men and two women were exposed for 8 hours to a 100 ppm EGBE concentration. No changes in blood pressure, erythrocyte fragility, or pulse rate were observed. Again, nasal and throat irritation followed by ocular irritation and a disturbing metallic taste were experienced. Two subjects reported headaches.

There are a number of case reports of acute ingestion of EGBE, consisting primarily of accidental or intentional ingestion. Bauer et al. (1992, 100087) reported the effects of acute ingestion of 500 mL of window cleaner containing 9.1% EGBE and 2.5% ethanol by a 53-year-old alcoholic male. He was comatose with metabolic acidosis, shock and noncardiogenic pulmonary edema when brought to a hospital, approximately 10 hours after ingestion. He had increased heart rate, decreased blood pressure, and transient polyuria and hypoxemia. Hypochromic anemia was evident with an Hb concentration of 9.1 g/100 mL, a Hct of 25%, and thrombocytopenia. The patient recovered and was discharged after 15 days.

Gijsenbergh et al. (1989, 100134) reported that a 23-year-old woman weighing 64 kg ingested approximately 25-30 g of EGBE (~400-500 mg/kg) and ethanol (~4:1 ratio) as a window cleaner in an apparent suicide attempt. She was comatose when admitted to the hospital, exhibiting dilated pupils, obstructive respiration, and metabolic acidosis, including depression of blood Hb concentration and hematuria. The presence of EGBE in the blood and dialysis fluid was confirmed. Treatment consisted of supportive therapy, forced diuresis, bicarbonate administration, and hemodialysis. Her Hb concentration fell from 11.9 g Hb/100 mL upon admission to 8.9 g Hb/100 mL. She was discharged after 8 days.

Gualtieri et al. (2003, 100140) reported a case of a suicide attempt with an industrial-strength window cleaner. The 18-year-old male weighed 71 kg; he consumed between 360 and 480 mL of a concentrated glass cleaner that contained 22% EGBE, a dose equivalent to 1,131-1,509 mg/kg. He was admitted to the hospital with no abnormalities other than epigastric discomfort within 3 hours postingestion. Approximately 10 hours postadmission, the patient was

noticeably lethargic, weak, and hyperventilating, symptoms consistent with the onset of metabolic acidosis. BAA was measured; the highest serum concentration found was 4.86 mmol/L, collected approximately 16 hours postingestion. The patient was transferred to a tertiary care hospital where hemodialysis was initiated at approximately 24 hours postingestion. Ethanol therapy was started 30 minutes later. Treatment also consisted of intravenous doses of 100 mg thiamine and 50 mg folic acid every 12 hours and 50 mg pyridoxine every 6 hours. Following 4 hours of dialysis, the patient was alert and remained hemodynamically stable. Ten days after discharge, the patient was readmitted following a second ingestion of 480 mL of the same cleaner, an EGBE dose equivalent to 1,509 mg/kg. Treatment included ethanol therapy and hemodialysis, and was initiated within a few hours of ingestion to control the metabolic acidosis. Due to this early treatment, ethanol therapy had an impact on the disposition of EGBE and BAA. As with the first episode, metabolic acidosis was manifest. This high-dose oral ingestion was nearly 1.1-1.5 g EGBE/kg body weight. The highest serum BAA concentration was 2.07 mmol/L, collected 22 hours postingestion. No evidence of hemolysis or renal abnormalities was detected.

A 50-year-old woman ingested approximately 250-500 mL of a window cleaner containing 12% EGBE, representing ~30-60 mL, in an apparent suicide attempt (Rambourg-Schepens et al., 1988, 100191). She was diagnosed with metabolic acidosis, hypokalemia, a rise in serum creatinine level, and a marked increase in urinary excretion of oxalate crystals. Moderate hemoglobinuria appeared on the third day postexposure, and a progressive erythropenia was noted. In the absence of more complete hematologic details from this and other similar case studies, it is not possible to determine whether these effects were due to hemolysis or other factors related to the profound blood chemistry changes observed. The clinical status improved gradually and the patient was discharged on the 10th day.

Burkhart and Donovan (1998, 056375) summarized the case of a 19-year-old male who ingested 20-30 ounces, or ~590-885 mL, of a product that contained 25-35% EGBE (an exposure equivalent to ~177-265 mL, estimated at >3,000 mg/kg) along with 15-25% propylene glycol, 5-10% monoethanolamine, and 1-3% potassium hydroxide. On his arrival at the hospital 3.5 hours after ingestion, the patient was deeply comatose with severe hypotension. Hematuria developed on the second day, with no evidence of renal or hepatic toxicity; however, pulmonary toxicity consisting of severe aspiration pneumonia was present. The patient had a significant recovery, despite severe neurologic deficits that were slow to resolve.

Osterhoudt (2002, 100186) reported on a 16-month-old girl who ingested an unknown amount of cleaning solution containing EGBE (10-30%), monoethanolamine (5-10%), alkoxylated linear alcohols (1-5%), ethylenediaminetetraacetic acid (1-5%), and potassium hydroxide (1-5%). Metabolic acidosis was manifest, and a single dose (15 mg/kg) of the aldehyde

dehydrogenase (ALDH) inhibitor fomepizole was administered. Within 2 hours, the metabolic acidosis was completely resolved, and there was no evidence of alkaline mucosal injury, hepatic or renal dysfunction, or hemolysis.

Dean and Krenzelok (1991, 597279) reported that 24 children, aged 7 months to 9 years, were observed subsequent to oral ingestion of at least 5 mL of glass window cleaner containing EGBE in the 0.5-9.9% range. Two children drank more than 15 mL and were treated by gastric lavage. No symptoms of EGBE poisoning, such as metabolic acidosis, and no hemolysis were observed in any of the children.

Raymond et al. (1998, 100193) reported on seven clerical workers who were evaluated 8 months after they entered a file room where the supervisor believed that EGBE had been applied overnight to strip the floor. Exact details of the product used were unknown, but based on containers found and exposure symptoms of noted intense eye and respiratory irritation, marked dyspnea, nausea, and faintness, the authors suggested that they were exposed to EGBE concentrations of 200-300 ppm. Of major concern were skin spots—cherry angiomas—that appeared between 4 and 22 weeks after exposure in six of the seven workers. All workers continued to experience recurrent eye and tracheobronchial irritation; four had a dry cough. Workplace air sampling conducted by a certified industrial hygienist 1 week after the floor stripping found no detectable EGBE, although traces (0.1-0.2 ppm) of formaldehyde were identified. Five years after the exposure, four of the workers who could be contacted reported that they continued to have outbreaks of new cherry angiomas. It should be noted that no other studies linking EGBE exposure to outbreaks of cherry angiomas are available in the literature. The authors included the observation that, since this report, they had seen three patients who they believe were also exposed to EGBE vapor in an unrelated incident, and who did not develop any skin spots. Cherry angiomas are the most common cutaneous vascular lesion; they are benign and formed by a proliferation of dilated venules. The spots occur more frequently with increasing age but can appear in younger individuals. There are reports in the literature of cherry angiomas appearing following individual exposure to other chemicals, such as bromides (Cohen et al., 2001, 100096), glutaraldehyde (Raymond et al., 1998, 100193), and sulfur mustard gas (Firooz et al., 1999, 100115).

A cross section of 31 male workers, aged 22-45 years, employed for 1-6 years, who were exposed to low levels of EGBE in a beverage packing production plant were monitored by Haufroid et al. (1997, 042040). The effect of external EGBE exposure and internal BAA levels on erythrocyte lineage were investigated by monitoring: RBC count, Hb, Hct, MCV, mean corpuscular hemoglobin (MCH), mean corpuscular hemoglobin concentration (MCHC), haptoglobin (Hp), reticulocyte count, and osmotic resistance (OR), a measure of osmotic fragility. Also studied were serum glutamic-oxaloacetic and glutamic-pyruvic transaminases and renal creatinine and urinary retinol binding protein parameters. The average airborne

concentration of EGBE was 2.91 mg/m^3, or 0.6 ppm (standard deviation [SD] of ±1.30 mg/m^3 or 0.27 ppm). In addition, there was coexposure to methyl ethyl ketone. Single determinations of BAA in postshift urine samples were used to assess exposure to low levels of EGBE. No differences were observed for RBC counts, Hb, MCV, MCH, Hp, reticulocyte count, or OR between exposed and control workers. The only statistically significant change observed in exposed workers when compared with a matched control group (n = 21) was a 3.3% decrease in Hct (p = 0.03) and a 2.1% increase in MCHC (p = 0.02). The implications of these small erythroid effects are unclear. Both values are within their corresponding normal clinical ranges and, given that no statistically significant changes were observed in other erythroid parameters, they do not appear to be related to the more severe adverse effects observed in laboratory animals. Furthermore, no correlation was found between any of the nine erythroid parameters measured and the parameters of internal exposure. No significant differences were observed in hepatic and renal biomarkers.

Several human studies investigated the dermal absorption of EGBE. Jakasa et al. (2004, 100151) dermally exposed six male research subjects, ages 22-55 years, to 50%, 90%, or neat EGBE for 4 hours on the forearm over an area of 40 cm^2. The dermal absorption of EGBE from aqueous solutions was markedly higher than from neat EGBE. In Jones et al. (2003, 100161), four research subjects were exposed via inhalation of 50 ppm EGBE for 2 hours on nine separate occasions, with each occasion separated by 3 weeks, at varying temperatures and humidity levels. Results show that "baseline" dermal contribution to total body absorption of EGBE vapor in appropriately dressed workers was, on average, 11%. Higher temperature (30°C, mean 14%, p = 0.03) and greater humidity (65% relative humidity, mean 13%, p = 0.1) both increased dermal absorption. The wearing of whole-body overalls did not attenuate absorption (mean 10%). By combining several factors together in the industrial scenario, dermal absorption of vapors was reported to be as high as 39% of the total absorbed dose.

For more detail on Susceptible Populations, exit to the toxicological review, Section 4.7 (PDF)

I.A.5. Confidence in the Chronic Oral RfD

Study — High
Database — Medium/High
RfD — Medium/High

The overall confidence in the RfD is medium to high because the RfD has been calculated using a route-to-route extrapolation from the PBPK/benchmark concentration (BMC) method used to derive the RfC. This method accounts for pharmacokinetic differences between rats and humans using a validated PBPK model (Corley et al., 1994, 041977; Corley et al., 1997,

041984). There is high confidence in the NTP (2000, 196293) study because it was a chronic study, employed both male and female rats and mice, had a wide range of exposure levels, and animals were observed twice daily. There is medium-to-high confidence in the database, because data are available for a variety of animal species, including humans. Confidence in the database is not high, because the potential for effects in humans from repeated, long-term exposures has not been investigated.

For more detail on Characterization of Hazard and Dose Response, exit to the toxicological review, Section 6 (PDF).

I.A.6. EPA Documentation and Review of the Chronic Oral RfD

Source Document — U.S. EPA (2010, 597544)

This document was provided for review to EPA scientists, interagency reviewers from other federal agencies and White House offices, and the public, and peer reviewed by independent scientists external to EPA. A summary and EPA's disposition of the comments received from the independent external peer reviewers and from the public is included in Appendix A of the *Toxicological Review of Ethylene Glycol Monobutyl Ether* (U.S. EPA, 2010, 597544). ***To review this appendix, exit to the toxicological review, Appendix A, Summary of and Response to External Peer Review Comments (PDF)***.

I.A.7. EPA Contacts

Please contact the IRIS Hotline for all questions concerning this assessment or IRIS, in general, at (202) 566-1676 (phone), (202) 566-1749 (fax), or hotline.iris@epa.gov (email address).

I.B. Reference Concentration (RfC) for Chronic Inhalation Exposure

Substance Name — Ethylene glycol monobutyl ether (EGBE)
CASRN — 111-76-2
Section I.B. Last Revised — 3/31/2010

The RfC is an estimate (with uncertainty spanning perhaps an order of magnitude) of a continuous inhalation exposure to the human population (including sensitive subgroups) that is likely to be without an appreciable risk of deleterious effects during a lifetime. The RfC considers toxic effects for both the respiratory system (portal of entry) and for effects

peripheral to the respiratory system (extrarespiratory effects). The inhalation RfC (generally expressed in units of mg/m^3) is analogous to the oral RfD and is similarly intended for use in risk assessments for health effects known or assumed to be produced through a nonlinear (presumed threshold) mode of action.

Inhalation RfC values are derived according to *Methods for Derivation of Inhalation Reference Concentrations and Application of Inhalation Dosimetry* (U.S. EPA, 1994, 006488). Because RfC values can also be derived for the noncarcinogenic health effects of substances that are carcinogens, it is essential to refer to other sources of information concerning the carcinogenicity of this chemical substance. If the U.S. EPA has evaluated this substance for potential human carcinogenicity, a summary of that evaluation will be contained in Section II of this file.

The previous RfC for EGBE (posted on the IRIS database in 1999 (U.S. EPA, 1999, 597365)) was 13 mg/m^3, based on an NTP (1998, 594421) subchronic inhalation study in rats using changes in mean RBC count as the critical effect. C_{max} (peak blood concentrations) for BAA in arterial blood of female rats following inhalation exposure was estimated using the PBPK model of Lee et al. (1998, 041983). The BMD_{05} was calculated to be 225 µM, using the 95% lower confidence limit of the dose-response curve expressed in terms of the C_{max} for BAA in blood. The PBPK model of Corley et al. (1994, 041977; 1997, 041984) was used to "back-calculate" to a human equivalent concentration (HEC) of 78 ppm (380 mg/m^3) assuming continuous exposure (24 hours/day). The RfC was calculated by applying a UF of 30 (10 for intrahuman variability and 3 for extrapolation from a LOAEL) to the benchmark concentration, 95% lower bound (BMCL) HEC of 380 mg/m^3.

I.B.1. Chronic Inhalation RfC Summary

Critical Effect	Point of Departure*	UF	Chronic RfC
Hemosiderin deposition in the liver **Chronic (rat and mouse) inhalation study** **NTP (2000, 196293)**	BMCL(HEC): 16 mg/m^3 (PBPK and $BMCL_{10}$)	10	1.6 mg/m^3

*Conversion Factors and Assumptions - For the purposes of deriving an RfC for EGBE, hemosiderin staining data were evaluated in male and female rats from the 2 year chronic study by NTP (2000). A 10% extra risk was used as a BMR level for quantal data as this is at or near the limit of sensitivity in most cancer bioassays and in some noncancer bioassays as

well. Because the hemosiderin staining endpoint was observed in control animals and a 10% increase in incidence was within the observable range of the data, 10% extra risk was considered an appropriate BMR and a $BMCL_{10}$ an appropriate POD for derivation of the RfC (U.S. EPA, 1995, 005992; U.S. EPA, 2000, 052150).

The AUC was selected as the appropriate dose metric due to the nature of the endpoint, hemosiderin deposition. This endpoint increased in severity with increased duration (subchronic to chronic) and is believed to be the result of the cumulative exposure to EGBE as opposed to a peak event. A $BMCL_{10}$ of 133 µmol hour/L for hemosiderin staining in liver of male rats chronically exposed to EGBE (NTP, 2000, 196293) was used as the POD to calculate the RfC. A human PBPK model (Corley et al., 1997, 041984) was used to back-calculate to an HEC of 16 mg/m^3 (3.4 ppm) for the $BMCL_{HEC}$.

I.B.2. Principal and Supporting Studies

National Toxicology Program (NTP) (2000, 196293) technical report on the toxicology and carcinogenesis studies of 2 butoxyethanol (CAS No. 111 76 2) in F344/N rats and B6C3F$_1$ mice (inhalation studies). http://ntp.niehs.nih.gov/?objectid=070AC403-B110-CA79-3A23AF79DE7B752A**;** http://ntp.niehs.nih.gov/ntp/htdocs/LTrpts/tr484.pdf

See Section 1.A.2 for a complete description.

I.B.3. Uncertainty Factors

UF = 10
= 10 (UF_H) × 1(UF_A) × 1(UF_D).

A UF of 10 was selected to account for the uncertainty associated with the variability of the human response (UF_H) to the effects of EGBE. Potentially susceptible subpopulations include individuals with enhanced metabolism or decreased excretion of BAA and individuals whose RBC membranes are more susceptible to the lysis caused by BAA, the precursor step to developing hemosiderin staining in the liver. Human in vitro studies suggest that the elderly and patients with fragile RBCs would not be more sensitive to the hemolytic effects of EGBE than normal adults. Laboratory animal studies suggest that older animals are more sensitive than neonates and that females are more sensitive than males. While developmental studies do not reveal increased susceptibility in infants, none of the developmental studies examined fetal or infant blood for signs of effects from prenatal exposure to EGBE. Additionally, human responses to EGBE have not been observed under a broad range of exposure conditions (e.g., repeated or long-term exposures) and potentially sensitive subjects (e.g., individuals predisposed to hemolytic anemia or infants).

A UF of 1 was selected to account for the uncertainty associated with interspecies variability resulting from toxicodynamic and toxicokinetic differences between animals and humans (UF_A). Traditionally, these components (toxicodynamic and toxicokinetic) are individually represented by partial UFs of 3 for a total UF of 10 in the absence of chemical-specific information; thus, application of a full UF of 10 would depend on two areas of uncertainty (i.e., toxicokinetic and toxicodynamic uncertainties). In this assessment, the toxicokinetic uncertainty is addressed by the determination of an HEC, using a combination of measured internal blood levels in the test animals and PBPK modeling. A value of 1 was selected for the toxicokinetic portion of the UF_A. Regarding toxicodynamics, in vivo (Carpenter et al., 1956, 066464) and in vitro (Ghanayem and Sullivan, 1993, 041609; Udden, 2002, 042111; Udden and Patton, 1994, 056374) studies indicate that humans may be significantly less sensitive than rats to the hematological effects of EGBE. A value of 1 was selected for the toxicodynamic portion of the UF_A.

A UF to account for extrapolation from subchronic to chronic exposure (UF_S) was not needed because the RfC was derived from a chronic inhalation study.

A UF to account for the extrapolation from a LOAEL to a NOAEL (UF_L) was not applied because the current approach is to address this extrapolation as one of the considerations in selecting a benchmark response (BMR) for BMD modeling. In this case, EPA concluded a 10% increase in hemosiderin staining, indicating a precursor to an adverse effect, is appropriate for use in deriving the RfC under the assumption that it represents a minimal biologically significant change.

A UF of 1 was selected to account for deficiencies in the database (UF_D). Studies that are available include chronic and subchronic studies for two species (rats and mice), and several reproductive and developmental studies, including a two-generation reproductive toxicity study. There are also limited human studies available following short-term inhalation exposure.

I.B.4. Additional Studies/Comments

See Section 1.A.4. for additional information.

For more detail on Susceptible Populations, exit to the toxicological review, Section 4.7 (PDF)

I.B.5. Confidence in the Chronic Inhalation RfC

Study — High
Data Base — Medium/High
RfC — Medium/High

The overall confidence in the RfC is medium to high because the RfC was derived from internal dose measures (PBPK method and combined PBPK/BMC method) which account for pharmacokinetic differences between rats and humans using PBPK models (Corley et al., 1997, 041984; Corley et al., 2005, 100100; Lee et al., 1998, 041983) and actual measurements of internal blood concentrations in test animals of interest were used (Dill et al., 1998, 041981). There is high confidence in the NTP (2000, 196293) study because it was a chronic study, employed both male and female rats and mice, had a wide range of exposure levels, and animals were observed twice daily. There is medium-to-high confidence in the database, because data are available for a variety of animal species, including humans. Confidence is not high, because the potential for effects in humans from repeated, long-term exposures has not been investigated.

For more detail on Characterization of Hazard and Dose Response, exit to the toxicological review, Section 6 (PDF)

I.B.6. EPA Documentation and Review of the Chronic Inhalation RfC

Source Document — U.S. EPA (2010, 597544)

This document was provided for review to EPA scientists, interagency reviewers from other federal agencies and White House offices, and the public, and peer reviewed by independent scientists external to EPA. A summary and EPA's disposition of the comments received from the independent external peer reviewers and from the public is included in Appendix A of the *Toxicological Review of Ethylene Glycol Monobutyl Ether* (U.S. EPA, 2010, 597544). ***To review this appendix, exit to the toxicological review, Appendix A, Summary of and Response to External Peer Review Comments (PDF)***.

I.B.7. EPA Contacts

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II. Carcinogenicity Assessment for Lifetime Exposure

Substance Name — Ethylene glycol monobutyl ether (EGBE)
CASRN — 111-76-2
Last Revised — 3/31/2010

This section provides information on three aspects of the carcinogenic assessment for the substance in question: the weight-of-evidence judgment of the likelihood that the substance is a human carcinogen, and quantitative estimates of risk from oral and inhalation exposure. Users are referred to Section I of this file for information on long-term toxic effects other than carcinogenicity.

The rationale and methods used to develop the carcinogenicity information in IRIS are described in the *Guidelines for Carcinogen Risk Assessment* (U.S. EPA, 2005, 086237) and the *Supplemental Guidance for Assessing Susceptibility from Early-Life Exposure to Carcinogens* (U.S. EPA, 2005, 088823). The quantitative risk estimates are derived from the application of a low-dose extrapolation procedure, and are presented in two ways to better facilitate their use. First, route-specific risk values are presented. The "oral slope factor" is a plausible upper bound on the estimate of risk per mg/kg-day of oral exposure. Similarly, a "unit risk" is a plausible upper bound on the estimate of risk per unit of concentration, either per µg/L drinking water (see Section II.B.1.) or per µg/m^3 air breathed (see Section II.C.1.). Second, the estimated concentration of the chemical substance in drinking water or air when associated with cancer risks of 1 in 10,000, 1 in 100,000, or 1 in 1,000,000 is also provided.

This assessment revises the current carcinogenicity assessment of 1999 (U.S. EPA, 1999, 597365) in which the human carcinogen potential could not be determined at that time.

II.A. Evidence for Human Carcinogenicity

II.A.1. Weight-Of-Evidence Characterization

Under the *Guidelines for Carcinogen Risk Assessment* (U.S. EPA, 2005, 086237), EGBE is deemed "not likely to be carcinogenic to humans" at environmental concentrations at or below the RfD and RfC, based on laboratory animal evidence, mode-of-action information, and limited human study information. The available data indicate that carcinogenic effects from EGBE are not likely to occur in humans in the absence of the critical noncancer effects, including hepatic hemosiderin staining and irritant effects at the portal of entry, and are not likely to be carcinogenic to humans exposed at levels at or below the RfC and RfD values established in this assessment. Carpenter et al. (1956, 066464) reported that no changes in erythrocyte osmotic fragility were found in human subjects exposed to up to 195 ppm (942

mg/m^3; ~600 times the RfC) for two 4-hour periods separated by a 30-minute break. At oral doses of 400-500 mg/kg with a one-time bolus dose, hematuria has been noted in two human case reports. This dose is 3,000-3,500 times the RfD and would need to be sustained for a significant period of time to produce hemosiderin deposition. This is unlikely to occur because the primary response of humans to high oral doses of EGBE, as shown in the case studies, is metabolic acidosis, which, if not treated, can lead to shock and eventually death. No information is available on the carcinogenic effects of EGBE via the oral or inhalation route in humans. A 2 year inhalation bioassay with mice and rats (NTP, 2000, 196293) reported tumors of the liver in male mice, forestomach tumors in female mice, and tumors of the adrenal medulla in female rats. Non-neoplastic effects in rats included hyaline degeneration of the olfactory epithelium and Kupffer cell pigmentation. Non-neoplastic effects in mice included forestomach ulcers and epithelial hyperplasia, hematopoietic cell proliferation, Kupffer cell pigmentation, hyaline degeneration of the olfactory epithelium (females only), and bone marrow hyperplasia (males only).

EGBE has been tested in conventional genotoxicity tests for its potential to induce gene mutations in vitro and for cytogenicity in both in vitro and in vivo assays. The available data do not support a mutagenic or clastogenic mechanism for EGBE. Two laboratories (Elias et al., 1996, 042011; Hoflack et al., 1995, 100147) reported weak genotoxicity responses in vitro at high treatment concentrations, but results were not replicated in five other labs reporting negative results.

The hypothesized MOA for the tumors observed following EGBE treatment involves exposure to high doses for prolonged periods of time. The weight of evidence indicates that EGBE is not likely to be carcinogenic to humans at expected environmental concentrations.

For more detail on Characterization of Hazard and Dose Response, exit to the toxicological review, Section 6 (PDF)

For more detail on Susceptible Populations, exit to the toxicological review, Section 4.7 (PDF)

II.A.2. Human Carcinogenicity Data

There are currently no human studies addressing the potential carcinogenicity of EGBE.

II.A.3. Animal Carcinogenicity Data

NTP (2000, 196293) conducted a 2-year inhalation study on EGBE in both genders of F344/N rats and B6C3F$_1$ mice. Rats (50/gender/group) were exposed to concentrations of 0, 31, 62.5,

and 125 ppm (0, 150, 302, and 604 mg/m^3) and mice (50/gender/group) were exposed to concentrations of 0, 62.5, 125, and 250 pm (0, 302, 604, and 1,208 mg/m^3). The NTP report stated that the highest exposure was selected to produce a 10-15% depression in hematologic indices and survival was significantly decreased in male mice at 125 and 250 ppm (54.0 and 53.1%, respectively). While the NTP researchers report that no effect on survival was observed in rats, the female rats appeared to show a trend toward decreased survival that may have been attributable to the hematological effects. Mean body weights of rats exposed to 31 and 62.5 ppm were similar to those of control animals. Mean body weights of the exposed mice were generally less than for controls, with females experiencing greater and earlier reductions. From week 17 to the end of the study, the mean body weights of 125 ppm female rats were generally less than those of controls.

At the end of the 2-year chronic bioassay (NTP, 2000, 196293), neoplastic effects were observed in female rats and in male and female mice. In female rats, the combined incidence of benign and/or malignant pheochromocytoma of the adrenal medulla was 3/50, 4/50, 1/49, and 8/49. The incidence in the high-dose group (16%) did not represent a statistically significant increase over the chamber control group (6%), but it exceeded the historical control (6.4 ± 3.5%; range 2-13%) for this effect.

The low survival rate in male mice exposed to 125 and 250 ppm EGBE may have been due to carcinogenic effects in the liver. A high rate of hepatocellular carcinomas was found in these exposure groups (10/50 [control], 11/50, 16/50, 21/50); the increase at the high-exposure level was statistically significant ($p < 0.01$). However, when hepatocellular adenomas and carcinomas were combined, no significant increase was observed in any exposure group. The incidence of hemangiosarcomas in males exposed to 250 ppm (8%) was also significantly increased ($p = 0.046$) relative to chamber controls (0/50, 1/50, 2/49, 4/49) and exceeded the range of historical controls (14/968; 1.5 ± 1.5%; range 0-4%). No significant increases in benign or malignant hepatocellular tumors or hemangiosarcomas were noted in the female mice, and the incidence of hepatocellular adenomas actually decreased significantly ($p < 0.05$) in relation to the control chamber group (16/50, 8/50, 7/49, 8/49). It should be noted that in light of the high survival rate of the exposed female mice relative to controls (29/50, 31/50, 33/50, 36/50), the high exposure of 250 ppm may not have provided the maximum tolerated dose.

Forestomach squamous cell papillomas and carcinomas, combined, were significantly increased (trend test = 0.003) in female mice relative to the chamber control group (0/50, 1/50, 2/50, 6/50). The incidence of these tumor types (12%) at the highest exposure level was also statistically significant and exceeded the range for the occurrence of these tumors in historical controls (0.9 ± 1.1%; range 0-3%). The first incidence of these tumors appeared in the group exposed to 250 ppm at 582 days, as compared to 731 days at 62.5 and 125 ppm, indicating a

decreased latency period in the highest exposure group. While the incidence of these types of forestomach tumors was not significantly increased over controls in male mice (1/50, 1/50, 2/50, 2/50), the incidence of squamous cell papillomas (4%) in the two highest exposure groups exceeded the range for historical controls (0.5 ± 0.9%; range 0-2%). The increased incidence of forestomach neoplasms in males, as in females, occurred in groups with ulceration and hyperplasia.

The NTP (2000, 196293) study concluded that there was no evidence showing carcinogenic activity in male F344/N rats and equivocal evidence of carcinogenic activity in female F344/N rats, based on increased combined incidences of benign (mainly) and malignant pheochromo¬cytoma of the adrenal medulla. The researchers reported some evidence of carcinogenic activity in male $B6C3F_1$ mice based on increased incidences of hemangiosarcoma of the liver and an increase in the incidence of hepatocellular carcinoma, as well as some evidence of carcinogenic activity in female $B6C3F_1$ mice based on increased incidence of forestomach squamous cell papilloma (mainly) or carcinoma.

With respect to the pheochromocytomas reported in female rats, while the data showed a positive trend ($p = 0.044$) and the high-dose tumor frequencies (16%) were above the upper range of historical controls (13%), the tumor incidence data were not statistically significant. Further, the NTP (2000, 196293) report noted that pheochromocytomas can be difficult to distinguish from non-neoplastic adrenal medullary hyperplasia. The presence of mild-to-moderate compression of the adjacent tissue is a primary criterion used to distinguish pheochromocytomas from medullary hyperplasia; most tumors observed were small and not substantially larger than the more severe grades of adrenal medullary hyperplasia. Interpretation of these tumors should be done cautiously. Given the marginal dose response, lack of tumor evidence in any other organ system of the rats, and reported difficulties in distinguishing pheochromocytomas from non-neoplastic adrenal medullary hyperplasia, this tumor type was not given significant weight in the qualitative or quantitative assessment of EGBE cancer potential.

II.A.4. Supporting Data for Carcinogenicity

Although weakly genotoxic responses have been obtained in two laboratories (Elias et al., 1996, 042011; Hoflack et al., 1995, 100147), EGBE is not expected to be mutagenic or clastogenic based on the available data. The NTP reported negative responses for mutagenicity when EGBE was tested in *Salmonella typhimurium* strains TA97, TA98, TA100, TA1535, and TA1537 at up to 10 mg/plate with and without metabolic activation (Zeiger et al., 1992, 095748). However, Hoflack et al. (1995, 100147) reported that at 38 µmol/plate (4.5 mg/plate), EGBE induced a weak mutagenic response in salmonella tester strain TA97a in the absence of S9 mix (Hoflack et al., 1995, 100147). The work of Hoflack and colleagues was

repeated by Gollapudi et al. (1996, 100137), and EGBE was found to be negative in these tester strains when evaluated at 0.5, 1.0, 2.5, 5.0, 8.5, and 10 mg/plate in the presence and absence of Aroclor-induced rat liver S9 mix. Thus, the weak positive result reported in salmonella TA97a by Hoflack et al. (1995, 100147) is unconfirmed. A plausible explanation put forth by Gollapudi et al. (1996, 100137) is that, given the sensitivity of the Ames test, perhaps the weak positive result reported by Hoflack et al. (1995, 100147) is attributed to an impurity in their test material.

Elias et al. (1996, 042011) reported that EGBE did not induce chromosomal aberrations in Chinese hamster V79 fibroblast cells but that EGBE, at treatment concentrations of ≥8.5 mM, weakly induced sister chromatid exchanges (SCEs) and micronuclei (MN) and potentiated the clastogenicity induced by methyl methanesulfonate. Elias et al. (1996, 042011) also reported that EGBE weakly induced aneuploidy (numerical chromosomal anomalies) in V79 cells; however, this response was found at very high concentrations (16.8 mM EGBE).

When tested at doses nearing toxicity, EGBE and its metabolite butoxyacetaldehyde (BAL) were not mutagenic in an in vitro gene mutation assay using Chinese hamster ovary (CHO) cells (CHO-AS52) (Chiewchanwit and Au, 1995, 041999). In contrast, Elias et al. (1996, 042011) reported that both EGBE and BAL weakly induced gene mutations in Chinese hamster V79 cells only at high treatment concentrations (≥7.5 mg/mL). It should be noted that Chiewchanwit and Au (1995, 041999) reported high cytotoxicity at 38.1 mM EGBE (4.5 mg/mL). The gene mutation data presented by Elias et al. (1996, 042011) is in graphic form only with mean values and no SDs presented. The presence or absence of cytotoxicity was not reported. BAL was also tested for induction of deoxyribonucleic acid (DNA) damage in the mouse endothelial cell line, SVEC4-10, using the comet assay. BAL failed to produce a statistically significant increase in DNA strand breaks at any of the concentrations or time points examined (Klaunig and Kamendulis, 2004, 594442; Klaunig and Kamendulis, 2005, 100165; Reed et al., 2003, 594436). Other lines of evidence indicate that direct interaction of BAL with the DNA molecules does not play a significant role in the carcinogenic activity of EGBE. First, BAL causes cytotoxicity at levels associated with chromosome effects, and cytotoxicity itself can have effects that result in chromosome damage, such as reduction in the repair of SCEs. Second, acetaldehyde is recognized as "weakly mutagenic" and structural comparisons of the aldehyde metabolites of glycol ethers shows that longer-chain aldehydes such as BAL are less mutagenic (Chiewchanwit and Au, 1995, 041999). Third, if BAL were a stable mutagenic metabolite in any of the in vitro assays exposed to EGBE, one would expect them to give positive results; however, the results were generally negative. Elias et al. (1996, 042011) suggested that the V79 cells possess neither ALDH nor alcohol dehydrogenase. The relevance of these studies, or of any systems that lack these enzymes, is of limited value in elucidating the MOA of toxicity in biological systems that possess these enzymes. BAA has been found negative for reverse mutations in *S. typhimurium* his^- with and without metabolic

activation (Hoflack et al., 1995, 100147). Concentrations of up to 8 µmol/plate were tested, and dose was limited by toxicity. BAA (up to 10 mM) was also found negative for induction of DNA damage in SVEC4-10 mouse endothelial cells (Klaunig and Kamendulis, 2005, 100165) and in an SCE assay in V79 cells (Elias et al., 1996, 042011). BAA was weakly positive for aneuploidy in V79 cells at 0.38 mM and positive for MN induction in the same cell line at 10 mM, as reported by Elias et al. (1996, 042011). As noted above, the data means are presented in graphic form without SDs and cannot be critically evaluated; no cytotoxicity data are reported.

EGBE did not increase the incidence of MN in the bone marrow cells of male mice or rats (NTP, 1996, 042064). Animals were given three intraperitoneal injections of EGBE 24 hours apart and sacrificed 24 hours after the last injection; rats were dosed at 0, 7, 14, 28, 56, 112.5, 225, or 450 mg/kg and mice were dosed at 0, 17, 34, 69, 137.5, 275, or 550 mg/kg (NTP, 1996, 042064). There was high mortality (2/5 mice survived) in mice injected with 1,000 mg/kg doses of EGBE. Keith et al. (1996, 041625) treated Sprague-Dawley rats and transgenic FVB/N mice carrying the v-Ha-ras oncogene with a single oral dose of 120 mg/kg EGBE; there was no increase in DNA adducts in the brain, liver, kidney, testes, or spleen of the rats, and no changes in DNA methylation patterns in either species.

II.B. Quantitative Estimate of Carcinogenic Risk from Oral Exposure

No reliable human epidemiological studies or chronic oral animal studies are available that address the potential carcinogenicity of EGBE. However, the NTP (2000) performed a 2-year inhalation bioassay with rats and mice and found no evidence of carcinogenic activity in male F344/N rats and equivocal evidence of carcinogenic activity in female F344/N rats, based on increased combined incidences of benign and malignant pheochromocytoma (mainly benign) of the adrenal medulla. The researchers reported some evidence of carcinogenic activity in male $B6C3F_1$ mice, based on an increased incidence of hemangiosarcoma of the liver and an increase in the incidence of hepatocellular carcinoma that may have been exposure related. They also reported some evidence of carcinogenic activity in female $B6C3F_1$ mice, based on an increased incidence of forestomach squamous cell papilloma or carcinoma (mainly papilloma).

The MOAs presented for the animal tumors indicate that both high doses and sustained periods of exposure are necessary for the carcinogenic response. The available human exposure/response information indicates that these conditions are unlikely to occur because the primary response of humans to high oral doses of EGBE, as shown in the case studies, is metabolic acidosis, which, if not treated, can lead to shock and eventually death. Further,

based on simulations from PBPK modeling, the maximum blood concentrations of BAA that could be produced in humans following exposure to a saturated atmosphere of EGBE would be below those needed to produce hemolysis (Corley et al., 2005, 100100).

The available data indicate that carcinogenic effects from EGBE are not likely to occur in humans in the absence of the critical noncancer effects, including hepatic hemosiderin staining and irritant effects at the portal of entry, and are not likely to be carcinogenic to humans exposed at levels at or below the RfD value established in this assessment. Based on its physical-chemical properties, toxicokinetic and dynamic factors, and MOA information, under existing EPA guidelines (U.S. EPA, 2005, 086237), EGBE is judged not likely to be carcinogenic to humans at expected environmental concentrations.

Following the U.S. EPA (2005, 086237) Guidelines for Carcinogen Risk Assessment, a nonlinear approach to dose-response assessment is taken for agents, such as EGBE, for which the most plausible mode of action at low doses is consistent with nonlinearity. The RfD of 0.1 mg/kg-day derived in Section 5.2 of the Toxicological Review represents the outcome of nonlinear assessment based on hemolytic effects (i.e., hemosiderin deposition) associated with oral and exposure to EGBE. Doses (or concentrations) of EGBE below the RfD would not be expected to produce hemolytic effects (i.e., hemosiderin deposition) and is therefore not expected to produce any increase in cancer risk.

II.C. Quantitative Estimate of Carcinogenic Risk from Inhalation Exposure

No reliable human epidemiological studies are available that address the potential carcinogenicity of EGBE. The NTP (2000, 196293) performed a 2-year inhalation bioassay with rats and mice and found no evidence of carcinogenic activity in male F344/N rats and equivocal evidence of carcinogenic activity in female F344/N rats, based on increased combined incidences of benign and malignant pheochromocytoma (mainly benign) of the adrenal medulla. The researchers reported some evidence of carcinogenic activity in male $B6C3F_1$ mice, based on an increased incidence of hemangiosarcoma of the liver and an increase in the incidence of hepatocellular carcinoma that may have been exposure related. They also reported some evidence of carcinogenic activity in female $B6C3F_1$ mice, based on an increased incidence of forestomach squamous cell papilloma or carcinoma (mainly papilloma).

The MOAs presented for the animal tumors indicate that both high doses and sustained periods of exposure are necessary for the carcinogenic response. The available human exposure/response information indicates that these conditions are unlikely to occur because

the primary response of humans to high oral doses of EGBE, as shown in the case studies, is metabolic acidosis, which, if not treated, can lead to shock and eventually death. Further, based on simulations from PBPK modeling, the maximum blood concentrations of BAA that could be produced in humans following exposure to a saturated atmosphere of EGBE would be below those needed to produce hemolysis (Corley et al., 2005, 100100).

The available data indicate that carcinogenic effects from EGBE are not likely to occur in humans in the absence of the critical noncancer effects, including hepatic hemosiderin staining and irritant effects at the portal of entry, and are not likely to be carcinogenic to humans exposed at levels at or below the RfC value established in this assessment. Based on its physical-chemical properties, toxicokinetic and dynamic factors, and MOA information, under existing EPA guidelines (U.S. EPA, 2005, 086237), EGBE is judged not likely to be carcinogenic to humans at expected environmental concentrations.

Following the U.S. EPA (2005, 086237) Guidelines for Carcinogen Risk Assessment, a nonlinear approach to dose-response assessment is taken for agents, such as EGBE, for which the most plausible mode of action at low doses is consistent with nonlinearity. The RfC of 1.6 mg/m^3 derived in Section 5.1 of the Toxicological Review (U.S. EPA, 2010, 597544) represents the outcome of a nonlinear assessment based on hemolytic effects (i.e., hemosiderin deposition) associated with inhalation exposures to EGBE. Doses (or concentrations) of EGBE below the RfC would not be expected to produce hemolytic effects (i.e., hemosiderin deposition) and is therefore not expected to produce any increase in cancer risk.

II.D. EPA Documentation, Review, And Contacts (Carcinogenicity Assessment)

II.D.1. EPA Documentation

Source Document — U.S. EPA (2010, 597544)

This document has been provided for review to EPA scientists, interagency reviewers from other federal agencies and White House offices, and the public, and peer reviewed by independent scientists external to EPA. A summary and EPA's disposition of the comments received from the independent external peer reviewers and from the public is included in Appendix A of the *Toxicological Review of Ethylene Glycol Monobutyl Ether* (U.S. EPA, 2010, 597544). ***To review this appendix, exit to the toxicological review, Appendix A, Summary of and Response to External Peer Review Comments (PDF)***.

II.D.2. EPA Review

Agency Consensus Date — 3/31/2010

II.D.3. EPA Contacts

Please contact the IRIS Hotline for all questions concerning this assessment or IRIS, in general, at (202) 566-1676 (phone), (202) 566-1749 (fax), or hotline.iris@epa.gov (email address).

III. [reserved]
IV. [reserved]
V. [reserved]

VI. Bibliography

Ethylene glycol monobutyl ether (EGBE)
CASRN — 111-76-2

VI.A. Oral RfD References

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VII. Revision History

Ethylene glycol monobutyl ether (EGBE)
CASRN — 111-76-2
File First On-Line — 12/30/1999

Date	Section	Description
12/30/1999	I., II., VI.	RfD, RfC, and carcinogenicity assessment first on line
12/03/2002	I.A.6., I.B.6., II.D.2.	Screening-Level Literature Review Findings message has been added.
03/31/2010	I., II., VI.	RfD, RfC, and cancer assessment sections updated.

VIII. Synonyms

Ethylene glycol monobutyl ether (EGBE)
CASRN — 111-76-2
Section VII. Last Revised — 3/31/2010

- Bucs
- Butoxyethanol
- N-Butoxyethanol
- 2-Butoxyethanol
- 2-Butoxy-1-Ethanol
- Butyl Cellosolve
- O-Butyl Ethylene Glycol

- Butyl Glycol
- Butyl Oxitol
- Dowanol EB
- Ektasolve EB
- Ethylene Glycol N-Butyl
- Gafcol EB
- Glycol Butyl Ether
- Glycol Ether EB
- Glycol Ether EB Acetate
- Glycol Monobutyl Ether
- Jeffersol EB
- Monobutyl Ether Of Ethylene Glycol
- Monobutyl Glycol Ether
- 3-Oxa-1-Heptanol
- Poly-Solv EB

Attachment 7

2-Butoxyethyl benzoate (2-BEB): Estimation of vapor pressure using MpBp from US EPA's EPISuite

Experimental Database Structure Match: no data

SMILES : CCCCOCCOC(=O)c1ccccc1
CHEM :
MOL FOR: C13 H18 O3
MOL WT : 222.29
---------- SUMMARY MPBPWIN v1.43 ----------

Boiling Point: 300.80 deg C (Adapted Stein and Brown Method)

Melting Point: 54.09 deg C (Adapted Joback Method)
Melting Point: 61.97 deg C (Gold and Ogle Method)
Mean Melt Pt : 58.03 deg C (Joback; Gold,Ogle Methods)
Selected MP: 58.03 deg C (Mean Value)

Vapor Pressure Estimations (25 deg C):
(Using BP: 300.80 deg C (estimated))
(Using MP: 58.03 deg C (estimated))
VP: 0.000716 mm Hg (Antoine Method)
: 0.0955 Pa (Antoine Method)
VP: 0.000924 mm Hg (Modified Grain Method)
: 0.123 Pa (Modified Grain Method)
VP: 0.00166 mm Hg (Mackay Method)
: 0.222 Pa (Mackay Method)
Selected VP: 0.000924 mm Hg (Modified Grain Method)
: 0.123 Pa (Modified Grain Method)
Subcooled liquid VP: 0.00187 mm Hg (25 deg C, Mod-Grain method)
: 0.249 Pa (25 deg C, Mod-Grain method)

TYPE	NUM	BOIL DESCRIPTION	COEFF	VALUE
Group	1	-CH3	21.98	21.98
Group	5	-CH2-	24.22	121.10
Group	1	-O- (nonring)	25.16	25.16
Group	1	-COO- (ester)	78.85	78.85
Group	5	CH (aromatic)	28.53	142.65
Group	1	-C (aromatic)	30.76	30.76
*		Equation Constant		198.18

RESULT-uncorr| BOILING POINT in deg Kelvin | 618.68
RESULT- corr | BOILING POINT in deg Kelvin | 573.96
| BOILING POINT in deg C | 300.80

TYPE	NUM	MELT DESCRIPTION	COEFF	VALUE
Group	1	-CH3	-5.10	-5.10
Group	5	-CH2-	11.27	56.35
Group	1	-O- (nonring)	22.23	22.23
Group	1	-COO- (ester)	53.60	53.60
Group	5	CH (aromatic)	8.13	40.65
Group	1	-C (aromatic)	37.02	37.02
*		Equation Constant		122.50
RESULT		MELTING POINT in deg Kelvin		327.25
		MELTING POINT in deg C		54.09

Attachment 8

2-Butoxyethyl benzoate (2-BEB): Emissions from Manufacturing

INITIAL REVIEW ENGINEERING REPORT
CBI: Yes
Existing Chemical: 19 2BEB MANUF
Standard Review Draft 5/30/2019
PV (kg/yr): 275,000 NX
ENGINEER: Ashish C. Jachak \
SUBMITTER: The Dow Chemical Company
USE:
OTHER USES:
MSDS: No
Label: No
TLV/PEL:

CRSS :
Chemical Name: 2 Butoxyethyl benzoate (2 BEB)
S H20: 0.087 g/L @ 20.00
Physical State and Misc CRSS Info:
MW: 222.28 %<500 %<1000
VP: 2.9E 4 torr @ 20.00
Consumer Use:
SAT (concerns) :
Migration to groundwater:
PBT rating: PBT
Health:
Eco:
OCCUPATIONAL EXPOSURE RATING: 2A
NOTES & KEY ASSUMPTIONS:
Generated by the 09/30/2013 version of ChemSTEER.
POLLUTION PREVENTION CONSIDERATIONS:
EXPOSURE BASED REVIEW: No

INITIAL REVIEW ENGINEERING REPORT
CBI: Yes
Existing Chemical: 19 2BEB MANUF
User defined Manufacturing
Number of Sites/ Location: 1
Days/yr: 20
Basis:
Process Description:
ENVIRONMENTAL RELEASES ESTIMATE SUMMARY
IRER Note: The daily releases listed for any source below may coincide with daily releases from the other sources to the same medium.

Water
Typical: 2.4E+0 kg/site day over 10 days/yr from 1 site
or 2.4E+1 kg/site yr from 1 site or 2.4E+1 kg/yr all sites
Worst Case: 2.4E+0 kg/site day over 10 days/yr from 1 site
or 2.4E+1 kg/site yr from 1 site or 2.4E+1 kg/yr all sites
to:
from: Aqueous Wash of Organic Mass
basis: EPA/OPPT Water Saturation Loss Model.
Water
Typical: 5.5E+2 kg/site day over 10 days/yr from 1 site
or 5.5E+3 kg/site yr from 1 site or 5.5E+3 kg/yr all sites
Worst Case: 5.5E+2 kg/site day over 10 days/yr from 1 site
or 5.5E+3 kg/site yr from 1 site or 5.5E+3 kg/yr all sites
to:
from: Distillation Column Bottoms Disposal
basis: User Defined Loss Rate Model.
Water
Typical: 5.5E+2 kg/site day over 10 days/yr from 1 site
or 5.5E+3 kg/site yr from 1 site or 5.5E+3 kg/yr all sites
Worst Case: 5.5E+2 kg/site day over 10 days/yr from 1 site
or 5.5E+3 kg/site yr from 1 site or 5.5E+3 kg/yr all sites
to:
from: Equipment Cleaning Losses of Liquids from Multiple Vessels
basis: EPA/OPPT Multiple Process Vessel Residual Model, CEB standard 2% residual.
Air
Typical: 8.1E 8 kg/site day over 10 days/yr from 1 site
or 8.1E 7 kg/site yr from 1 site or 8.1E 7 kg/yr all sites
Worst Case: 6.5E 7 kg/site day over 10 days/yr from 1 site
or 6.5E 6 kg/site yr from 1 site or 6.5E 6 kg/yr all sites
to:
from: Sampling Liquid Product
basis: EPA/OPPT Penetration Model.
Air
Typical: 4.7E 5 kg/site day over 10 days/yr from 1 site
or 4.7E 4 kg/site yr from 1 site or 4.7E 4 kg/yr all sites
Worst Case: 9.3E 5 kg/site day over 10 days/yr from 1 site
or 9.3E 4 kg/site yr from 1 site or 9.3E 4 kg/yr all sites
to:
from: Loading Liquid Product into Drums
basis: EPA/OAQPS AP 42 Loading Model.
Air

Typical: 1.8E 4 kg/site day over 10 days/yr from 1 site
or 1.8E 3 kg/site yr from 1 site or 1.8E 3 kg/yr all sites
Worst Case: 1.8E 4 kg/site day over 10 days/yr from 1 site
or 1.8E 3 kg/site yr from 1 site or 1.8E 3 kg/yr all sites
to:
from: Equipment Cleaning Losses of Liquids from Multiple Vessels
basis: EPA/OPPT Mass Transfer Coefficient Model.
RELEASE TOTAL

1.1E+4 kg/yr all sites
OCCUPATIONAL EXPOSURES ESTIMATE SUMMARY
Tot. # of workers exposed via assessed routes: 3
Basis:

Inhalation:
Exposure to Mist (non volatile) (Class I)
Typical:
> Potential Dose Rate: 0.0E+0 mg/day over 10 days/yr
> Lifetime Average Daily Dose: 0.0E+0 mg/kg day over 10 days/yr
> Average Daily Dose: 0.0E+0 mg/day over 10 days/yr
> Acute Potential Dose: 0.0E+0 mg/day over 10 days/yr
Worst Case:
> Potential Dose Rate: 0.0E+0 mg/day over 10 days/yr
> Lifetime Average Daily Dose: 0.0E+0 mg/kg day over 10 days/yr
> Average Daily Dose: 0.0E+0 mg/day over 10 days/yr
> Acute Potential Dose: 0.0E+0 mg/day over 10 days/yr
Number of workers (all sites) with inhalation exposure: 1
Basis: Aqueous Wash of Organic Mass; User defined Inhalation Model.
NOTE: The respirator class is: I. Particulate (including solid or liquid droplets).
INHALATION MONITORING DATA REVIEW
1) Uncertainty (estimate based on model, regulatory limit,
or data not specific to industry):
Yes
2)a) Exposure level > 1 mg/day?
No
OR
b) Hazard Rating for health of 2 or greater?
No
=> Inhalation Monitoring Data Desired? No
Exposure to Vapor (non volatile) (Class II)
Typical:
> Potential Dose Rate: 3.9E 5 mg/day over 10 days/yr
> Lifetime Average Daily Dose: 8.7E 9 mg/kg day over 10 days/yr
> Average Daily Dose: 1.5E 8 mg/day over 10 days/yr
> Acute Potential Dose: 5.6E 7 mg/day over 10 days/yr
Worst Case:
> Potential Dose Rate: 9.4E 3 mg/day over 10 days/yr
> Lifetime Average Daily Dose: 2.1E 6 mg/kg day over 10 days/yr
> Average Daily Dose: 3.7E 6 mg/day over 10 days/yr
> Acute Potential Dose: 1.3E 4 mg/day over 10 days/yr
Number of workers (all sites) with inhalation exposure: 1
Basis: Sampling Liquid Product; EPA/OPPT Mass Balance Model.
NOTE: The respirator class is: II. Gas/vapor (all substances in the gas form).
INHALATION MONITORING DATA REVIEW
1) Uncertainty (estimate based on model, regulatory limit,
or data not specific to industry):
Yes
2)a) Exposure level > 1 mg/day?
No

OR
b) Hazard Rating for health of 2 or greater?
No

=> Inhalation Monitoring Data Desired? No
Exposure to Vapor (non volatile) (Class II)
Typical:
> Potential Dose Rate: 2.2E 2 mg/day over 10 days/yr
> Lifetime Average Daily Dose: 5.0E 6 mg/kg day over 10 days/yr
> Average Daily Dose: 8.8E 6 mg/day over 10 days/yr
> Acute Potential Dose: 3.2E 4 mg/day over 10 days/yr
Worst Case:
> Potential Dose Rate: 1.3E+0 mg/day over 10 days/yr
> Lifetime Average Daily Dose: 3.0E 4 mg/kg day over 10 days/yr
> Average Daily Dose: 5.3E 4 mg/day over 10 days/yr
> Acute Potential Dose: 1.9E 2 mg/day over 10 days/yr
Number of workers (all sites) with inhalation exposure: 1
Basis: Loading Liquid Product into Drums; EPA/OPPT Mass Balance Model.
NOTE: The respirator class is: II. Gas/vapor (all substances in the gas form).
INHALATION MONITORING DATA REVIEW
1) Uncertainty (estimate based on model, regulatory limit,
or data not specific to industry):
Yes
2)a) Exposure level > 1 mg/day?
Yes
OR
b) Hazard Rating for health of 2 or greater?
No
=> Inhalation Monitoring Data Desired? No
Dermal:

Exposure to Liquid at 100.00% concentration
Typical:
> Potential Dose Rate: 7.5E+2 mg/day over 10 days/yr
> Lifetime Average Daily Dose: 1.7E 1 mg/day over 10 days/yr
> Average Daily Dose: 2.9E 1 mg/day over 10 days/yr
> Acute Potential Dose: 1.1E+1 mg/day over 10 days/yr
Worst Case:
> Potential Dose Rate: 2.2E+3 mg/day over 10 days/yr
> Lifetime Average Daily Dose: 5.0E 1 mg/day over 10 days/yr
> Average Daily Dose: 8.8E 1 mg/day over 10 days/yr
> Acute Potential Dose: 3.2E+1 mg/day over 10 days/yr
Number of workers (all sites) with dermal exposure: 1
Basis: Aqueous Wash of Organic Mass; EPA/OPPT 2 Hand Dermal Contact with Liquids Model.
Exposure to Liquid at 100.00% concentration
Typical:
> Potential Dose Rate: 3.7E+2 mg/day over 10 days/yr
> Lifetime Average Daily Dose: 8.4E 2 mg/day over 10 days/yr
> Average Daily Dose: 1.5E 1 mg/day over 10 days/yr

> Acute Potential Dose: 5.4E+0 mg/day over 10 days/yr
Worst Case:
> Potential Dose Rate: 1.1E+3 mg/day over 10 days/yr
> Lifetime Average Daily Dose: 2.5E 1 mg/day over 10 days/yr
> Average Daily Dose: 4.4E 1 mg/day over 10 days/yr
> Acute Potential Dose: 1.6E+1 mg/day over 10 days/yr
Number of workers (all sites) with dermal exposure: 1
Basis: Sampling Liquid Product; EPA/OPPT 1 Hand Dermal Contact with Liquids Model.
Exposure to Liquid at 100.00% concentration
Typical:
> Potential Dose Rate: 7.5E+2 mg/day over 10 days/yr
> Lifetime Average Daily Dose: 1.7E 1 mg/day over 10 days/yr
> Average Daily Dose: 2.9E 1 mg/day over 10 days/yr
> Acute Potential Dose: 1.1E+1 mg/day over 10 days/yr
Worst Case:
> Potential Dose Rate: 2.2E+3 mg/day over 10 days/yr
> Lifetime Average Daily Dose: 5.0E 1 mg/day over 10 days/yr
> Average Daily Dose: 8.8E 1 mg/day over 10 days/yr
> Acute Potential Dose: 3.2E+1 mg/day over 10 days/yr
Number of workers (all sites) with dermal exposure: 1
Basis: Loading Liquid Product into Drums; EPA/OPPT 2 Hand Dermal Contact with Liquids Model.

CALL BY:
CALL TO:
Organization:
Date:
Time:
Existing Chemical: 19 2BEB MANUF

Attachment 9

2-Butoxyethyl benzoate (2-BEB): Emissions from Processing

INITIAL REVIEW ENGINEERING REPORT
CBI: Yes
Existing Chemical: 19 BEB Processing
Standard Review Draft 6/7/2019
PV (kg/yr): 265,000 NX
ENGINEER: Ashish C. Jachak \
SUBMITTER: The Dow Chemical Company
USE:
OTHER USES:
MSDS: No
Label: No
TLV/PEL:

CRSS :
Chemical Name: 2 Butoxyethyl benzoate (2 BEB)
S H20: 0.087 g/L @ 20.00
Physical State and Misc CRSS Info:
MW: 222.28 %<500 %<1000
VP: 2.9E 4 torr @ 20.00
Consumer Use:
SAT (concerns) :
Migration to groundwater:
PBT rating: PBT
Health:
Eco:
OCCUPATIONAL EXPOSURE RATING: 2A
NOTES & KEY ASSUMPTIONS:
Generated by the 09/30/2013 version of ChemSTEER.
POLLUTION PREVENTION CONSIDERATIONS:
EXPOSURE BASED REVIEW: No

INITIAL REVIEW ENGINEERING REPORT
CBI: Yes
Existing Chemical: 19 BEB Processing
User defined Processing
Number of Sites/ Location: 1
Days/yr: 250
Basis:
Process Description:
ENVIRONMENTAL RELEASES ESTIMATE SUMMARY
IRER Note: The daily releases listed for any source below may coincide with daily releases from the other sources to the same medium.

Water
Typical: 2.1E+1 kg/site day over 250 days/yr from 1 site
or 5.3E+3 kg/site yr from 1 site or 5.3E+3 kg/yr all sites
Worst Case: 2.1E+1 kg/site day over 250 days/yr from 1 site
or 5.3E+3 kg/site yr from 1 site or 5.3E+3 kg/yr all sites
to:
from: Equipment Cleaning Losses of Liquids from Multiple Vessels
basis: EPA/OPPT Multiple Process Vessel Residual Model, CEB standard 2% residual.
Water
Typical: 2.6E+1 kg/site day over 250 days/yr from 1 site
or 6.6E+3 kg/site yr from 1 site or 6.6E+3 kg/yr all sites
Worst Case: 3.2E+1 kg/site day over 250 days/yr from 1 site
or 8.0E+3 kg/site yr from 1 site or 8.0E+3 kg/yr all sites
to:
from: Cleaning Liquid Residuals from Drums Used to Transport the Raw Material
basis: EPA/OPPT Drum Residual Model, CEB standard 3% residual.
Air
Typical: 9.0E 5 kg/site day over 250 days/yr from 1 site
or 2.2E 2 kg/site yr from 1 site or 2.2E 2 kg/yr all sites
Worst Case: 1.8E 4 kg/site day over 250 days/yr from 1 site
or 4.5E 2 kg/site yr from 1 site or 4.5E 2 kg/yr all sites
to:
from: Unloading Liquid Raw Material from Drums
basis: EPA/OAQPS AP 42 Loading Model.
Air
Typical: 2.5E 3 kg/site day over 250 days/yr from 1 site
or 6.3E 1 kg/site yr from 1 site or 6.3E 1 kg/yr all sites
Worst Case: 2.5E 3 kg/site day over 250 days/yr from 1 site
or 6.3E 1 kg/site yr from 1 site or 6.3E 1 kg/yr all sites
to:
from: Vapor Release from Open Liquid Surfaces
basis: User defined Vapor Generation Rate Model.
Air
Typical: 8.1E 8 kg/site day over 250 days/yr from 1 site
or 2.0E 5 kg/site yr from 1 site or 2.0E 5 kg/yr all sites
Worst Case: 6.5E 7 kg/site day over 250 days/yr from 1 site
or 1.6E 4 kg/site yr from 1 site or 1.6E 4 kg/yr all sites
to:
from: Sampling Liquid Product
basis: EPA/OPPT Penetration Model.

Air
Typical: 9.0E 5 kg/site day over 250 days/yr from 1 site
or 2.2E 2 kg/site yr from 1 site or 2.2E 2 kg/yr all sites
Worst Case: 1.8E 4 kg/site day over 250 days/yr from 1 site
or 4.5E 2 kg/site yr from 1 site or 4.5E 2 kg/yr all sites
to:
from: Loading Liquid Product into Drums
basis: EPA/OAQPS AP 42 Loading Model.

Air
Typical: 1.8E 4 kg/site day over 250 days/yr from 1 site
or 4.4E 2 kg/site yr from 1 site or 4.4E 2 kg/yr all sites
Worst Case: 1.8E 4 kg/site day over 250 days/yr from 1 site
or 4.4E 2 kg/site yr from 1 site or 4.4E 2 kg/yr all sites
to:
from: Equipment Cleaning Losses of Liquids from Multiple Vessels
basis: EPA/OPPT Mass Transfer Coefficient Model.
Air
Typical: 2.9E 6 kg/site day over 250 days/yr from 1 site
or 7.3E 4 kg/site yr from 1 site or 7.3E 4 kg/yr all sites
Worst Case: 2.9E 6 kg/site day over 250 days/yr from 1 site
or 7.3E 4 kg/site yr from 1 site or 7.3E 4 kg/yr all sites
to:
from: Cleaning Liquid Residuals from Drums Used to Transport the Raw Material
basis: EPA/OPPT Penetration Model.
RELEASE TOTAL
1.3E+4 kg/yr all sites
OCCUPATIONAL EXPOSURES ESTIMATE SUMMARY
Tot. # of workers exposed via assessed routes: 5
Basis:

Inhalation:
Exposure to Vapor (non volatile) (Class II)
Typical:
> Potential Dose Rate: 2.8E 2 mg/day over 250 days/yr
> Lifetime Average Daily Dose: 1.5E 4 mg/kg day over 250 days/yr
> Average Daily Dose: 2.7E 4 mg/day over 250 days/yr
> Acute Potential Dose: 4.0E 4 mg/day over 250 days/yr
Worst Case:
> Potential Dose Rate: 1.7E+0 mg/day over 250 days/yr
> Lifetime Average Daily Dose: 9.3E 3 mg/kg day over 250 days/yr
> Average Daily Dose: 1.6E 2 mg/day over 250 days/yr
> Acute Potential Dose: 2.4E 2 mg/day over 250 days/yr
Number of workers (all sites) with inhalation exposure: 1
Basis: Unloading Liquid Raw Material from Drums; EPA/OPPT Mass Balance Model.
NOTE: The respirator class is: II. Gas/vapor (all substances in the gas form).
INHALATION MONITORING DATA REVIEW
1) Uncertainty (estimate based on model, regulatory limit,
or data not specific to industry):
Yes
2)a) Exposure level > 1 mg/day?
Yes
OR
b) Hazard Rating for health of 2 or greater?
No
=> Inhalation Monitoring Data Desired? No
Exposure to Vapor (non volatile) (Class II)
Typical:
> Potential Dose Rate: 0.0E+0 mg/day over 250 days/yr

> Lifetime Average Daily Dose: 0.0E+0 mg/kg day over 250 days/yr
> Average Daily Dose: 0.0E+0 mg/day over 250 days/yr
> Acute Potential Dose: 0.0E+0 mg/day over 250 days/yr
Worst Case:
> Potential Dose Rate: 0.0E+0 mg/day over 250 days/yr
> Lifetime Average Daily Dose: 0.0E+0 mg/kg day over 250 days/yr
> Average Daily Dose: 0.0E+0 mg/day over 250 days/yr
> Acute Potential Dose: 0.0E+0 mg/day over 250 days/yr
Number of workers (all sites) with inhalation exposure: 1
Basis: Vapor Release from Open Liquid Surfaces; EPA/OPPT Mass Balance Model.
NOTE: The respirator class is: II. Gas/vapor (all substances in the gas form).
INHALATION MONITORING DATA REVIEW
1) Uncertainty (estimate based on model, regulatory limit,
or data not specific to industry):
Yes
2)a) Exposure level > 1 mg/day?
No
OR

b) Hazard Rating for health of 2 or greater?
No
=> Inhalation Monitoring Data Desired? No
Exposure to Vapor (non volatile) (Class II)
Typical:
> Potential Dose Rate: 3.9E 5 mg/day over 250 days/yr
> Lifetime Average Daily Dose: 2.2E 7 mg/kg day over 250 days/yr
> Average Daily Dose: 3.8E 7 mg/day over 250 days/yr
> Acute Potential Dose: 5.6E 7 mg/day over 250 days/yr
Worst Case:
> Potential Dose Rate: 9.4E 3 mg/day over 250 days/yr
> Lifetime Average Daily Dose: 5.2E 5 mg/kg day over 250 days/yr
> Average Daily Dose: 9.2E 5 mg/day over 250 days/yr
> Acute Potential Dose: 1.3E 4 mg/day over 250 days/yr
Number of workers (all sites) with inhalation exposure: 1
Basis: Sampling Liquid Product; EPA/OPPT Mass Balance Model.
NOTE: The respirator class is: II. Gas/vapor (all substances in the gas form).
INHALATION MONITORING DATA REVIEW
1) Uncertainty (estimate based on model, regulatory limit,
or data not specific to industry):
Yes
2)a) Exposure level > 1 mg/day?
No
OR
b) Hazard Rating for health of 2 or greater?
No
=> Inhalation Monitoring Data Desired? No
Exposure to Vapor (non volatile) (Class II)
Typical:
> Potential Dose Rate: 2.8E 2 mg/day over 250 days/yr
> Lifetime Average Daily Dose: 1.5E 4 mg/kg day over 250 days/yr

> Average Daily Dose: 2.7E 4 mg/day over 250 days/yr
> Acute Potential Dose: 4.0E 4 mg/day over 250 days/yr
Worst Case:
> Potential Dose Rate: 1.7E+0 mg/day over 250 days/yr
> Lifetime Average Daily Dose: 9.3E 3 mg/kg day over 250 days/yr
> Average Daily Dose: 1.6E 2 mg/day over 250 days/yr
> Acute Potential Dose: 2.4E 2 mg/day over 250 days/yr
Number of workers (all sites) with inhalation exposure: 1
Basis: Loading Liquid Product into Drums; EPA/OPPT Mass Balance Model.
NOTE: The respirator class is: II. Gas/vapor (all substances in the gas form).
INHALATION MONITORING DATA REVIEW
1) Uncertainty (estimate based on model, regulatory limit,
or data not specific to industry):
Yes
2)a) Exposure level > 1 mg/day?
Yes
OR

b) Hazard Rating for health of 2 or greater?
No
=> Inhalation Monitoring Data Desired? No
Exposure to Vapor (non volatile) (Class II)
Typical:
> Potential Dose Rate: 9.0E 4 mg/day over 250 days/yr
> Lifetime Average Daily Dose: 5.1E 6 mg/kg day over 250 days/yr
> Average Daily Dose: 8.8E 6 mg/day over 250 days/yr
> Acute Potential Dose: 1.3E 5 mg/day over 250 days/yr
Worst Case:
> Potential Dose Rate: 2.7E 2 mg/day over 250 days/yr
> Lifetime Average Daily Dose: 1.5E 4 mg/kg day over 250 days/yr
> Average Daily Dose: 2.7E 4 mg/day over 250 days/yr
> Acute Potential Dose: 3.9E 4 mg/day over 250 days/yr
Number of workers (all sites) with inhalation exposure: 1
Basis: Cleaning Liquid Residuals from Drums Used to Transport the Raw Material; EPA/OPPT Mass Balance Model.
NOTE: The respirator class is: II. Gas/vapor (all substances in the gas form).
INHALATION MONITORING DATA REVIEW
1) Uncertainty (estimate based on model, regulatory limit,
or data not specific to industry):
Yes
2)a) Exposure level > 1 mg/day?
No
OR
b) Hazard Rating for health of 2 or greater?
No
=> Inhalation Monitoring Data Desired? No
Dermal:

Exposure to Liquid at 2.00% concentration
Typical:
> Potential Dose Rate: 1.5E+1 mg/day over 250 days/yr
> Lifetime Average Daily Dose: 8.4E 2 mg/day over 250 days/yr
> Average Daily Dose: 1.5E 1 mg/day over 250 days/yr
> Acute Potential Dose: 2.1E 1 mg/day over 250 days/yr
Worst Case:
> Potential Dose Rate: 4.5E+1 mg/day over 250 days/yr
> Lifetime Average Daily Dose: 2.5E 1 mg/day over 250 days/yr
> Average Daily Dose: 4.4E 1 mg/day over 250 days/yr
> Acute Potential Dose: 6.4E 1 mg/day over 250 days/yr
Number of workers (all sites) with dermal exposure: 1
Basis: Unloading Liquid Raw Material from Drums; EPA/OPPT 2 Hand Dermal Contact with Liquids Model.
Exposure to Liquid at 2.00% concentration
Typical:
> Potential Dose Rate: 7.5E+0 mg/day over 250 days/yr
> Lifetime Average Daily Dose: 4.2E 2 mg/day over 250 days/yr
> Average Daily Dose: 7.3E 2 mg/day over 250 days/yr
> Acute Potential Dose: 1.1E 1 mg/day over 250 days/yr
Worst Case:
> Potential Dose Rate: 2.2E+1 mg/day over 250 days/yr
> Lifetime Average Daily Dose: 1.3E 1 mg/day over 250 days/yr
> Average Daily Dose: 2.2E 1 mg/day over 250 days/yr
> Acute Potential Dose: 3.2E 1 mg/day over 250 days/yr
Number of workers (all sites) with dermal exposure: 1
Basis: Sampling Liquid Product; EPA/OPPT 1 Hand Dermal Contact with Liquids Model.
Exposure to Liquid at 2.00% concentration
Typical:
> Potential Dose Rate: 1.5E+1 mg/day over 250 days/yr
> Lifetime Average Daily Dose: 8.4E 2 mg/day over 250 days/yr
> Average Daily Dose: 1.5E 1 mg/day over 250 days/yr
> Acute Potential Dose: 2.1E 1 mg/day over 250 days/yr
Worst Case:
> Potential Dose Rate: 4.5E+1 mg/day over 250 days/yr
> Lifetime Average Daily Dose: 2.5E 1 mg/day over 250 days/yr
> Average Daily Dose: 4.4E 1 mg/day over 250 days/yr
> Acute Potential Dose: 6.4E 1 mg/day over 250 days/yr
Number of workers (all sites) with dermal exposure: 1
Basis: Loading Liquid Product into Drums; EPA/OPPT 2 Hand Dermal Contact with Liquids Model.
Exposure to Liquid at 2.00% concentration

Typical:
> Potential Dose Rate: 1.5E+1 mg/day over 250 days/yr
> Lifetime Average Daily Dose: 8.4E 2 mg/day over 250 days/yr
> Average Daily Dose: 1.5E 1 mg/day over 250 days/yr
> Acute Potential Dose: 2.1E 1 mg/day over 250 days/yr
Worst Case:
> Potential Dose Rate: 4.5E+1 mg/day over 250 days/yr
> Lifetime Average Daily Dose: 2.5E 1 mg/day over 250 days/yr

> Average Daily Dose: 4.4E 1 mg/day over 250 days/yr
> Acute Potential Dose: 6.4E 1 mg/day over 250 days/yr
Number of workers (all sites) with dermal exposure: 1
Basis: Cleaning Liquid Residuals from Drums Used to Transport the Raw Material; EPA/OPPT 2 Hand Dermal Contact with Liquids Model.

CALL BY:
CALL TO:
Organization:
Date:
Time:
Existing Chemical: 19 BEB Procesing

Attachment 10

2-Butoxyethyl benzoate (2-BEB): E-FAST Report for Manufacturing
INITIAL REVIEW EXPOSURE REPORT

Chemical ID: BEB Assessor:

ENVIRONMENTAL RELEASES

Scenario#:1 Number of Release Sites: 1.

Release Activity:

Release Description:	WATER	LANDFILL Non-sludge/Sludge	STACK	FUGITIVE
Total Releases:	N/A	N/A	0.00	2.80E-03
	(kg/yr)	(kg/yr)	(kg/yr)	(kg/yr)

		Non-sludge/Sludge		
Release Days/yr:	N/A	0.00/0.00	0.00	20.00
Per Site Release:	N/A	N/A/0.00	0.00	1.40E-04
	(kg/site/day)	(kg/site/day)	(kg/site/day)	(kg/site/day)

Remarks:

INITIAL EXPOSURE REVIEW REPORT

Chemical ID: BEB

INHALATION EXPOSURE ESTIMATES (POST-TREATMENT)

SCENARIO #: 1 RELEASE ACTIVITY:

RELEASE DESCRIPTION:

METHOD OF CALCULATION: Screen3

EXPOSED POPULATION: Adult

Number of Sites:	1.	
Per Site Fugitive Release:	1.40E-04	kg/site/day
Fugitive Release Days per Year:	20.00	days
% Removal via Fugitive Release:	0.00	%
Total Fugitive Release:	2.80E-03	kg/yr
Max Annual Average Air Concentration (Fugitive):	7.98E-05	$\mu g/m^3$
Max 24 Hour Average Air Concentration(Fugitive):	1.82E-02	$\mu g/m^3$
Per Site Stack Release:	NA	kg/site/day
Stack Release Days per Year:	NA	days
% Removal via Stack Release:	0.00	%
Total Stack Release:	NA	kg/yr
Max Annual Average Air Concentration (Stack):	0.00	$\mu g/m^3$
Max 24 Hour Average Air Concentration (Stack):	0.00	$\mu g/m^3$

Exposure Units	Results (Stack)	Results (Fugitive)	ASSUMPTIONS			
			ED (years)	AT (years)	BW (kg)	Inh. Rate (m^3/hr)
Cancer						
$LADD_{pot}$ (mg/kg/day)	0.00	6.18E-09	33.00	78.00	80.00	0.61
$LADC_{pot}$ (mg/m^3)	0.00	3.38E-08	33.00	78.00	NA	NA
Acute						
ADR_{pot} (mg/kg/day)	0.00	3.33E-06	NA	1 day	80.00	0.61

Inhalation Comments:

Stack Parameter Data		Fugitive Parameter Data		
Stack Height	10.00	Release Height:	3.00	m
Inside Stack Diameter:	0.10	Length of Release Opening:	10.00	m
Stack Gas Exit Velocity:	0.10	Width of Release Opening:	10.00	m
Stack Gas Temperature:	293.00			

Meteorological and Terrain Information:

Surrounding Land Use:	Urban	
Terrain Height:	0.00	m
Distance to Residence of Interest:	10.00	m
Meteorological Class:	Full	
Stability Class:	NA	
Wind Speed:	NA	

Downwash Information:

Facility Length:	NA	m
Facility Width:	NA	m
Facility Height:	NA	m

Attachment 11

2-Butoxyethyl benzoate (2-BEB): E-FAST Report for Processing
INITIAL REVIEW EXPOSURE REPORT

Chemical ID: BEB Assessor:

ENVIRONMENTAL RELEASES

Scenario#:1 Number of Release Sites: 1.

Release Activity:

Release Description:	WATER	LANDFILL Non-sludge/Sludge	STACK	FUGITIVE
Total Releases:	N/A	N/A	0.00	0.76
	(kg/yr)	(kg/yr)	(kg/yr)	(kg/yr)

		Non-sludge/Sludge		
Release Days/yr:	N/A	0.00/0.00	0.00	250.00
Per Site Release:	N/A	N/A/0.00	0.00	3.06E-03
	(kg/site/day)	(kg/site/day)	(kg/site/day)	(kg/site/day)

Remarks:

INITIAL EXPOSURE REVIEW REPORT

Chemical ID: BEB

INHALATION EXPOSURE ESTIMATES (POST-TREATMENT)

SCENARIO #: 1 RELEASE ACTIVITY:

RELEASE DESCRIPTION:

METHOD OF CALCULATION: Screen3

EXPOSED POPULATION: Adult

Number of Sites:	1.	
Per Site Fugitive Release:	3.06E-03	kg/site/day
Fugitive Release Days per Year:	250.00	days
% Removal via Fugitive Release:	0.00	%
Total Fugitive Release:	0.76	kg/yr
Max Annual Average Air Concentration (Fugitive):	2.18E-02	$\mu g/m^3$
Max 24 Hour Average Air Concentration(Fugitive):	0.40	$\mu g/m^3$
Per Site Stack Release:	NA	kg/site/day
Stack Release Days per Year:	NA	days
% Removal via Stack Release:	0.00	%
Total Stack Release:	NA	kg/yr
Max Annual Average Air Concentration (Stack):	0.00	$\mu g/m^3$
Max 24 Hour Average Air Concentration (Stack):	0.00	$\mu g/m^3$

Exposure Units	Results (Stack)	Results (Fugitive)	ASSUMPTIONS			
			ED (years)	AT (years)	BW (kg)	Inh. Rate (m^3/hr)
Cancer						
$LADD_{pot}$ (mg/kg/day)	0.00	1.69E-06	33.00	78.00	80.00	0.61
$LADC_{pot}$ (mg/m^3)	0.00	9.22E-06	33.00	78.00	NA	NA
Acute						
ADR_{pot} (mg/kg/day)	0.00	7.28E-05	NA	1 day	80.00	0.61

Inhalation Comments:

Stack Parameter Data		Fugitive Parameter Data		
Stack Height	10.00	Release Height:	3.00	m
Inside Stack Diameter:	0.10	Length of Release Opening:	10.00	m
Stack Gas Exit Velocity:	0.10	Width of Release Opening:	10.00	m
Stack Gas Temperature:	293.00			

Meteorological and Terrain Information:

Surrounding Land Use:	Urban	
Terrain Height:	0.00	m
Distance to Residence of Interest:	10.00	m
Meteorological Class:	Full	
Stability Class:	NA	
Wind Speed:	NA	

Downwash Information:

Facility Length:	NA	m
Facility Width:	NA	m
Facility Height:	NA	m

Attachment 12

2-Butoxyethyl benzoate (2-BEB): E-FAST Report for Water to Air Releases
INITIAL REVIEW EXPOSURE REPORT

Chemical ID: BEB Assessor:

ENVIRONMENTAL RELEASES

Scenario#:1 Number of Release Sites: 1.

Release Activity:

Release Description:	WATER	LANDFILL Non-sludge/Sludge	STACK	FUGITIVE
Total Releases:	N/A	N/A	0.00	98.55
	(kg/yr)	(kg/yr)	(kg/yr)	(kg/yr)

		Non-sludge/Sludge		
Release Days/yr:	N/A	0.00/0.00	0.00	365.00
Per Site Release:	N/A	N/A/0.00	0.00	0.27
	(kg/site/day)	(kg/site/day)	(kg/site/day)	(kg/site/day)

Remarks:

INITIAL EXPOSURE REVIEW REPORT

Chemical ID: BEB

INHALATION EXPOSURE ESTIMATES (POST-TREATMENT)

SCENARIO #: 1 RELEASE ACTIVITY:

RELEASE DESCRIPTION:

METHOD OF CALCULATION: Screen3

EXPOSED POPULATION: Adult

Number of Sites:	1.	
Per Site Fugitive Release:	0.27	kg/site/day
Fugitive Release Days per Year:	365.00	days
% Removal via Fugitive Release:	0.00	%
Total Fugitive Release:	98.55	kg/yr
Max Annual Average Air Concentration (Fugitive):	2.08E-04	µg/m^3
Max 24 Hour Average Air Concentration(Fugitive):	2.61E-03	µg/m^3
Per Site Stack Release:	NA	kg/site/day
Stack Release Days per Year:	NA	days
% Removal via Stack Release:	0.00	%
Total Stack Release:	NA	kg/yr
Max Annual Average Air Concentration (Stack):	0.00	µg/m^3
Max 24 Hour Average Air Concentration (Stack):	0.00	µg/m^3

Exposure Units	Results (Stack)	Results (Fugitive)	ASSUMPTIONS			
			ED (years)	AT (years)	BW (kg)	Inh. Rate (m^3/hr)
Cancer						
$LADD_{pot}$ (mg/kg/day)	0.00	1.61E-08	33.00	78.00	80.00	0.61
$LADC_{pot}$ (mg/m^3)	0.00	8.80E-08	33.00	78.00	NA	NA
Acute						
ADR_{pot} (mg/kg/day)	0.00	4.78E-07	NA	1 day	80.00	0.61

Inhalation Comments:

Stack Parameter Data		Fugitive Parameter Data		
Stack Height	10.00	Release Height:	3.00	m
Inside Stack Diameter:	0.10	Length of Release Opening:	1.00E+04	m
Stack Gas Exit Velocity:	0.10	Width of Release Opening:	1.00E+04	m
Stack Gas Temperature:	293.00			

Meteorological and Terrain Information:

Surrounding Land Use:	Urban	
Terrain Height:	0.00	m
Distance to Residence of Interest:	10.00	m
Meteorological Class:	Full	
Stability Class:	NA	
Wind Speed:	NA	

Downwash Information:

Facility Length:	NA	m
Facility Width:	NA	m
Facility Height:	NA	m