Method Version: GreenScreen® Version 1.2

Verified or Non-Verified: VERIFIED

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<th>October 22, 2013</th>
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<td>Expiration Date:</td>
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<tr>
<td>Date:</td>
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<td>Verification Review Plan Prepared By:</td>
<td>Dr. Eric Rosenblum</td>
</tr>
<tr>
<td>Verified GreenScreen® Prepared by Licensed Profiler:</td>
<td>Organization: ToxServices LLC</td>
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<tr>
<td>Date:</td>
<td>October 15, 2013</td>
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Glucose (CAS #50-99-7) GreenScreen® Assessment

Prepared for:

Clean Production Action

Date:

October 15, 2013
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GreenScreen® Executive Summary for Glucose (CAS #50-99-7)

Glucose is a chemical that functions as a food component and additive, a nutrient replenisher in pharmaceuticals and a fluid replenisher.

Glucose (anhydrous solid) was assigned a GreenScreen® Benchmark Score of 3 (“Use But Still Opportunity for Improvement”) as it has moderate Rx (Reactivity) (Appendix B). This corresponds to GreenScreen® benchmark classification 3d in CPA 2011. A data gap exists for E (Endocrine Activity). Glucose meets the criteria for a benchmark 3 chemical despite the data gap. In a worst case scenario, if glucose were assigned a score of High for E, it would be classified as a GreenScreen® benchmark 1 chemical.

GreenScreen® Benchmark Score for Relevant Route of Exposure:
All exposure routes (oral, dermal and inhalation) were evaluated together, as a standard approach for GreenScreen® evaluations, so the GreenScreen® Benchmark Score of 3 (“Use But Still Opportunity for Improvement”) is applicable for all routes of exposure.

### GreenScreen® Hazard Ratings for Glucose

<table>
<thead>
<tr>
<th>Group I Human</th>
<th>AT</th>
<th>ST</th>
<th>N</th>
<th>SnS*</th>
<th>SnR*</th>
<th>IrE</th>
<th>IrE</th>
<th>AA</th>
<th>CA</th>
<th>P</th>
<th>B</th>
<th>Rx</th>
<th>F</th>
</tr>
</thead>
<tbody>
<tr>
<td>L</td>
<td>L</td>
<td>L</td>
<td>L</td>
<td>L</td>
<td>L</td>
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<td>L</td>
<td>L</td>
<td>L</td>
<td>L</td>
<td>L</td>
<td>L</td>
<td>L</td>
</tr>
</tbody>
</table>

Note: Hazard levels (Very High (vH), High (H), Moderate (M), Low (L), Very Low (vL)) in italics reflect estimated (modeled) values, authoritative B lists, screening lists, weak analogues, and lower confidence. Hazard levels in BOLD font are used with good quality data, authoritative A lists, or strong analogues. Group II Human Health endpoints differ from Group II* Human Health endpoints in that they have four hazard scores (i.e., vH, H, M and L) instead of three (i.e., H, M and L), and are based on single exposures instead of repeated exposures. Please see Appendix A for a glossary of hazard acronyms.
GreenScreen® Assessment for Glucose (CAS #50-99-7)

GreenScreen® Version 1.2 Assessment

Chemical Name: Glucose
CAS Number: 50-99-7

GreenScreen® Assessment Prepared By:
Name: Bingxuan Wang, Ph.D.
Title: Toxicologist
Organization: ToxServices LLC
Date: April 9, 2013 (draft); May 31, 2013
(Revision #1); October 1, 2013 (Revision #2)

Quality Control Performed By:
Name: Dr. Margaret H. Whittaker, Ph.D.,
Title: Managing Director and Chief Toxicologist
Organization: ToxServices LLC
Date: April 11, 2013 (draft); June 3, 2013
(Revision # 1), October 15, 2013 (revision #2)

Confirm application of the de minimus rule¹: Not applicable; glucose is not a mixture

Chemical Structure(s):

\[
\begin{array}{c}
\text{HO} \\
\text{O} \\
\text{O} \\
\text{H} \\
\end{array}
\begin{array}{c}
\text{O} \\
\text{H} \\
\text{O} \\
\text{H} \\
\end{array}
\]

Glucose (CAS #50-99-7)

Also called:
D-Glucose, anhydrous; Dextrose [USAN]; Glucose [JAN]; alpha-D-Glucopyranose; Corn sugar; Dextrose; Cartose; Cerelose; Grape sugar; Dextrosol

Chemical Structure(s) of Chemical Surrogates Used in the GreenScreen®:
Sufficient data were identified for glucose to meet the requirements of its assigned benchmark score; use of chemical surrogates was not needed.

Identify Applications/Functional Uses:
1. Food component and additive
2. Nutrient (carbohydrate) replenisher in pharmaceuticals
3. Fluid replenisher

GreenScreen® Summary Rating for Glucose²: Glucose (anhydrous solid) was assigned a GreenScreen® Benchmark Score of 3 (“Use But Still Opportunity for Improvement”) as it has

¹ Every chemical in a material or formulation should be assessed if it is:
   1. intentionally added and/or
   2. present at greater than or equal to 100 ppm
² For inorganic chemicals with low human and ecotoxicity across all hazard endpoints and low bioaccumulation potential, persistence alone will not be deemed problematic. Inorganic chemicals that are only persistent will be evaluated under the criteria for Benchmark 4.
moderate Rx (Reactivity) (Appendix B). This corresponds to GreenScreen® benchmark classification 3d in CPA 2011. A data gap exists for E (Endocrine Activity). Glucose meets the criteria for a benchmark 3 chemical despite the data gap. In a worst case scenario, if glucose were assigned a score of High for E, it would be classified as a GreenScreen® benchmark 1 chemical.

![Figure 1: GreenScreen® Hazard Ratings for Glucose](image)

<table>
<thead>
<tr>
<th>Group I Human</th>
<th>Group II and II* Human</th>
<th>Ecotox</th>
<th>Fate</th>
<th>Physical</th>
</tr>
</thead>
<tbody>
<tr>
<td>C</td>
<td>M</td>
<td>R</td>
<td>D</td>
<td>E</td>
</tr>
<tr>
<td>L</td>
<td>L</td>
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</table>

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

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

Glucose occurs naturally and in the free state in fruits and other parts of plants. It is a primary energy source for most living organisms. Based on its molecular formula, possible combustion products of glucose are CO and CO₂, which are naturally occurring, ambient substances and not relevant with respect to the GreenScreen® score for glucose.

**Introduction**
Glucose or sugar is a common component of food. It can be obtained in the diet as a monosaccharide or metabolized from disaccharides, oligosaccharides and polysaccharides in the human small intestine. Glucose is a source of energy for cells, and it is the most important simple sugar in human metabolism.

ToxServices assessed Glucose against GreenScreen® Version 1.2 (CPA 2013) following procedures outlined in ToxServices’ SOP 1.37 (GreenScreen® Hazard Assessment) (ToxServices 2013). In order to identify relevant environmental fate, environmental toxicity, and human health effects data, multiple sources were searched for data. These sources include on-line databases such as: ChemIDplus (which indexes databases such as HSDB, DART, EMIC, CCRIS, IRIS, Medline, and Toxline), TSCATS (which catalogs toxicity studies submitted to EPA under TSCA), ExPub (which indexes databases such as RTECS), NICNAS and ECHA. In addition, the World Wide Web is also used to search for material safety data sheets (MSDS) and other relevant data.

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3 A moiety is a discrete chemical entity that is a constituent part or component of a substance. A moiety of concern is often the parent substance itself for organic compounds. For inorganic compounds, the moiety of concern is typically a dissociated component of the substance or a transformation product.
Due to its wide use as food and known association with diabetes, many of the identified studies for D-glucose are non-standard toxicity studies. The susceptibility of diabetic patients to the potential adverse effects of glucose is taken into consideration in this report, as they are relevant to the health of human population.

**GreenScreen® List Translator Screening Results**

The GreenScreen® List Translator identifies specific authoritative or screening lists that should be searched to screen for GreenScreen® benchmark 1 chemicals (CPA 2012b). Pharos (Pharos 2013) is an online list-searching tool that is used to screen chemicals against the List Translator electronically. The output indicates benchmark or possible benchmark scores for each human health and environmental endpoint. The output for glucose can be found in Appendix C and a summary of the results can be found below:

Glucose is on the Restricted List of German FEA as a Substance Hazardous to Waters (VwVwS). It is categorized as a Class 1 (low hazard to waters) chemical. It is exempted from REACH Annex I listing due to intrinsic safety.

**PhysioChemical Properties of Glucose**

Glucose is a monosaccharide that is a colorless crystal or white granular powder at room temperature. It is heavier than water and is highly soluble in water.

<table>
<thead>
<tr>
<th>Property</th>
<th>Value</th>
<th>Reference</th>
</tr>
</thead>
<tbody>
<tr>
<td>Molecular formula</td>
<td>C₆H₁₂O₆</td>
<td>ChemIDplus 2013</td>
</tr>
<tr>
<td>SMILES Notation</td>
<td>OC[C@H][C@H][C@H]</td>
<td>ChemIDplus 2013</td>
</tr>
<tr>
<td>Molecular weight</td>
<td>180.1548 g/mol</td>
<td>ChemIDplus 2013</td>
</tr>
<tr>
<td>Physical state</td>
<td>Solid</td>
<td>HSDB 2002</td>
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<tr>
<td>Appearance</td>
<td>Colorless crystals or white granular powder</td>
<td>HSDB 2002</td>
</tr>
<tr>
<td>Melting point</td>
<td>146 °C</td>
<td>HSDB 2002</td>
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<tr>
<td>Vapor pressure</td>
<td>NA</td>
<td></td>
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<tr>
<td>Water solubility</td>
<td>1.2 g/mL at 30°C</td>
<td>HSDB 2002</td>
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<tr>
<td>Dissociation constant</td>
<td>12.92 at 0°C</td>
<td>HSDB 2002</td>
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<tr>
<td>Density/specific gravity</td>
<td>1.544 g/cm³</td>
<td>HSDB 2002</td>
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<tr>
<td>Partition coefficient</td>
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<td>HSDB 2002</td>
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Hazard Classification Summary Section:

Group I Human Health Effects (Group I Human)

Carcinogenicity (C) Score (H, M or L): L
Glucose was assigned a score of L for carcinogenicity based on weight of evidence indicating lack of carcinogenicity. GreenScreen® criteria classify chemicals as a Low hazard for carcinogenicity when there are adequate negative data available, the chemicals have no structural alerts and are not classified by GHS (CPA 2012a).

- Authoritative and Screening Lists
  - Authoritative: not listed in any authoritative lists.
  - Screening: not listed in any screening lists.

- IOM 2005
  - One case-control study in 928 humans suggested that foods rich in sugars, total sucrose intake, sucrose-to-dietary fiber ratio, and glycemic index were associated with increased risk of lung cancer.
  - There are inconsistent data on the association of sugars intake and breast cancers in humans.
  - Five case-control studies showed an increased risk in developing colorectal polyps and colorectal cancer across intakes of sugars and foods rich in sugars. Fiber and starch had been shown to decrease the risk of colorectal cancer. It has been suggested that “the positive association between high sugars consumption and colorectal cancer reflects a global dietary habit that is generally associated with increased risk of colorectal cancer and may not indicate a biological effect of sugars on colon carcinogenesis”.

- U.S. EPA 1990
  - In a 1-year study in rats, glucose water solution (20%, 1 mL) was administered to the animals every other day. No tumors were found. No further information is provided.

- Bayer AG 1998
  - In a chronic dietary study, Sprague-Dawley rats (50/dose/sex) were treated with increasing concentrations of glucose for 16 weeks and then 30% glucose in the diet from the 17th to the 112th week. A concurrent control group with equal number of animals was also included. Additional 10 animals/sex were treated for 14 months and sacrificed for interim examination. The incidence of islet cell adenomas in the pancreas of male rats was significantly (statistical significance not specified) increased, and the incidence of cortical adenomas in the adrenals of females was decreased (statistical significance not specified). The incidence of mammary gland adenomas in females and the Leydig cell tumors of the testes in males was also decreased.
  - In a chronic drinking water study, Syrian golden hamsters (60/dose/sex) received glucose at 0 or 20% in water for 80 weeks. The Incidence of adrenocortical adenomas was increased in females (statistical significance not reported), and no other neoplastic changes were observed.
  - The authors concluded that the changes in the incidence of benign neoplasms in hormone-sensitive tissues (i.e., pancreas, adrenal gland, mammary gland and testis) observed in rats and hamsters as described above appear to be the result of nutritionally/metabolism-induced modulation of the homeostasis in these tissues rather than the result of chronic glucose administration.

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4 Glycemic index is a measure of how quickly blood glucose levels rise after eating a particular type of food.
• The above data showed equivocal associations between sugar intake and lung and breast cancer risk in humans. Several other epidemiological studies suggest that the association of increased sugar intake and increased colorectal cancer risk reflects a global dietary habit rather than a specific biological effect of glucose. Epidemiological studies have inherent limitations in establishing causal relationships due to the inter-individual variations in many aspects such as dietary preferences and genetic background. In the 1 year rat study, no evidence of tumorigenesis was found. In another controlled study in rats and hamsters, both increased and decreased incidences of benign tumor formations were found in hormone-sensitive tissues, indicating that these effects were due to nutritionally-induced disturbances to homeostasis rather than chronic glucose administration. In addition, glucose is an essential cellular nutrient. Therefore, the weight of evidence indicates that the carcinogenic potential of glucose is low.

**Mutagenicity/Genotoxicity (M) Score (H, M or L): L**
Glucose was assigned a score of L for mutagenicity/genotoxicity based on mostly negative studies and weight of evidence. GreenScreen® criteria classify chemicals as a Low hazard for mutagenicity/genotoxicity when there are adequate negative data available, the chemicals have no structural alerts and are not classified by GHS (CPA 2012a).

- **Authoritative and Screening Lists**
  - **Authoritative:** not listed in any authoritative lists.
  - **Screening:** not listed in any screening lists.

- **CCRIS 2001**
  - Glucose tested positive in a mouse lymphoma L5178 thymidine kinase locus assay without metabolic activation at concentrations of 0.179 – 0.235 mol/L.
  - Glucose tested negative in an Ames test using *Salmonella typhimurium* strain TA98 with metabolic activation. No further details are provided.

- **GENE-TOX 1992**
  - Glucose was tested in an *in vivo* micronucleus test in mammalian polychromatic erythrocytes. No conclusion was drawn from the study. No further information was provided.
  - Glucose was tested negative in male mice for clastogenicity in an *in vivo* sperm morphology study. Glucose was not found to cause structural chromosomal aberrations in mitotically-dividing mouse sper®atogonial cells (Wyrobeck et al. 1983).

- **RTECS 2012**
  - Glucose was not cytotoxic in human chondrocytes or genotoxic in human lymphocytes (comets assay) *in vitro.*
  - High glucose (30 mM for 9 – 14 days) induced DNA damage in cultured human endothelial cells as demonstrated by accelerated rate of alkali unwinding indicative of an increased number of single strand breaks, and increased amount of hydroxyl-urea-resistant thymidine incorporation indicative of increased DNA repair synthesis.
  - Reducing sugars such as glucose could produce spectral changes of DNA, and the changed DNA had reduced transfection potential. The rate of inactivation by glucose-6-phosphate (150 mM/L) is 25 times that of glucose. The accumulation of modified DNA may be a mechanism for the decreased genetic viability characteristic of the aged organism.

- **Hansen et al. 2008**
  - Sucrose, glucose or fructose was fed to male Big Blue rats at 30% in the diet. All the sugars increased the mutation rates and the bulky DNA adduct levels in the colon to a
similar extent. No information was provided on the duration of the study or the extent of increase in mutation/DNA adducts levels compared to controls in the abstract.

- Positive results from mouse lymphoma studies may not reflect intrinsic mutagenicity. These results can arise from changes in pH, osmolality, or high levels of cytotoxicity (OECD 1997). At very high concentrations glucose may react with DNA through physiological processes. The last three studies above are non-standard tests with high levels of glucose and therefore not relevant to this GreenScreen® evaluation. Based on the weight of evidence, the genotoxic potential for glucose is low.

**Reproductive Toxicity (R) Score (H, M, or L): L**
Glucose was assigned a score of L for reproductive toxicity based on the weight of evidence according to GHS. The level of confidence was low. Animal studies have limited data. Elevated blood glucose levels in pregnant women are associated with an increased risk of fetal macrosomia, however these are multifactorial conditions and glucose is not a known reproductive toxicant in humans. Glucose is also an essential nutrient in healthy individuals and has a known history of safe use. GreenScreen® criteria classify chemicals as a Low hazard for reproductive toxicity when they are not classifiable under GHS (CPA 2012a).

- **Authoritative and Screening Lists**
  - **Authoritative:** not listed in any authoritative lists.
  - **Screening:** not listed in any screening lists.

- **Reprotox 2011**
  - In humans, women who develop gestational diabetes in mid or late pregnancy have an increased risk of pregnancy complications. Women with elevated blood glucose, due to either diabetes or excessive weight gain during gestation, are at increased risk of fetal macrosomia, which may pose challenges at delivery. This is further discussed in the Developmental Toxicity section.

- **Ruff et al. 2013**
  - Mice (strain and number not specified) were fed human-relevant concentrations of added sugar (25% kcal from a mixture of fructose and glucose to mimic high fructose corn syrup) (duration not specified) and allowed to compete with control mice for territories, resources and mates. Fructose/glucose-fed females had a 2-fold increase in mortality and fructose/glucose-fed males controlled 26% fewer territories and produced 25% less offspring. The authors concluded that physiological adversity was identified in the presence of only minor clinical disruptions using this novel Organismal Performance Assay. However, this reduction in the number of offspring produced may not be the direct result of glucose’s impact on reproductive performance, but may rather be the results of a combination of factors. In addition, this study addressed the effects of added sugar (in addition to normal intake required to sustain physiological processes).

- **RTECS 2012**
  - When administered intraperitoneally to rats (strain and number not reported) for 30 days during pregnancy, TDLo was established at 300,000 mg/kg based on maternal effects on ovaries, fallopian tubes, uterus, cervix and vagina (unspecified). No further information was provided. Since this was administered via an irrelevant route (i.e. intraperitoneal) at extremely high doses, ToxServices disregarded this study in the evaluation of this endpoint.
  - Pregnant hamsters (number not reported) were treated with 4,000 mg/kg of D- or L-isomers of glucose or water via injection (unspecified) for a total of five times, including on gestation day 6 (3pm), day 7 (8 am and 3 pm), and day 8 (8am and 3 pm). D-glucose
trea®ent produced alternating periods of hyperglycemia and normoglycemia and enlarged placentae in the maternal animals. This study was conducted to simulate very high doses of glucose intake via an irrelevant route of exposure (injection). Therefore, the relevance of the reproductive effects observed is questionable.

Based on the data above, elevated blood glucose during gestation is associated with (likely causally) increased risk of fetal macrosomia in pregnant women, which may lead to complications during parturition. The adverse effects on parturition are secondary to fetal macrosomia. Women with diabetes or excessive weight gain during gestation are especially susceptible to elevated blood glucose after glucose ingestion but diabetes is a multifactorial condition that is not solely attributed to high glucose intake. The two animal studies identified have limited details reported, were administered through irrelevant routes (intraperitoneal injection and/or i.v. injection) and used very high doses. Therefore, these studies are of limited relevance to humans. Glucose is an essential energy source in the human body. It is not a known reproductive toxicant in humans (not present on any of the authoritative and screening lists), and is not GHS classified. Based on the weight of evidence, D-glucose is not likely to be a reproductive toxicant to the healthy population.

**Developmental Toxicity incl. Developmental Neurotoxicity (D) Score (H, M or L): L**

Glucose was assigned a score of L for developmental toxicity based the potential teratogenic effects in the sensitive subpopulation of diabetic pregnant women. The level of confidence was low due to the many factors that contribute this teratogenic effect. GreenScreen® criteria classify chemicals as a Low hazard for developmental toxicity when they are not classified under GHS and adequate negative data are available (CPA 2012a).

- **Authoritative and Screening Lists**
  - **Authoritative:** not listed in any authoritative lists.
  - **Screening:** not listed in any screening lists.

- **Reprotox 2011**
  - Abnormally high blood glucose is associated with abnormal embryo development in diabetic pregnancies. It has been reported that infants of diabetic women have an increased incidence (6 – 13%) of congenital anomalies. The most common abnormalities are cardiac and neural tube defects. Macrosomia may also be a result of maternal diabetes or excessive weight gain during gestation, but typically resolves uneventfully for the newborn during the first month after birth. The exact etiology of gestational diabetes is not clear, but the potentially detrimental (to fetuses) sharp rise in blood sugar after meals is thought to be stimulated by the placental hormones (Mayo Clinic 2013).
  - With tight control of maternal diabetes using insulin and close monitoring, the congenital anomaly rate appears to be decreased, provided such controls are instituted very early in the pregnancy. This suggests, but does not prove, that the factors associated with the elevation in maternal blood glucose are responsible for the observed teratogenic effects in diabetic pregnancies
  - In early (2-8 cells) hamster embryos in vitro, the presence of small amounts of glucose in the culture medium inhibits development.
  - Cultured rat embryos with glucose concentrations many times higher than those in diabetic women led to the production of anomalies, particularly involving the central nervous system.
  - Animal experiments using I-glucose, the non-metabolizable isomer of glucose indicate that osmotic effects may play a role in the development of some of the defects associated with elevated serum glucose.
• Jones 1992
  o For most of gestation, fetal tissues are highly dependent on glucose for growth and to meet energy needs; this is reflected in the limited capacity of fetal tissues to metabolize fuels other than glucose.

• RTECS 2012
  o The frequency of several neonatal complications and maternal complications in relation to glucose tolerance was studied in 249 women in the 3rd trimester of pregnancy. None of them had previous evidence of diabetes and all had normal results on an oral glucose-tolerance test. Women were divided into three groups based on their 2-h plasma glucose levels: A (glucose<100 mg/dL), B (glucose between 120 – 164 mg/dL) and C (glucose between 120 – 164 mg/dL). The higher 2-h plasma glucose levels were associated with a significant increase in the incidence of macrosomia, congenital abnormalities (e.g. craniofacial including nose and tongue) and toxemia, C-section, or both (statistical significance not reported). There was also a significant correlation between the infant’s weight and the mother’s 2-h plasma glucose level. The author concluded that even limited degrees of maternal hyperglycemia, which were considered normal under current criteria, may affect the outcome of pregnancy. These developmental effects were not the direct result of glucose administered in the test, but rather the disruption of glucose homeostasis reflected by the test in the pregnant women.
  o Pregnant hamsters (number not reported) were treated with D- or L-isomers of glucose or water at 4,000 mg/kg via injection (unspecified) for a total of five times on gestation day 6 (3pm), day 7 (8 am and 3 pm), and day 8 (8am and 3 pm). In this study, high doses were administered at set intervals to simulate the effect of maternal diabetes in humans. Therefore, the observed effects were relevant only to infants of mothers with gestational diabetes. D-glucose produced fetuses with small urinary bladders, microphthalmia and skeletal abnormalities of sternum, caudal vertebrae, pelvic bones and femora. L-glucose did not produce these developmental effects. This study was conducted via an irrelevant route of exposure (injection) and therefore, the relevance of the developmental effects observed is questionable.

• Although high maternal blood glucose levels are associated with teratogenic effects in humans, this effect is only seen in the sensitive subpopulation of pregnant women with diabetes, and results from the metabolism of many dietary components as well as by the ingestion of glucose. High blood glucose may be the result of direct glucose intake or food intake that can be converted to glucose after digestion, under abnormal metabolic regulation in those who are diabetic. The exact cause of gestational diabetes, however, is not clear; and it is not expected to be directly caused by glucose intake alone. The developmental effects observed in the epidemiological study identified in RTECS (2012) were not the direct effect of glucose administration, but rather reflected the disrupted status of maternal glucose homeostasis. The animal study in hamsters identified in RTECS (2012) was designed to study the effects of maternal diabetes on fetal development. It should be noted that glucose is indispensable for the development of the fetus. Therefore, a score of Low for developmental toxicity was given, considering the lack of definitive data that glucose levels are the causative agent for the potential teratogenic effects in the sensitive subpopulation of diabetic pregnant women and the limitations with epidemiological studies with regard to confounders. Controversies exist regarding the causal relationships of sugar intake with these teratogenic effects. However, in healthy individuals, glucose is not expected to be developmentally toxic.
Endocrine Activity (E) Score (H, M or L): DG
Glucose was assigned a score of DG for endocrine disruption due to the lack of testing data for multiple endocrine pathways.

- **Authoritative and Screening Lists**
  - **Authoritative:** not listed in any authoritative lists.
  - **Screening:** not listed in any screening lists.
- Not listed as a potential endocrine disruptor on the EU Priority List of Suspected Endocrine Disruptors.
- Not listed as a potential endocrine disruptor on the OSPAR List of Chemicals of Possible Concern.
- **Brandt undated.**
  - Insulin is a peptide hormone secreted by the β-cells in the pancreas. Insulin is released in response to elevated plasma glucose, mannose and some amino acids. Prolonged high blood glucose levels may exhaust the β-cells’ insulin store and exceed the ability of them to synthesize additional hormone, resulting in hyperglycemia and diabetes.
- **Diamanti-Kandarakis et al. 2009**
  - Epidemiological studies have established the link between several endocrine disrupting chemicals and diabetes as well as prediabetic disturbances. Glucose is not among them.
- Blood glucose level is regulated by insulin and it also affects insulin secretion, both of which are physiological phenomenon. In diabetic patients, abnormal regulation of blood glucose by insulin is found. Diabetes is a multifactorial condition that is not solely attributed to high glucose intake. Most of the available studies on endocrine disruptors focus on the interaction of other chemicals with the glucose-regulation system rather than the effect of glucose. Glucose itself has not been reported to be an endocrine disruptor. However, data are lacking for other endocrine pathways.

**Group II and II* Human Health Effects (Group II and II* Human)**
*Note: Group II and Group II* endpoints are distinguished in the v 1.2 Benchmark system. For Systemic Toxicity and Neurotoxicity, Group II and II* are considered sub-endpoints and test data for single or repeated exposures may be used. If data exist for single OR repeated exposures, then the endpoint is not considered a data gap. If data are available for both single and repeated exposures, then the more conservative value is used.*

**Acute Mammalian Toxicity (AT) Group II Score (vH, H, M or L): L**
Glucose was assigned a score of L for acute toxicity based on an oral LD$_{50}$ of 25,800 mg/kg in rats. GreenScreen® criteria classify chemicals as a Low hazard for acute toxicity when oral LD$_{50}$ values are greater than 2,000 mg/kg (CPA 2012a).

- **Authoritative and Screening Lists**
  - **Authoritative:** not listed in any authoritative lists.
  - **Screening:** not listed in any screening lists.
- **ChemIDplus 2013**
  - An oral LD$_{50}$ value of 25,800 mg/kg has been established in rats.

**Systemic Toxicity/Organ Effects incl. Immunotoxicity (ST)**
*Group II Score (single dose) (vH, H, M or L): L*
Glucose was assigned a score of L for systemic toxicity (single dose) based on the fact that glucose is an essential energy source in humans and that acute adverse effects only occur at extremely high doses. GreenScreen® criteria classify chemicals as a Low hazard for systemic toxicity (single dose) when adequate negative data are available, and they are not classified under GHS (CPA 2012a).
• Authoritative and Screening Lists
  o **Authoritative**: not listed in any authoritative lists.
  o **Screening**: not listed in any screening lists.

• RTECS 2012
  o In several acute toxicity studies through intraperitoneal (i.p.) and oral routes of exposure, hyperglycemia was reported in rodents and humans.
  o A single oral dose of glucose caused coma, cyanosis, hypermotility and diarrhea in rats. The LD$_{50}$ was of 25,800 mg/kg.

• The weight of evidence indicates that glucose is not classified into GHS Category 1, 2 or 3 for specific target organ toxicity after single exposure.

**Group II* Score (repeated dose) (H, M, or L): L**
Glucose was assigned a score of L for systemic toxicity (repeated dose) based on the maximum recommended intake level of 460 mg/kg/day for humans. GreenScreen® criteria classify chemicals as a Low hazard for systemic toxicity (repeated dose) when the oral effect levels are greater than 100 mg/kg/day (CPA 2012a).

• Authoritative and Screening Lists
  o **Authoritative**: not listed in any authoritative lists.
  o **Screening**: not listed in any screening lists.

• IOM 2005
  o The Recommended Dietary Allowances (RDAs) for carbohydrate are 130 g/day for humans except for 60 – 95 g/day for infants under 1 year old, 175 g/day for pregnant women and 210 g/day for lactating women. The RDAs were based on the role of glucose as the primary energy source for the brain. The Acceptable Macronutrient Distribution Range (AMDR)$^5$ for carbohydrates is established at 45 – 65 g/day based on its role as a source of kilocalories to maintain body weight. Starch and sugar are the major type of carbohydrates evaluated in the report. No defined intake level at which potential adverse effects of total digestible carbohydrate was identified. It was suggested that the maximal intake of added sugars be limited to providing no more than 25% of energy based on the decreased intake of some micronutrients of American subpopulations exceeding this level. This is equivalent to approximately 32.5 g/day (130 g/day x 25%) assuming all the added sugars are in the form of glucose. This is equivalent to 460 mg/kg/day for a 70 kg adult (32.5 g/day ÷ 70 kg = 0.46 g/kg/day). It should be noted that this effect level is the amount of glucose consumed in addition to the baseline consumption from all other sources of digestible carbohydrates.

  o **Dental caries**: Sugars play a significant role in the development of dental caries. However, as dental caries is of multifactorial causation, an intake level of sugars at which increased risk of dental caries can occur has not been determined.

  o **Plasma triacylglycerol, HDL and LDL cholesterol**: There is some evidence that increased intake of sugars including glucose is positively associated with plasma triacylglycerol and low density lipoprotein (LDL) cholesterol concentrations. Most epidemiological studies have shown an inverse relationship between sugar intake and high density lipoprotein (HDL) cholesterol concentration. These are risk factors for cardiovascular diseases.

---

$^5$ AMDR is “the range of intake for a particular energy source that is associated with reduced risk of chronic disease while providing intakes of essential nutrients. If an individual consumes in excess of the AMDR, there is a potential of increasing the risk of chronic disease and/or insufficient intakes of essential nutrients” (IOM 2005).
o **CHD:** Four epidemiological studies showed no risk of coronary heart disease (CHD) from consuming naturally occurring or added sugars. One study showed increased risk of CHD with increasing glycemic index, but only for those with a body mass index greater than 23.

o **Insulin sensitivity and type 2 diabetes:** Insulin controls the glucose metabolism in human bodies. Obesity is related to decreased insulin sensitivity, which can be contributed by sugars and fat intakes. Type 2 diabetes is a chronic disease with high blood glucose levels. It results from insulin insufficiency or insensitivity. In general, prospective data showed no association, and several dietary studies showed an inverse association between total carbohydrate intake and diabetes incidence. However, this observation was confounded by the fact that diets lower in carbohydrate are higher in fat, which predicts diabetes risk due to increased obesity. Some other studies reported that a history of consumption of foods with a high glycemic load predicts the development of type 2 diabetes. Although it is widely believed that individuals with diabetes should avoid sugar to maintain glycemic control, debate exists on whether high-sugar diets have adverse effects on glucose control in those who are diabetic (Howard and Wylie-Rosett 2002).

o **Obesity:** Increased added sugars intake has been shown to cause increased energy intake for children and adults. However, there is no clear and consistent association between increased intake of added sugars and body mass index. Published reports disagree on if a direct link exists between the trend toward increased intakes of sugars and increased rates of obesity.

- Glucose is an essential cellular nutrient in living organisms. Increased added sugar intake has been associated with increased risk of dental caries, cardiovascular diseases, coronary heart disease, diabetes and obesity. However, many of these conditions such as cardiovascular diseases, coronary heart disease, diabetes and obesity are also associated with other risk factors (such as dietary fat intake and exercise habits) due to the limitations with epidemiological studies with regard to confounders, and controversies exist regarding the causal relationships of sugar intake with these diseases. In addition, the increased risks of developing these conditions are likely associated with excess consumption of sugar, which exceeds the levels specified in GreenScreen® hazard assignment criteria. The Institute of Medicine’s recommended maximum level of sugar intake of 460 mg/kg/day for humans is not associated with adverse effects, and glucose is classified as a Low hazard for the repeated dose toxicity endpoint.

**Neurotoxicity (N)**

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

Glucose was assigned a score of L for neurotoxicity (single dose) based on the absence of adverse effects in humans. GreenScreen® criteria classify chemicals as a Low hazard for neurotoxicity (single dose) when adequate negative data are available, and they are not classified under GHS (CPA 2012a).

- **Authoritative and Screening Lists**
  - **Authoritative:** not listed in any authoritative lists.
  - **Screening:** not listed in any screening lists.

- **Not classified as a developmental neurotoxicant (Grandjean and Landrigan 2006).**

- **RTECS 2012**
  - In a human study, 120 volunteers consumed a 25-g glucose drink or a placebo. Tracking but not memory was enhanced by glucose.
**Group II* Score (repeated dose) (H, M, or L): L**

Glucose was assigned a score of L for neurotoxicity (repeated dose) based on the RDA of 130 g/day (460 mg/kg/day) for carbohydrate which is based on the energy requirement of the brain and indicates that glucose is not classified as GHS category 1 or 2 for this endpoint. GreenScreen® criteria classify chemicals as a Low hazard for neurotoxicity (repeated dose) when adequate negative data are available, and they are not classified under GHS (CPA 2012a).

- **Authoritative and Screening Lists**
  - **Authoritative**: not listed in any authoritative lists.
  - **Screening**: not listed in any screening lists.
- **Not classified as a developmental neurotoxicant** (Grandjean and Landrigan 2006).
- **IOM 2005**
  - It has been proposed that sugars may lead to hyperactivity, especially in children. A number of studies have been conducted to examine this association. A meta-analysis of 23 studies conducted over a 12-year period concluded that sugar intake does not affect either behavior or cognitive performance in children.
  - Recommended Dietary Allowances (RDAs) for carbohydrate is 130 g/day (460 mg/kg/day) for humans except infants under 1 year old (RDA is 60 – 95 g/day for infants under 1 year old). The RDA for pregnant women is 175 g/day and for lactating women 210 g/day. The RDAs were based on its role as the primary energy source for the brain.
- **Tomlinson and Gardiner 2008**
  - **Diabetic neuropathy**: Hyperglycemia induces cellular oxidative stress, which can lead to diminished neurotrophic support, disturbed excitability and impulse conduction and the generation of painful states. In the longer term, Schwann-cell death and axonal degeneration results in complete functional breakdown.
- Based on the weight of evidence, although prolonged high blood glucose level can lead to neuropathy, this condition happens in diabetic patients. Diabetes is a multifactorial disease and therefore cannot be attributed by glucose consumption alone. The risk of developing diabetic neuropathy through chronic consumption of glucose alone cannot be determined. The RDA of 130 g/day (460 mg/kg/day) for carbohydrate is based on the energy requirement of the brain and indicates that glucose is not classified as GHS category 1 or 2 for this endpoint.

**Skin Sensitization (SnS) Group II* Score (H, M or L): L**

Glucose was assigned a score of *L* for skin sensitization based on expert judgment by the European Union. The level of confidence was low as no measured data were available.

- **Authoritative and Screening Lists**
  - **Authoritative**: not listed in any authoritative lists.
  - **Screening**: not listed in any screening lists.
- **No relevant data were identified.**
- **EC 2011**
  - In the review of substances listed in Annex IV of Regulation (EC) No. 1907/2006, which are exempted from registration because they are considered to cause minimum risk due to their intrinsic properties, glucose passes the criteria for sensitization (i.e. “No evidence of sensitization potential from structural alerts, in animal tests and no human evidence of sensitization potential”) according to expert judgment.

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

Glucose was assigned a score of *L* for respiratory sensitization based expert judgment by the European Union. The level of confidence was low as no measured data were available.
• Authoritative and Screening Lists
  o **Authoritative**: not listed in any authoritative lists.
  o **Screening**: not listed in any screening lists.
• No relevant data were identified.
• EC 2011
  o In the review of substances listed in Annex IV of Regulation (EC) No. 1907/2006, which are exempted from registration because they are considered to cause minimum risk due to their intrinsic properties, glucose passes the criteria for sensitization (i.e. “No evidence of sensitization potential from structural alerts, in animal tests and no human evidence of sensitization potential”) according to expert judgment.

**Skin Irritation/Corrosivity (IrS) Group II Score (vH, H, M or L): L**
Glucose was assigned a score of L for skin irritation/corrosivity based on expert judgment. The level of confidence was low due to lack of experimental data.

• Authoritative and Screening Lists
  o **Authoritative**: not listed in any authoritative lists.
  o **Screening**: not listed in any screening lists.
• EC Undated
  o Glucose is not irritating to the skin based on the information from the World Health Organization (WHO)’s Joint Group of Experts on the Scientific Aspects of Marine Environmental Protection (GESAMP, source can’t be located), structure activity relationship (SAR) evaluation, and expert judgment.
  o Anhydrous glucose may cause skin redness and itching
• Sigma-Aldrich 2012
  o Glucose may be harmful if absorbed through skin and may cause skin irritation.
  o No measured data were found for this endpoint. The data source supporting the listed statements from material safety data sheets cannot be obtained. The opinion of EC was based on GESAMP, SAR and expert judgment without data, and the EC is a reliable source. In addition, glucose has a long history of safe use as an essential food additive, and no adverse irritating effects are known. Based on the weight of evidence, glucose is not likely to be irritating to the skin.

**Eye Irritation/Corrosivity (IrE) Group II Score (vH, H, M or L): L**
Glucose was assigned a score of M for eye irritation/corrosivity based on slight hazard of eye irritation in humans without measured data determined by the EC. The level of confidence was low due to lack of measured data. GreenScreen® criteria classify chemicals as a **Low** hazard for eye irritation/corrosivity when adequate data are available and negative, there are no structural alerts, and they are not classified under GHS (CPA 2012a).

• Authoritative and Screening Lists
  o **Authoritative**: not listed in any authoritative lists.
  o **Screening**: not listed in any screening lists.
• EC undated
  o Glucose is not irritating to the eye, but is slightly hazardous in case of eye contact (irritant) based on information from GESAMP, SAR, MSDS and expert judgment.
• ScholAR Chemistry 2012
  o Acute symptoms of exposure of anhydrous glucose on the eyes are redness, tearing, itching, burning and conjunctivitis
•Sigma-Aldrich 2012
  o D-glucose may cause eye irritation

•No measured data were found for this endpoint and the listed statements are from material safety data sheets, for which the data sources cannot be obtained. Based on the expert judgment of EC, there is a slight hazard for eye irritation.

**Ecotoxicity (Ecotox)**

**Acute Aquatic Toxicity (AA) Score (vH, H, M or L): L**
Glucose was assigned a score of L for acute aquatic toxicity based on the most conservative predicted acute aquatic toxicity value of 1.51 x 10^5 mg/L. The level of confidence was low as the assignment was based on modeled data. GreenScreen® criteria classify chemicals as a *Low* hazard for acute aquatic toxicity when acute aquatic toxicity values are higher than 100 mg/L (CPA 2012a).

- Authoritative and Screening Lists
  - Authoritative: not listed in any authoritative lists.
  - Screening: not listed in any screening lists.

- U.S. EPA 2013
  - 2-day LD₅₀ (zebra fish) = 2.5% v/v
  - 1 – 2-day LOEC (zebra fish) = 40 mM (7,200 mg/L)
  - 7-day EC₅₀ (inflated duckweed, population) < 100 mM (18,000 mg/L)

- U.S. EPA 2012
  - The available measured data for glucose does not include data for all three trophic levels, and are not from standard aquatic toxicity tests. Therefore, ECOSAR was used to estimate the aquatic toxicity of this chemical (Appendix D). Glucose has calculated acute aquatic L/EC₅₀ values of 3.63 x 10^6 mg/L in fish (96h), 1.31 x 10^6 mg/L in daphnia (48h) and 1.51 x 10^5 in green algae (96h). However, glucose may not be soluble enough to measure the effect in fish and daphnia.

**Chronic Aquatic Toxicity (CA) Score (vH, H, M or L): L**
Glucose was assigned a score of L for chronic aquatic toxicity based on the most conservative predicted chronic aquatic toxicity value of 14,501 mg/L in algae. The level of confidence was low as this assignment was based on modeled data. GreenScreen® criteria classify chemicals as a *Low* hazard for chronic aquatic toxicity when chronic aquatic toxicity values are greater than 10 mg/L (CPA 2012a).

- Authoritative and Screening Lists
  - Authoritative: not listed in any authoritative lists.
  - Screening: not listed in any screening lists.

- U.S. EPA 2013
  - 292-day NOEC (reed, population) = 4,493 lb/acre
  - 14-day NOAC (reed, population) = 8,986 lb/acre

- U.S. EPA 2012
  - No standard measured data are available for glucose, and the data identified above are of limited value due the fact that results are reported in a unit which cannot be converted to a mg/L dose level. Therefore, ECOSAR was used to estimate the aquatic toxicity of this chemical (Appendix D). Glucose has predicted chronic toxicity values of 2.08 x 10^5 mg/L in fish, 36,447 mg/L in daphnia and 14,501 mg/L in green algae.
Environmental Fate (Fate)

Persistence (P) Score (vH, H, M, L, or vL): vL
Glucose was assigned a score of vL for persistence based on the EPISuite prediction of ready biodegradability. The level of confidence was low as this assignment was based on modeled data. GreenScreen® criteria classify chemicals as a very Low hazard for persistence when the biodegradation half-lives meet the 10-day window (CPA 2012a).

- Authoritative and Screening Lists
  - Authoritative: not listed in any authoritative lists.
  - Screening: not listed in any screening lists.
- U.S. EPA 2011
  - No relevant data could be found for glucose. As a result, EPISuite was used to predict the biodegradability of this chemical (Appendix E). BIOWIN predicted that glucose is readily biodegradable.

Bioaccumulation (B) Score (vH, H, M, L, or vL): vL
Glucose was assigned a score of vL for bioaccumulation based on the predicted BCF of less than 100 and a measured log Kow of less than 4. The level of confidence was low as this assignment was based on modeled data. GreenScreen® criteria classify chemicals as a very Low hazard for bioaccumulation when BCF/BAF values are less than 100 or log Kow values are less than 4 (CPA 2012a).

- Authoritative and Screening Lists
  - Authoritative: not listed in any authoritative lists.
  - Screening: not listed in any screening lists.
- U.S. EPA 2011
  - No relevant data could be found for glucose. As a result, EPISuite was used to predict the biodegradability of this chemical (Appendix E). BCFBAF predicted a BCF of 0.893 based on a measured log Kow of -3.24 for glucose.

Physical Hazards (Physical)

Reactivity (Rx) Score (vH, H, M or L): M
Glucose was assigned a score of M for reactivity based on GHS categorization of Division 1.4 for explosiveness. GreenScreen® criteria classify chemicals as a Moderate hazard for reactivity when they are classified as GHS Division 1.4 or 1.5 chemicals (CPA 2012a).

- Authoritative and Screening Lists
  - Authoritative: not listed in any authoritative lists.
  - Screening: not listed in any screening lists.
- CHRIS 1999
  - Glucose solution does not react with water or other common materials. It is stable during transport.
- ICSC 1997
  - Finely dispersed particles of glucose form explosive mixtures in air.
- Data from ICSC (1997) indicate that glucose is a substance that presents a small hazard of explosion in the event of ignition or initiation. This classifies the chemical into Division 1.4 under GHS for explosives.
**Flammability (F) Score (vH, H, M or L): L**
Glucose was assigned a score of L for flammability based on weight of evidence indicating lack of flammability. GreenScreen® criteria classify chemicals as a Low hazard for flammability when adequate negative data are available and they are not classified under GHS (CPA 2012a).

- **Authoritative and Screening Lists**
  - **Authoritative:** not listed in any authoritative lists.
  - **Screening:** not listed in any screening lists.
- **CHRIS 1999**
  - Glucose solution is not flammable
- **ICSC 1997**
  - Glucose is combustible
- **Sigma-Aldrich 2012**
  - HMIS Classification for Flammability: 0
  - NFPA Rating for Fire: 0
- **Ward’s Science 2013**
  - HMIS Classification for Flammability: 1
  - NFPA Rating for Fire: 1
- **Information from the Sigma-Aldrich MSDS and from Ward’s Science MSDS is different regarding the flammability of glucose. Data from MSDS’s are not considered as reliable as the classifications provided by ICSC (from NIOSH) and CHRIS, which are national agencies. The weight of evidence indicates that glucose does not meet the GHS criteria for flammable solids, which are readily combustible (easily ignited by brief contact with an ignition source and the flame spreads rapidly), or may cause or contribute to fire through friction.**
References


APPENDIX A: Hazard Benchmark Acronyms
(in alphabetical order)

(AA) Acute Aquatic Toxicity

(AT) Acute Mammalian Toxicity

(B) Bioaccumulation

(C) Carcinogenicity

(CA) Chronic Aquatic Toxicity

(Cr) Corrosion/ Irritation (Skin/ Eye)

(D) Developmental Toxicity

(E) Endocrine Activity

(F) Flammability

(IrE) Eye Irritation/Corrosivity

(IrS) Skin Irritation/Corrosivity

(M) Mutagenicity and Genotoxicity

(N) Neurotoxicity

(P) Persistence

(R) Reproductive Toxicity

(Rx) Reactivity

(SnS) Sensitization- Skin

(SnR) Sensitization- Respiratory

(ST) Systemic/Organ Toxicity

(TD_{Lo}) Toxic Dose Low
APPENDIX B: Results of Automated GreenScreen® Score Calculation for Glucose

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<th>Table 1: Hazard Summary Table</th>
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**Datagap Criteria**

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**Final Green Screen Benchmark Score**

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Note: Chemical has not undergone a data gap assessment. Not a final GreenScreen Score.
APPENDIX C: Pharos Output for Glucose

GLUCOSE

CAS RN: 50-99-7
Synonyms: Anhydrous dextrose, corn sugar, dextrose, anhydrous glucose

Detailed Direct Hazard Listings

Quickscreen

Restricted List
German FEA - Substances Hazardous to Waters (VwVw5)
Class I Low Hazard to Waters - GreenScreen Benchmark Unspecified - occupational hazard only

Exempt
EC - REACH Exemptions
Exempted from REACH Annex I listing due to intrinsic safety

Lifecycle Hazard Quickscreen

Full Lifecycle Map

Research Status: Preliminary literature review drafted
The Pharos team has undertaken a preliminary literature review of some of the processes involved in the manufacture of this substance and identified the following chemicals. This list of chemicals is not exhaustive of all chemicals that may be involved in the production or life cycle of this substance.

May contain residual manufacturing chemicals that have a hazard of...

Cancer
SULFURIC ACID [7664-93-9] - Occasional/Rare Intermediate

Respiratory
SULFURIC ACID [7664-93-9] - Occasional/Rare Intermediate

Mammalian
HYDROGEN CHLORIDE (HCL) [7647-01-0] - Occasional/Rare Intermediate

Skin Irritation
SULFURIC ACID [7664-93-9] - Occasional/Rare Intermediate

Restricted List
STARCH [9005-25-8] - Integral Feedstock
APPENDIX D: ECOSAR Output for Glucose

ECOSAR Version 1.11 Results Page

SMILES : OCC1C(O)C(O)C(O)C(O)O1
CHEM : D-Glucose
CAS Num: 000050-99-7
ChemID1:
MOL FOR: C6 H12 O6
MOL WT : 180.16
Log Kow: -2.888     (EPISuite Kowwin v1.68 Estimate)
Log Kow:            (User Entered)
Log Kow: -3.24      (PhysProp DB exp value - for comparison only)
Melt Pt:            (User Entered for Wat Sol estimate)
Melt Pt: 83.00      (deg C, PhysProp DB exp value for Wat Sol est)
Wat Sol: 1E+006     (mg/L, EPISuite WSKowwin v1.43 Estimate)
Wat Sol:            (User Entered)
Wat Sol: 5E+005     (mg/L, PhysProp DB exp value)

---------------------------------------------------------------
Values used to Generate ECOSAR Profile
---------------------------------------------------------------
Log Kow: -2.888     (EPISuite Kowwin v1.68 Estimate)
Wat Sol: 5E+005     (mg/L, PhysProp DB exp value)

---------------------------------------------------------------
Available Measured Data from ECOSAR Training Set
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No Data Available

---------------------------------------------------------------
ECOSAR v1.1 Class-specific Estimations
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Neutral Organics

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<td>1.51e+005</td>
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<tr>
<td>Neutral Organics</td>
<td>Fish</td>
<td>ChV 2.08e+005</td>
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<tr>
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<td>Daphnid</td>
<td>ChV 36446.895</td>
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<td>Green Algae</td>
<td>ChV 14500.736</td>
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<tr>
<td>Neutral Organics</td>
<td>Fish (SW)</td>
<td>96-hr LC50</td>
<td>4.44e+006 *</td>
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<tr>
<td>Neutral Organics</td>
<td>Mysid</td>
<td>96-hr LC50</td>
<td>9.04e+007 *</td>
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<tr>
<td>Neutral Organics</td>
<td>Fish (SW)</td>
<td>ChV 24350.627</td>
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<tr>
<td>Neutral Organics</td>
<td>Mysid (SW)</td>
<td>ChV 3.33e+007</td>
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<tr>
<td>Neutral Organics</td>
<td>Earthworm</td>
<td>14-day LC50</td>
<td>1006.237</td>
<td></td>
</tr>
</tbody>
</table>

GreenScreen® Version 1.2 Reporting Template - Sept 2013
Note: * = asterisk designates: Chemical may not be soluble enough to measure this predicted effect. If the effect level exceeds the water solubility by 10X, typically no effects at saturation (NES) are reported.

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

Neutral Organics:

Maximum LogKow: 5.0 (Fish 96-hr LC50; Daphnid LC50, Mysid LC50)
Maximum LogKow: 6.0 (Earthworm LC50)
Maximum LogKow: 6.4 (Green Algae EC50)
Maximum LogKow: 8.0 (ChV)
APPENDIX E: EPISuite Output for Glucose

CAS Number: 50-99-7
SMILES : OCC1C(O)C(O)C(O)C(O)O1
CHEM : D-Glucose
MOL FOR: C6 H12 O6
MOL WT : 180.16

------------------------------------ EPI SUMMARY (v4.10) -----------------------------------

Physical Property Inputs:
  Log Kow (octanol-water):   -----
  Boiling Point (deg C) :   -----
  Melting Point (deg C) :   -----
  Vapor Pressure (mm Hg) :   -----
  Water Solubility (mg/L):   -----
  Henry LC (a®-m3/mole) :   -----

Log Octanol-Water Partition Coef (SRC):
  Log Kow (KOWWIN v1.68 estimate) = -2.89
  Log Kow (Exper. database match) = -3.24
   Exper. Ref: SANGSTER (1994)

Boiling Pt, Melting Pt, Vapor Pressure Estimations (MPBPVP v1.43):
  Boiling Pt (deg C):  380.68  (Adapted Stein & Brown method)
  Melting Pt (deg C):  132.79  (Mean or Weighted MP)
  VP(mm Hg,25 deg C):  1.33E-007  (Modified Grain method)
  VP (Pa, 25 deg C) :  1.78E-005  (Modified Grain method)
   MP  (exp database): < 25 deg C
   VP  (exp database):  8.02E-14 mm Hg (1.07E-011 Pa) at 25 deg C

Water Solubility Estimate from Log Kow (WSKOW v1.42):
  Water Solubility at 25 deg C (mg/L):  1e+006
   log Kow used: -3.24 (expkow database)
   no-melting pt equation used
  Water Sol (Exper. database match) =  1.2e+006 mg/L (30 deg C)
   Exper. Ref: MULLIN,JW (1972)
  Water Sol (Exper. database match) =  5e+005 mg/L (20 deg C)
   Exper. Ref: YALKOWSKY,SH & DANNENFELSER,RM (1992)

Water Sol Estimate from Fragments:
  Wat Sol (v1.01 est) =  1e+006 mg/L

ECOSAR Class Program (ECOSAR v1.00):
  Class(es) found:
   Neutral Organics

Henrys Law Constant (25 deg C) [HENRYWIN v3.20]:
  Bond Method :  9.72E-015 a®-m3/mole (9.85E-010 Pa-m3/mole)
  Group Method:  1.62E-026 a®-m3/mole (1.64E-021 Pa-m3/mole)
For Henry LC Comparison Purposes:
User-Entered Henry LC: not entered
Henrys LC [via VP/WSol estimate using User-Entered or Estimated values]:
  HLC: 3.153E-014 a®-m3/mole (3.195E-009 Pa-m3/mole)
  VP: 1.33E-007 mm Hg (source: MPBPVP)
  WS: 1E+006 mg/L (source: WSKOWWIN)

Log Octanol-Air Partition Coefficient (25 deg C) [KOAWIN v1.10]:
Log Kow used: -3.24 (exp database)
Log Kaw used: -12.401 (HenryWin est)
  Log Koa (KOAWIN v1.10 estimate): 9.161
  Log Koa (experimental database): None

Probability of Rapid Biodegradation (BIOWIN v4.10):
  Biowin1 (Linear Model) : 1.1081
  Biowin2 (Non-Linear Model) : 0.9315
Expert Survey Biodegradation Results:
  Biowin3 (Ultimate Survey Model): 3.5922 (days-weeks )
  Biowin4 (Primary Survey Model) : 4.2253 (days )
MITI Biodegradation Probability:
  Biowin5 (MITI Linear Model) : 1.0950
  Biowin6 (MITI Non-Linear Model): 0.8829
Anaerobic Biodegradation Probability:
  Biowin7 (Anaerobic Linear Model): 1.4659
Ready Biodegradability Prediction: YES

Hydrocarbon Biodegradation (BioHCwin v1.01):
  Structure incompatible with current estimation method!

Sorption to aerosols (25 Dec C)[AEROWIN v1.00]:
Vapor pressure (liquid/subcooled): 1.07E-011 Pa (8.02E-014 mm Hg)
Log Koa (Koawin est ) : 9.161
Kp (particle/gas partition coef. (m3/ug)):
  Mackay model : 2.81E+005
  Octanol/air (Koa) model: 0.000356
Fraction sorbed to airborne particulates (phi):
  Junge-Pankow model : 1
  Mackay model : 1
  Octanol/air (Koa) model: 0.0277

Atmospheric Oxidation (25 deg C) [AopWin v1.92]:
Hydroxyl Radicals Reaction:
  OVERALL OH Rate Constant = 104.3877 E-12 cm3/molecule-sec
  Half-Life = 0.102 Days (12-hr day; 1.5E6 OH/cm3)
  Half-Life = 1.230 Hrs
Ozone Reaction:
  No Ozone Reaction Estimation
Fraction sorbed to airborne particulates (phi):
  1 (Junge-Pankow, Mackay avg)
0.0277 (Koa method)
Note: the sorbed fraction may be resistant to atmospheric oxidation

Soil Adsorption Coefficient (KOCWIN v2.00):
$Koc = 10 \text{ L/kg (MCI method)}$
$\log Koc = 1.000 \text{ (MCI method)}$
$Koc = 0.01658 \text{ L/kg (Kow method)}$
$\log Koc = -1.781 \text{ (Kow method)}$

Aqueous Base/Acid-Catalyzed Hydrolysis (25 deg C) [HYDROWIN v2.00]:
Rate constants can NOT be estimated for this structure!

Bioaccumulation Estimates (BCFBAF v3.01):
$\log BCF$ from regression-based method = 0.500 ($BCF = 3.162 \text{ L/kg wet-wt}$)
$\log BCF$ Arnot-Gobas method (upper trophic) = -0.049 ($BCF = 0.893$)
$\log$ $Kow$ used: -3.24 (expkow database)

Volatile from Water:
Henry LC: 9.72E-015 a®-m3/mole (estimated by Bond SAR Method)
Half-Life from Model River: 8.085E+010 hours (3.369E+009 days)
Half-Life from Model Lake: 8.82E+011 hours (3.675E+010 days)

Removal In Wastewater Treatment:
Total removal: 1.85 percent
Total biodegradation: 0.09 percent
Total sludge adsorption: 1.75 percent
Total to Air: 0.00 percent
(using 10000 hr Bio P,A,S)

Removal In Wastewater Treatment:
Total removal: 92.06 percent
Total biodegradation: 91.72 percent
Total sludge adsorption: 0.33 percent
Total to Air: 0.00 percent
(using Biowin/EPA draft method)

Level III Fugacity Model:
<table>
<thead>
<tr>
<th>Mass Amount</th>
<th>Half-Life</th>
<th>Emissions</th>
</tr>
</thead>
<tbody>
<tr>
<td>(percent)</td>
<td>(hr)</td>
<td>(kg/hr)</td>
</tr>
<tr>
<td>Air</td>
<td>5.06e-007</td>
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<td>Soil</td>
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<td>416</td>
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<tr>
<td>Sediment</td>
<td>0.0592</td>
<td>1.87e+003</td>
</tr>
</tbody>
</table>
Persistence Time: 414 hr
Authorized Reviewers

Glucose GreenScreen® Evaluation Prepared By:

Bingxuan Wang, Ph.D.
Toxicologist
ToxServices LLC

Glucose GreenScreen® Evaluation QC’d By:

Managing Director and Chief Toxicologist
ToxServices LLC