GreenScreen™ Assessment for Dihydrogen Oxide (CAS# 7732-18-5)

GreenScreen™ Version 1.2 Criteria, Information Sources and Specified Lists - Draft Assessment
Note: Validation Has Not Been Performed on this Green Screen Assessment

Chemical Name: Dihydrogen Oxide (H_2O)

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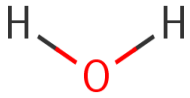
Confirm application of the *de minimus* rule[1]: (if no, what *de minimus* did you use?) Yes

Chemical Name (CAS #): Dihydrogen Oxide (CAS# 7732-18-5)

Also Called: Water, deionized water, distilled water, ice

Chemical Surrogates, analogs or moieties used in this assessment (CASs #): None

Chemical Structure(s):
*Note: Include chemical structure(s) of all surrogates, analogs (and /or moieties) used in the assessment.



H_2O

Notes related to production specific attributes[2]: Dihydrogen oxide is a naturally occurring inorganic liquid.
For Inorganic Chemicals and relevant particulate organics (*if not relevant, list NA*)
Define Properties:
1. Particle size (e.g. silica of respirable size): NA

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

2. Structure (e.g. amorphous vs. crystalline): Dihydrogen oxide is a liquid at standard temperature and pressure, but freezes to a solid crystalline form below 0^{o} C. Vapor forms at temperatures above 100^{o} C.
3. Mobility (e.g. Water solubility, volatility): Dihydrogen oxide is soluble in water. Vapor pressure is 3 mm Hg at 37^{o} C. (6)
4. Bioavailability: Dihydrogen oxide is a clear, odorless, tasteless liquid that is essential for animal and plant life and is an excellent solvent for many substances. A constant supply is needed to replenish fluids lost through normal physiological activities, such as photosynthesis, respiration, perspiration and urination. Dihydrogen oxide is also generated from food intake and metabolism of protein, fat and carbohydrates.

Identify Applications/Functional Uses:
(e.g. Cleaning product, TV casing)
1. Maintenance of biological systems and metabolism
2. Solvent

Green Screen Rating[3]: Dihydrogen oxide was assigned a Benchmark Score of 4 based on experimental data, expert judgment from its chemical and physical properties and general evidence. It scores High for Persistence due to its inorganic structure. Dihydrogen oxide is a naturally occurring substance, required by all living organisms for normal metabolic functions.

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

Note: Hazard levels (Very High (vH), High (H), Moderate (M), Low (L), Very Low (vL)) in *italics* reflect estimated values and lower confidence. Hazard levels in **BOLD** font reflect values based on test data (See Guidance). * = inorganic chemical

Transformation Products and Ratings:
Identify relevant fate and transformation products (i.e., dissociation products, transformation products, valence states) **and/or moieties of concern[4] :** NA

Functional Use	Life Cycle	Transformation Pathway	Transformation Products	CAS #	On CPA	Green Screen

[3] 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.
[4] 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.

	Stage				Red List[5]?	Rating[6]

Introduction

Dihydrogen oxide is a naturally occurring inorganic compound. It is essential for all living organisms for maintenance of metabolic and physiologic functions. It is also widely used as a solvent.

In experimental studies, dihydrogen oxide is often used as a negative control for comparison to a chemical being tested. A few specific experimental studies have been published to evaluate dihydrogen oxide itself; all of these have been negative. (3-7)

The US daily reference intake for water is 3.7 l/day for adult males and 2.7 l/day for adult females, including water contained in food, beverages and drinking water. An upper limit of consumption has not been set. (1)

Drinking water contains numerous elements and contaminants at low levels. In the US, these levels are controlled by the EPA through the National Primary and Secondary Drinking Water Regulations. The highest elemental secondary standard is for chloride at 250ppm. This is below a level of concern for toxicity. All other contaminants are below the *de minimus* level (100ppm) for intentionally or unintentionally added contaminants. (8)

Hazard Classification Summary Section:
Group I Human Health Effects (Group I Human)

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

Dihydrogen oxide was assigned a score of **Low** due to its use as a negative control in many experimental studies and long history of use with no carcinogenicity observed.

Authoritative and Screening Lists:

- Dihydrogen oxide was not listed on relevant authoritative or screening lists.

Results:

- Deionized water is used as the control substance in two-year carcinogenicity studies where the chemical of concern is dosed in water. (2)

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

Mutagenicity/Genotoxicity (M) Score (H, M or L): L
Dihydrogen oxide was assigned a score of **Low** for mutagenicity based on negative results in experimental studies.

Authoritative and Screening Lists:

- Dihydrogen oxide was listed on relevant authoritative or screening lists.

Results:

- Distilled water was tested at 100 – 10000 ug/plate in the bacterial reverse mutation assay (e.g. Ames test) with S. typhimurium TA97, TA98, TA100, TA1535 and TA1537 – with and without metabolic activation. All results were negative. (3)

Reproductive Toxicity (R) Score (H, M, or L): L
Dihydrogen oxide was assigned a score of **Low** for Reproductive Toxicity based on negative results in an experimental study.

Authoritative and Screening Lists:

- Dihydrogen oxide was not listed on relevant authoritative or screening lists.

Results:

- Five different types of drinking water – magnetized mineral water, activated water, purified water, mineral water, alkaline ionized water and natural water - were compared for effects on reproduction in mice. None of the water types effected pregnancy rate, gestation rate or birth livability of mice. (4)

Developmental Toxicity incl. Developmental Neurotoxicity (D) Score (H, M or L): L
Dihydrogen oxide was assigned a score of **Low** for Developmental Toxicity and Developmental Neurotoxicity based on negative results in an experimental study.

Authoritative and Screening Lists:

- Dihydrogen oxide was not listed on relevant authoritative or screening lists.

Results:

- A study was conducted to assess the combined effect of maternal drinking purified water and taking a magnesium deficient diet on postnatal development and behavior in the offspring of Sprague-Dawley rats. The four exposure groups were: control diet and control water, control diet and purified water, magnesium deficient diet and control water, and magnesium deficient diet and purified water, all from 5 weeks of age of the F0 generation to 3 weeks of the F1 generation. Reproductive and neurobehavioral parameters were measured. There were no significant differences of the reproductive outcome in the groups. Drinking purified water can decrease maternal magnesium level

slightly and induce offspring's developmental retardation, especially when there is a magnesium deficient diet. No other neurobehavioral effects were reported. (5)

Endocrine Activity (E) Score (H, M or L): *L*
Dihydrogen oxide was assigned a score of *Low* for endocrine activity although there was a lack of experimental data for this endpoint. Expert judgment used to assess this chemical classifies this substance as having low potential for Endocrine Activity based on its physical properties, such as solubility, lack of reactivity and general evidence as an essential chemical for normal biological and physiological function.

Authoritative and Screening Lists:
- Dihydrogen oxide was not listed on relevant authoritative or screening lists.

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
Dihydrogen oxide was assigned a score of **Low** for acute mammalian toxicity based on an oral LD50 study and human experience. Acute inhalation and dermal toxicity data were lacking, however, based on this chemical's physical properties, such as low volatility and solubility, expert judgment can be used to assess this substance as having low potential for acute toxicity.

Authoritative and Screening Lists:
- Dihydrogen oxide was not listed on relevant authoritative or screening lists.

Results:
- Oral LD50 study in rats was 89800 mg/kg. (6)
- TDLo following oral exposure to a human was reported to be 42.86 g/kg. (7)

Systemic Toxicity/Organ Effects incl. Immunotoxicity (ST) Group II Score (single dose: vH, H, M or L); *L*
Dihydrogen oxide was assigned a score of *Low* for systemic toxicity/ organ effects including immunotoxicity although direct experimental data are lacking. Expert judgment used to assess this chemical classifies this substance as having Low potential for systemic toxicity/organ effects including immunotoxicity, based on the chemical's physical properties, such as low volatility, lack of reactivity, solubility and general evidence as an essential chemical for normal biological and physiological function.

Authoritative and Screening Lists:

- Dihydrogen oxide was not listed on relevant authoritative or screening lists.

Group II* Score (repeated dose: H, M, L): *L*
Dihydrogen oxide was assigned a score of *Low* for systemic toxicity/ organ effects repeated dose toxicity although direct experimental data are lacking. Expert judgment used to assess this chemical classifies this substance as having low potential for repeated dose toxicity, based on the chemical's physical properties such as low volatility, lack of reactivity, solubility and general evidence as an essential chemical for normal biological and physiological function.

Authoritative and Screening Lists:

- Dihydrogen oxide was not listed on relevant authoritative or screening lists.

Neurotoxicity (N)
Group II Score (single dose: vH, H, M or L): *L*
Dihydrogen oxide was assigned a score of *Low* for single dose neurotoxicity although direct experimental data are lacking for this endpoint. Expert judgment used to assess this chemical classifies this substance as having low potential for neurotoxicity, based on the chemical's physical properties such as low volatility, lack of reactivity, solubility and general evidence as an essential chemical for normal biological and physiological function.

Authoritative and Screening Lists:

- Dihydrogen oxide was not listed on relevant authoritative or screening lists.

Group II* Score (repeated dose: H, M, L): *L*
Dihydrogen oxide was assigned a score of *Low* for repeated dose neurotoxicity although direct experimental data are lacking for this endpoint. Expert judgment used to assess this chemical classifies this substance as having low potential for neurotoxicity, based on the chemical's physical properties such as low volatility, lack of reactivity, solubility and general evidence as an essential chemical for normal biological and physiological function.

Authoritative and Screening Lists:

- Dihydrogen oxide was not listed on relevant authoritative or screening lists.

Skin Sensitization (SnS) Group II* Score (H, M or L): *L*
Dihydrogen oxide was assigned a score of *Low* for skin sensitization based on expert judgment. Expert judgment used to assess this chemical classifies this substance as having low potential for skin sensitization, based on the chemical's physical properties such as lack of reactivity, solubility and general evidence as an essential chemical for normal biological and physiological function.

Authoritative and Screening Lists:

- Dihydrogen oxide was not listed on relevant authoritative or screening lists.

Respiratory Sensitization (SnR) Group II* Score (H, M or L): *L*
Dihydrogen oxide was assigned a score of *Low* for respiratory sensitization based on expert judgment. Expert judgment was used to assess this substance as having *Low* hazard potential for respiratory sensitization based on the chemical's physical properties such as low volatility, lack of reactivity, solubility and general evidence as an essential chemical for normal biological and physiological function.

Authoritative and Screening Lists:

- Dihydrogen oxide was not listed on relevant authoritative or screening lists.

Skin Irritation/Corrosivity (IrS) Group II Score (vH, H, M or L): *L*
Dihydrogen oxide was assigned a score of *Low* for skin irritation/corrosivity based on expert judgment. Expert judgment used to assess this chemical classifies this substance as having low potential for skin irritation/ corrosivity, based on the chemical's physical properties such as neutral pH, lack of reactivity and general evidence.

Authoritative and Screening Lists:

- Dihydrogen oxide was not listed on relevant authoritative or screening lists.

Results:

- Prolonged skin contact with water can cause defatting of the skin, resulting in reversible redness. (5)

Eye Irritation/Corrosivity (IrE) Group II Score (vH, H, M or L): *L*
Dihydrogen oxide was assigned a score of *Low* for eye irritation/corrosivity. Expert judgment used to assess this chemical classifies this substance as having low potential for eye irritation/ corrosivity, based on the chemical's physical properties such as neutral pH, lack of reactivity and general evidence.

Authoritative and Screening Lists:

- Dihydrogen oxide was not listed on relevant authoritative or screening lists.

<u>Ecotoxicity (Ecotox)</u>

Acute Aquatic Toxicity (AA) Score (vH, H, M or L): L
Dihydrogen oxide was assigned a score of **Low** for acute aquatic toxicity. Expert judgment used to assess this chemical classifies this substance as having low potential for acute aquatic toxicity, based on the chemical's physical properties such as neutral pH, solubility, lack of reactivity and general evidence that aquatic organisms require dihydrogen oxide for their existence.

Authoritative and Screening Lists:

- Dihydrogen oxide was not listed on relevant authoritative or screening lists.

Chronic Aquatic Toxicity (CA) Score (vH, H, M or L): L
Dihydrogen oxide was assigned a score of **Low** for chronic aquatic toxicity. Expert judgment used to assess this chemical classifies this substance as having low potential for chronic aquatic toxicity, based on the chemical's physical properties such as neutral pH, solubility, lack of reactivity and general evidence that aquatic organisms require dihydrogen oxide for their existence.

Authoritative and Screening Lists:

- Dihydrogen oxide was not listed on relevant authoritative or screening lists.

Environmental Fate (Fate)

Persistence (P) Score (vH, H, M, L, or vL): H
Dihydrogen oxide was assigned a score of **High** for persistence in the environment based on the fact that it is a naturally occurring inorganic compound.

Authoritative and Screening Lists:

- Dihydrogen oxide was not listed on relevant authoritative or screening lists.

Results:

- Dihydrogen oxide is a naturally occurring inorganic compound that is persistent in the environment.

Bioaccumulation (B) Score (vH, H, M, L, or vL): *L*
Dihydrogen oxide was assigned a score of *Low* for bioaccumulation. Expert judgment used to assess this chemical classifies this substance as having low potential for bioaccumulation, based on the chemical's physical properties such as solubility and general evidence.

Authoritative and Screening Lists:

- Dihydrogen oxide was not listed on relevant authoritative or screening lists.

Physical Hazards (Physical)

Reactivity (Rx) Score (vH, H, M or L): L
Dihydrogen oxide was assigned a score of **Low** for reactivity based on its stability and lack of reactivity with most materials.

Authoritative and Screening Lists:

- Dihydrogen oxide was not listed on relevant authoritative or screening lists.

Results:

- Dihydrogen oxide is a stable inorganic compound.
- Dihydrogen oxide can react violently when in contact with alkaline metals, aluminum-alkyl compounds, metal hydrides or non-metal hydrides, acid anhydrides, acid chlorides, metal- or non-mental oxides. (6)

Flammability (F) Score (vH, H, M or L): L

Dihydrogen oxide was assigned a score of **Low** for flammability based on its physical property of non-flammability.

Authoritative and Screening Lists:

- Dihydrogen oxide was not listed on relevant authoritative or screening lists.

Results:

- Dihydrogen oxide is non-flammable.

References

1) Dietary Reference Intakes: Water, Potassium, Sodium, Chloride and Sulfate. Consuensus Report, Food and Nutrition Board, February 11, 2004. Accessed on July 2, 2012. Available at http://www.iom.edu/Reports/2004/Dietary-Reference-Intakes-Water-Potassium-Sodium-Chloride-and-Sulfate.aspx

2) NTP - http://ntp.niehs.nih.gov/?objectid=36305D16-F1F6-975E-79776DAD38EC101E - National Toxicology Program, Description of NTP Study Types, 2-Year Study Protocol. Accessed on July 2, 2012

3) Zeiger,E, Anderson,B, Haworth,S, Lawlor,T and Mortelmans,K; Salmonella Mutagenicity Tests. V. Results from the Testing of 311 Chemicals; Environ. Mol. Mutagen. 19(Suppl.21):2-141, 1992.

4) Zhou,YH, Geng, GY, Feng, SQ, Chung, K, Kung, K, Wei, S; Effects of new Types of Drinking Water on Reproduction and Antioxidation of Mice; China Public Health, 19(12):1429-30, 2003 Dec.

5) Zeng, H, Shu, VVQ, Zhao, Q, Chen, Q; Reproductive and Neurobehavioral Outcome of Drinking Purified Water Under Magnesium Deficiency in the Rat's Diet; Food Chem Toxicol. 46(5): 1495-502, 2008, May.

6) GESTIS Substance Database - http://gestis-en.itrust.de/nxt/gateway.dll/gestis_en/000000.xml?f=templates$fn=default.htm$3.0, Food Research, Vol 21, pg 348, 1956. Accessed on July 2, 2012.

7) TOXNET - http://toxnet.nlm.nih.gov/cgi-bin/sis/htmlgen?CHEM, Journal of Pharmacology and Experimental Therapeutics. Vol. 29, Pg. 135, 1926. Accessed on July 2, 2012.

8) US EPA Drinking Water Contaminants, List of Contaminants and their MCLs http://water.epa.gov/drink/contaminants/index.cfm#List. Accessed on July 2, 2012.

1) **Appendix X**[7]

Modeling Results

Attach: Inorganic compounds, such as dihydrogen oxide, are not recommended for modeling by these programs

- **EPISuite Results for Chemical Name (CAS #)**
- **ECOSAR Results for Chemical Name (CAS #)**
- **Other**

[7] Attach separate Appendix for each set of modeling results