# HYDROGEN PEROXIDE, PERACETIC ACID AND SODIUM PERCARBONATE
## (October 2010)

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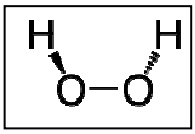
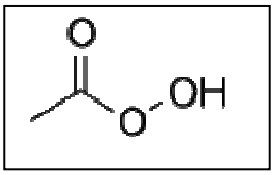


**HYDROGEN PEROXIDE**



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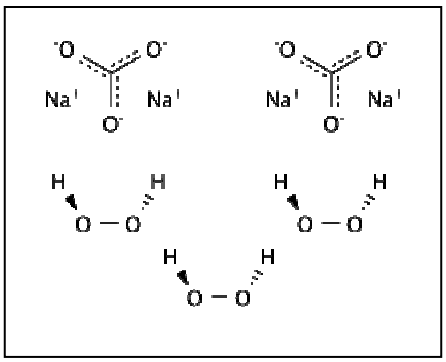

**SODIUM PERCARBONATE**

## BACKGROUND

Hydrogen peroxide is a reactive oxidizing substance that may form a number of addition compounds with different physical and chemical properties. Peracetic acid and sodium percarbonate are organic addition compounds that are also reactive oxidants and/or break down to hydrogen peroxide.

Hydrogen peroxide and peracetic acid were first registered in the United States as pesticides in 1977 and 1985, respectively for use as disinfectants, sanitizers and sterilants. As of the 1993 Reregistration Eligibility Decision (R.E.D.) document for peroxy compounds published by the U.S. EPA, there were 11 products containing hydrogen peroxide and 11 containing peracetic acid as active ingredients (EPA, 1993a,b). Sodium percarbonate was first registered as a pesticide by the U.S. EPA in 2002 for use as an algaecide and fungicide on ornamental plants and turf (Fed Reg., 2002). Sodium percarbonate was first registered in an herbicide product in 2004 (EPA, 2004a,b). A Memorandum of Understanding between EPA and the Food and Drug Administration gives the EPA primary regulatory jurisdiction over peroxy compounds (EPA, 1993a,b).

## REGISTERED PRODUCTS IN MASSACHUSETTS

The current list of aquatic herbicides containing hydrogen peroxide that are registered in Massachusetts can be accessed at http://www.state.ma.us/dfa/pesticides/water/Aquatic/Herbicides.htm on the Massachusetts Department of Agricultural Resources (DAR) Aquatic Pesticide Website. The DAR updates this list regularly with changes. In addition, the DAR can be contacted directly at (617) 626-1700 for more specific questions regarding these products.

## USES AND APPLICATION

Hydrogen peroxide-based products are used as aquatic herbicides/microbiocides to manage algae, cyanobacteria, fungi and microorganisms in water. These products work upon contact to oxidize plants.

Application of these products can be made in several ways, depending on the formulation used. In general, these products are most effective when application is made while algae are not yet well established and when growth first begins to appear. Both sunlight and higher temperatures enhance the effect so application early in the day under calm, sunny conditions is best. In water bodies with floating mats of algae, the best results are obtained by

breaking up the mats either before or during product application. Dead and/or floating plant material should be removed before it sinks and decays as an accumulation of decaying matter will provide additional nutrients to the water that will stimulate regrowth of algae and further blooms. These products may be applied via either a spot treatment or a whole-lake treatment.

Methods of application vary with the formulation and include, for liquid products, spot application directly over the infested area on the water surface from a boat or shore or injection via a piping system. For granular forms of the product, broadcast application by hand or via a mechanical spreader, spreading the product in burlap bags dragged behind a boat or aerially, via conventional aerial application equipment (BioSafe Systems, 2006; BioSafe Systems, 2008).

## MECHANISM OF ACTION

Hydrogen-peroxide-based products work by oxidizing organic material with which they come into contact. Both hydrogen peroxide and peracetic acid are strong oxidizing agents. Although the discussion below addresses hydrogen peroxide, the oxidizing mechanism of peracetic acid is similar. More specific information about peracetic acid is presented later in this document.

Hydrogen peroxide is one in a series of reactive oxygen species characterized by structures that possess unpaired electrons. This makes them highly reactive and gives them the ability to damage cellular macromolecules including lipids, proteins and nucleic acids (CSU, 2003). For example, lipid peroxidation is a process in which oxygen radicals react with unsaturated fatty acids in cell membrane phospholipids. Damage is produced as a chain reaction in which, the oxygen radical removes a hydrogen from the fatty acid, which leaves a carbon-centered radical within the fatty acid, which then reacts with oxygen to produce a peroxy radical, which can then react with other fatty acids or proteins. The process of lipid peroxidation is illustrated in Figure 1.

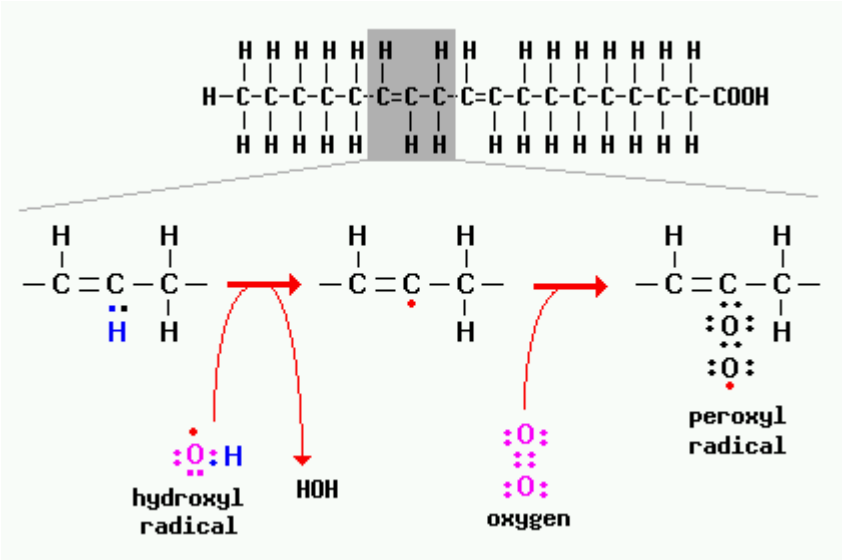


**Figure 1. Lipid Peroxidation (CSU, 2003)**

There is a "background" level of hydrogen peroxide in cells as all cells, with the exception of anaerobic bacteria, produce reactive oxygen species as a normal part of cellular metabolism (ECJRC, 2003). The process of cellular metabolism, known as oxidative phosphorylation, occurs in the cell mitochondria. This process converts energy released by the oxidation of nutrients to adenosine triphosphate (ADP), a useable form of energy for the cell. In this process, an electron is passed down the electron transport chain in a series of oxidation-reduction reactions in which the last electron acceptor should be oxygen, to form water. In a small percentage of cases, however, oxygen is

instead prematurely and incompletely reduced to yield a superoxide radical that may then be converted to hydrogen peroxide. (Wikipedia, 2009; CSU,2003) Other biological processes that may produce reactive oxygen species include production by white blood cells to kill invading pathogens; and production by cells exposed to abnormally low or high oxygen conditions, certain oxidizing drugs or ionizing radiation, (especially in well-oxygenated tissues) (CSU, 2003). Hydrogen peroxide is one of the major products formed that can set off a chain of oxidative damage (CSU, 2003).

Because endogenously produced hydrogen peroxide and other oxygenated radicals may cause damage to cells, cells are protected by antioxidant protection systems including endogenously produced antioxidant enzymes as well as antioxidant scavengers. Three important antioxidant chemicals produced by cells include superoxide dismutase, which converts superoxide ($O_2^-$) to hydrogen peroxide and water, as well as catalase and glutathione peroxidase, both of which degrade hydrogen peroxide to water and oxygen (see Figure 2). Vitamins C and E are examples of antioxidant scavengers. The antioxidant enzyme systems are important factors in the breakdown of oxidant chemicals in the environment as well as within organisms.

SOD:

$2\ O_2{-}\bullet + 2H+ \rightarrow H_2O_2 + O_2$ (SOD:superoxide dismutase)

GSPx:

$H_2O_2 + 2\ GSH \rightarrow 2\ H_2O + GSSG$ (GSPx:glutathione peroxidase)

CAT:

$2\ H_2O_2 \rightarrow 2\ H_2O + O_2$ (CAT: catalase)

**Figure 2. Enzymatic Reactions in the Elimination of Reactive Oxygen Species (ECJRC, 2003)**

Like hydrogen peroxide, peracetic acid is an oxidant and damages cells by oxidation and disruption of cell membranes via the hydroxyl radical. Unlike hydrogen peroxide though, peracetic acid is not deactivated in the same way by catalase and peroxidase enzymes of microorganisms which break down hydrogen peroxide, so is quite an effective antimicrobial compound. However, once peracetic acid does break down, contingent on the degree to which the peracetic acid solution is stabilized, the $H_2O_2$ formed is broken down by these enzymes, the gradual elimination of which will ultimately affect the equilibrium of this substance in solution (HERA, 2002; Wikipedia, 2009).

## ENVIRONMENTAL FATE AND TRANSPORT

The physical and chemical characteristics of hydrogen peroxide, peracetic acid and sodium percarbonate are summarized in Appendix Tables A-1-3.

### HYDROGEN PEROXIDE

Pure hydrogen peroxide solution is relatively stable. The stability of the solution increases with increasing hydrogen peroxide concentration. Hydrogen peroxide is highly reactive with other substances, organic compounds, elements, radiation or cells. Generally speaking, degradation of hydrogen peroxide proceeds rapidly due to the many degradation mechanisms that exist. Hydrogen peroxide solution is often mixed with a number of stabilizers to retard degradation, including mineral acids to maintain an acidic solution, complexing/chelating agents to inhibit

metal-catalyzed decomposition, to neutralize small amounts of colloidal catalysts or adsorb/absorb nutrients (ECJRC, 2003).

In aqueous solution, hydrogen peroxide may break down via either biological processes (i.e., in the presence of antioxidant enzymes) or abiotically, in which it reacts with transition metals, heavy metals, metals or other impurities that may be present and that may serve as catalysts for degradation. The rate of decomposition depends on the types and amount of catalyst or enzyme available, as well as on temperature and light conditions. Hydrogen peroxide is most stable at a pH of about 3.5-4.5. Highest degradation rates occur under alkaline conditions. In natural waters, hydrogen peroxide reacts readily with copper, manganese and iron.

Fenton's reagent, composed of hydrogen peroxide and ferrous (+2 oxidation state) iron, produces a large number of oxygen radicals and dramatically increases the oxidation potential of hydrogen peroxide. Hydrogen peroxide will also react with organic compounds, especially aliphatic and aromatic amines, aldehydes, and organic acids (forming peracids). Typical addition compounds formed include organic and inorganic peroxo compounds or epoxides (formed when hydrogen peroxide (or peracids) react with olefinic double bonds). Hydrogen peroxide will not readily react with benzene saturated alkanes, benzene, toluene and ethanol (ECJRC, 2003).

## PERACETIC ACID

Peracetic acid added to water rapidly dissociates but will eventually reach an equilibrium condition. At ambient temperatures, peracetic acid will reach equilibrium in several days (HERA, 2002). Peracetic acid has a pH of less than 1. The rate of decomposition of peracetic acid in the aquatic environment is pH- and temperature-dependent. At acidic pH, decomposition or hydrolysis will occur in about 7-12 days; at neutral or alkaline pH, decomposition may occur in less than one day.

## SODIUM PERCARBONATE

Sodium percarbonate decomposes rapidly in water to form sodium, carbonate and hydrogen peroxide. The hydrogen peroxide component decomposes as described above. Carbonate generation will result in an increase in alkalinity and a tendency to raise the pH of the water. However, the magnitude of any change is dependent upon the buffering capacity of the body of water. A 1% solution of sodium percarbonate has a moderately alkaline pH of about 10.5. A commercial formulation of sodium percarbonate has a purity of about 85%. Up to 15% of the formulation is composed of organic salts. A common industrial use of this chemical is as a bleaching agent in laundry detergents.

Table 1 provides estimates of the amount of sodium carbonate (a component of sodium percarbonate) needed to raise the pH of water from a theoretical pH of 8.3 to pHs of 9, 10 or 11 in solutions of differing buffering capacity (i.e., bicarbonate concentrations). The buffering capacity of a waterbody is generally determined by the natural background concentration of bicarbonate. In general, during summer months, the pH of a lake is between 7.5 and 8.5 for the upper part of a lake or a productive or eutrophic lake. It is typically between 6.5 and 7.5 in the lower part of a lake or in less productive lakes. Lakes that receive large volumes of acid rain typically have a lower pH and lose their buffering capacity (Lake Access, 2009).

The breakdown products of sodium percarbonate, hydrogen peroxide, carbon and sodium, are also present as background constituents in the environment. Hydrogen peroxide is mainly introduced to the aquatic environment through wet and dry deposition, through photochemical or biological formation and through oxidation of metals. Typical environmental concentrations of hydrogen peroxide are less than 10 μg/L although much higher concentrations have been reported (HERA, 2002). Sodium is naturally present in the aquatic environment as a result of weathering of rocks and minerals. In addition, sodium is also introduced to the aquatic ecosystem via anthropogenic sources of sodium, a large contributor of which is road salt. A study of 21 European lakes indicated background sodium percentile concentrations ranging from 1.9 mg/L ($10^{th}$ percentile) to 56 mg/L ($50^{th}$ percentile) to 92 mg/L ($90^{th}$ percentile) (HERA, 2002). While carbonate levels in aquatic ecosystems are low, bicarbonate levels

are readily measurable. The same study of 21 European rivers cited above for sodium found bicarbonate concentrations ranging from 15 ($10^{th}$ percentile) to 128 mg/L ($50^{th}$ percentile) to 233 ($90^{th}$ percentile) (HERA, 2002).

**Table 1. Concentration of Sodium Carbonate (mg/L) That Would Increase a pH of 8.3 in a Theoretical Waterbody to Values of 9.0, 10.0 and 11.0 (De Groot et al., 2002).**

| Buffer capacity[A] | Final pH[B] | | |
|---|---|---|---|
| | 9.0 | 10.0 | 11.0 |
| 0 mg/L $HCO_3^-$ (distilled water) | 1.1 (0.6) | 16 (6.1) | 603 (61) |
| 15 mg/L $HCO_3^-$ ($10^{th}$ percentile of 21 European rivers) | 2.3 (16) | 28 (21) | 725 (76) |
| 128 mg/L $HCO_3^-$ (mean value of 21 European rivers) | 12 (129) | 120 (134) | 1646 (189) |
| 233 mg/L $HCO_3^-$ ($90^{th}$ percentile of 21 European rivers) | 20 (234) | 206 (239) | 2502 (294) |

[A] The initial pH of a bicarbonate solution with a concentration of 15-233 mg/L is 8.3 (calculated) (HERA, 2002)
[B] Between brackets the final concentration of bicarbonate is given.

## MAMMALIAN TOXICITY

### HYDROGEN PEROXIDE

#### Pharmacokinetics

$H_2O_2$ is a normal by-product of cellular metabolism in aerobic cells. It passes readily through biological membranes and diffuses through the cell. From animal studies, it is estimated that about 75% of all $H_2O_2$ produced is in the liver. Of this amount, almost half (i.e, 47%) is attributed to microsomes through normal electron transport reactions and various oxidase reactions. The rest is produced in mitochondria, peroxisomes and soluble enzymes. $H_2O_2$, along with other reactive species, is important in defending the cells against invading organisms. It can destroy malignant or normal cells and also can alter the function of erythrocytes, platelets, neutrophils or lymphocytes.

The main metabolizing enzyme systems in the cell include glutathione peroxidase (GSH) and catalase, which control $H_2O_2$ concentration in different parts of the cell and the blood. In biological systems, $H_2O_2$ may also react with iron and other transition metals resulting in formation of hydroxyl radicals. Superoxide dismutase (SOD) also plays a role in the $H_2O_2$ balance of the cell as it catalyzes the conversion of two superoxides into $H_2O_2$ and oxygen.

#### Acute toxicity

Information from animal studies indicates that exposures to high concentrations of $H_2O_2$ via inhalation, ingestion and dermal exposure lead to higher rates of absorption, which leads to oxygen bubble formation in blood

vessels. In particular, ingestion and inhalation exposure may be harmful. Under some conditions, pulmonary, cerebral and other systemic embolization (i.e., formation of bubbles) may also occur.

Observations in humans include two cases of accidental ingestion of 35% $H_2O_2$, leading to cerebral embolism. One of these cases involved an 84-year old man, who ingested a dose of about 150 mg/kg and experienced severe brain damage. Another case involved accidental ingestion of 3% $H_2O_2$ at a dose of about 600 mg/kg by a 16 month-old child, leading to death. A 54-year-old male patient receiving irrigation of an infected wound with $H_2O_2$ under pressure experienced a sudden loss of consciousness and cardiac shock, and fell into 15-minute coma. Although the patient recovered, the cause was attributed to widespread embolization of oxygen microbubbles, especially to the cerebral and coronary arteries (ATSDR, 2002, ECJRC, 2003).

Subchronic/Chronic (i.e., Repeat Dose Toxicity)

Results of animal studies demonstrate that $H_2O_2$ is both irritating and corrosive to skin and especially to eyes. Respiratory system irritation and skin bleaching were seen in occupational studies.

Repeated dose toxicity studies indicated a decreased body weight gain in animal studies (i.e., at dose levels of 50-500 mg/kg/day in rats) as well as changes in blood chemistry parameters. Reversible hyperplasia was also noted at 1000-3000 ppm. While repeated dose inhalation toxicity is not as well characterized as for ingestion, studies in rats and dogs indicate that thickening, bleaching and hair loss (e.g., effects on skin) airways and lungs may occur at about 10 $mg/m^3$. The occupational literature reports a human case of an interstitial lung disease in a worker exposed to 12 $mg/m^3$ of $H_2O_2$ for most of the workday and transient exposures to 41 $mg/m^3$. In addition, six aseptic packaging workers exposed to high (2-3 $mg/m^3$ 8-hr time-weighted average with peaks to 11 $mg/m^3$) for one year, followed by another year exposure at 0.5-0.7 $mg/m^3$ 8-hr time-weighted average) demonstrated that three of the workers experienced eye and airway irritation, headache and bronchitis-sinusitis. Two of three workers experienced bronchoconstriction and only recovered once they reduced their exposure and were administered inhaled corticosteroids (ATSDR, 2002, ECJRC, 2003).

Mutagenicity

$H_2O_2$ has produced positive results in a variety of *in vitro* test systems. In bacterial tests, most gene mutation assays (in the Ames assay, especially in strains sensitive to reactive oxygen species) and DNA damage/repair assays produced positive results. In mammalian cells, most positive results were produced in gene mutation assays, DNA damage and repair assays, UDS assays, SCE assays and cytogenetic assays for chromosomal aberrations. The results also show that the tests conducted with metabolic activation show a clear reduction in genotoxicity, indicating that the S9 mix contains $H_2O_2$ degrading enzymes. The responses were altered by the presence of catalase, the Fenton reaction and the repair capacity of the cells.

Several *in vivo* tests, conducted using modern methodologies all produced negative results. These included evaluation of DNA repair in liver cells of rats administered $H_2O_2$ intravenously; micronucleus formation in a mouse orally administered $H_2O_2$ in drinking water or after a single intra-peritoneal injection with $H_2O_2$. Solutions of $H_2O_2$ in concentrations of 0.2-3.2% in ethanol were applied to the skin of Sencar mice twice weekly for four weeks to evaluate local mutagenicity in tissue. At these low concentrations and low application frequency, $H_2O_2$ did not induce mutagenicity in tissue.

The European Union (EU) concluded that $H_2O_2$ is not mutagenic. They acknowledge however that additional data would be helpful and that while there is evidence that cells are adapted to repair DNA damages produced by oxidants, there is also evidence that $H_2O_2$ may inhibit repair of DNA lesions produced by other reactive chemicals. However, based on the above information, particularly on the fact that $H_2O_2$ produces DNA damage, the possibility of mutagenicity may not be ruled out (ATSDR, 2002, ECJRC, 2003).

Carcinogenicity

A drinking water study in which catalase-deficient mice were exposed to $H_2O_2$ in drinking water produced duodenal hyperplasia and localized low frequency carcinomas. Other studies indicated a strong negative correlation

between the incidence of duodenal hyperplasia or neoplasia and catalase activity in duodenal mucosa, blood and liver. These results were not seen in comparable rat studies. Squamous cell papillomas of the forestomach were seen in rats consuming drinking water with 1% $H_2O_2$ for 32 weeks. Several studies have demonstrated a promoting effect of $H_2O_2$ in rat intestinal cancer whereas these have not indicated any promoter activity.

Overall, the results suggest that $H_2O_2$ has the potential to induce localized cancer in the duodenum of a sensitive mouse strain. Cessation of treatment may cause a regression or reversal of this effect. Whether $H_2O_2$ is a carcinogen is unclear. Mechanisms of action may include direct action on DNA, interference with DNA repair mechanisms and/or chronic inflammations. Possible promotion-type activity and/or complete carcinogenicity might be indicated based on the results presented above. Since mammalian cells have an endogenous defense system to protect themselves against reactive oxygen species, the damage produced by $H_2O_2$ may have a dose or dose ratio threshold. However, both the EU and IARC have concluded that there is insufficient information to classify $H_2O_2$ as to its carcinogenicity to humans (ATSDR, 2002, ECJRC, 2003).

Developmental/Reproductive Toxicity

The developmental/reproductive database for $H_2O_2$ is inadequate. Two studies conducted in mice and rats exposed to $H_2O_2$ in drinking water did not produce reproductive effects in either males or females. However, these studies had inadequacies due to lack of a control group, too few animals and/or poor reporting. A 90-day carcinogenicity study in catalase-deficient mice did not produce target organ toxicity in testes or ovaries. The only available developmental study which was conducted in rats administered $H_2O_2$ in feed showed fetotoxic effects. However, the study contained some reported uncertainties about exposure/effect mechanisms. Thus, it is not clear whether $H_2O_2$ causes developmental/reproductive effects due to the limited database for these endpoints (ATSDR, 2002, ECJRC, 2003).

## SODIUM PERCARBONATE

Pharmacokinetics

When sodium percarbonate comes into contact with physiological fluids, it dissolves into hydrogen peroxide, carbonate and sodium. The toxicity of hydrogen peroxide is addressed above. Both carbonate and sodium that result from intake of sodium percarbonate are not expected to be systemically available in the human body. Both substances are regulated through normal physiological processes.

With regard to carbonate, normal physiological pH is 7.4, with a range of 7.0 to 7.8. If pH of the blood decreases (i.e., metabolic acidosis) it results in hyperventilation (increased excretion of carbon dioxide) and increased renal absorption of $HCO^{-3}$. If pH of the blood increases (i.e., metabolic alkalosis), it results in hypoventilation (decreased excretion of carbon dioxide) and increased excretion of $HCO^{-3}$. In addition, if sodium percarbonate is ingested, gastric acid, with a pH close to 2, will easily neutralize percarbonate to bicarbonate and/or carbon dioxide.

With regard to sodium, the main regulation of sodium concentrations in the body occurs in the kidney. The amount of sodium that would be contributed through an oral intake of sodium percarbonate would not be expected to cause an increase in physiological sodium level (HERA, 2002).

Acute Toxicity

Sodium percarbonate produces localized acute oral and dermal toxicity, due to its irritant and corrosive properties. Acute oral LD50s are in 1034 mg/kg/day in the rat and 2000 mg/kg/day in the mouse while the acute dermal LD50 is >2000 mg/kg/day in the rabbit. Sodium percarbonate is also highly irritating to the eye. The irritant/corrosive nature of this compound can be attributed to the presence of hydrogen peroxide (HERA, 2002).

Repeat Dose Systemic Toxicity

While there are no repeat dose systemic studies available for sodium percarbonate, the toxicity of hydrogen peroxide has been described above.

**PERACETIC ACID**

Pharmacokinetics

Peracetic acid is not readily absorbed into the circulatory system due to its high water solubility, its low octanol water partition coefficient and the fact that it may form micro-bubbles in capillaries and tissues surrounding exposed tissues. It is readily absorbed through skin damaged by peracetic acid's corrosivity.

The degree to which peracetic acid may be distributed through the body via physiological fluids is limited by its degradation rate. peracetic acid may be degraded non-enzymatically via hydrolysis to hydrogen peroxide and water, via a dismutation reaction in the presence of metal ions to acetic acid and water, or via reaction with reducing agents such as cysteine or glutathione, which convert peracetic acid to acetic acid. In addition, peracetic acid may be degraded enzymatically via catalase or peroxidases. However, the breakdown of peracetic acid is not dependent on the peracetic acid concentration, so the reaction may be saturated. Since hydrogen peroxide is also being removed from the system via degradation, the equilibrium between peracetic acid, hydrogen peroxide and acetic acid will be affected (UCETC, 2001).

Acute Toxicity

Peracetic acid is acutely toxic to skin, eyes and mucous membranes due to its irritating and corrosive properties. Table 2 summarizes some of these effects by percent concentration. An RD50 (i.e., concentration producing a 50% reduction of respiratory rate) for peracetic acid was found at 21.5-24.1 mg/m$^3$ peracetic acid.

**Table 2. Acute Toxicity Characteristics of Peracetic Acid**

| Concentration | Effect |
|---|---|
| 0.034 – 0.35% | non- to slightly irritating to rabbit eyes |
| > 0.2% | corrosive or severely irritating to rabbit eyes |
| < 10% | low oral toxicity |
| > 10% | highly corrosive to rabbit skin after 3 minutes of application |

Repeat Dose Systemic Toxicity

The database for repeat dose toxicity information for peracetic acid suffers from inadequacies in histopathological examination, deficiencies in reporting including uncertainties about the composition, concentration and stability of the test substance and limitations in the number of dose levels tested. However, the types of effects noted were generally a result of the irritant and corrosive properties of peracetic acid. Peracetic acid could become systemically available if the physiological detoxifying enzyme systems are saturated. Under such conditions, it would possible for peracetic acid to reach target organs before it is degraded.

The genotoxicity database for peracetic acid is limited and shows some conflicting results. In general, most bacterial mutagenicity tests were negative; however, peracetic acid is bactericidal so the significance of these results is not clear. Two DNA repair tests in human fetal lung cells were also negative. *In vitro* tests were generally negative except for one positive result which was found at cytotoxic levels. Two mouse micronucleus studies were negative as was an *in vivo/ex vivo* assay of unscheduled DNA synthesis (UDS) in rats exposed orally. Investigators reported positive results in a series of *in vivo* chromosomal aberration tests with single intraperitoneal and dermal administration; however, these studies were questionable due to serious deficiencies in experimental protocol and reporting (UCETC, 2001).

Although there is no specific information on chronic toxicity or on carcinogenicity, an initiation-promotion study on mouse skin indicates possible tumor-promoting activity of peracetic acid.

Information on reproductive toxicity is limited. Based on available data on multiple generation studies, no effects on developmental and reproductive toxicity were reported.

## ECOTOXICOLOGICAL TOXICITY

### AVIAN AND BENEFICIAL INSECT SPECIES

Product labels for various hydrogen peroxide-based products warn that these products are toxic to birds (as well as to bees and other beneficial insects) (Biosafe Systems, 2006, 2008). However, no quantitative acute toxicity information was found in the literature for hydrogen peroxide-based products for these endpoints.

A study in which quail fed commercial bird mash with 750 ppm peracetic acid did not show adverse health effects. However, since the peracetic acid concentration in the mash was not measured and peracetic acid is relatively unstable, the actual peracetic acid concentration is not known so the significance of this study is limited (UCETC, 2001).

### AQUATIC SPECIES

Aquatic organisms have antioxidant enzymes, usually concentrated in organs of the digestive system (e.g., in the liver of fish, in the digestive gland of mollusks, etc.) They have the capacity to process some excess hydrogen peroxide; however, this capacity varies between cells, individuals, and species as well as with age and time of year among species (ECJRC, 2003).

Tables 3,4,5 and 6 list some short-term toxicity test results for aquatic species exposed to hydrogen peroxide, sodium percarbonate and peracetic acid, respectively.

**Table 3. Hydrogen Peroxide Aquatic Toxicity Data**

| Species | Test Type | Duration (hours) | Value (mg/L) | Reference |
|---|---|---|---|---|
| FISH | | | | |
| *Pimephales promelas* | Semi-static LC50 | 96 | 16.4 | Shurtleff,1989a |
| *Leuciscus idus* | Static LC50 | 72 | 35 | Degussa, 1977 |
| *Ictalurus punctatus* | Semi-static LC50 | 96 | 37.4 | Kay et al., 1982 |
| INVERTEBRATES | | | | |
| *Daphnia pulex* | Semi-static E50 | 48 | 2.4 | Shurtleff,1989b |
| *Daphnia magna* | Static EC50 | 24 | 2.3 (2.0-2.6) | Bringmann and Kuhn, 1982 |
| *Gammarus sp.* | Semi-static EC50 | 96 | 4.4 | Kay et al., 1982 |
| *Physa sp.* | Semi-static-EC50 | 96 | 17.7 | Kay et al., 1982 |

(Table adapted from Tables 3.17 and 3.18 in ECJRC, 2003)

In a recent study in which *Daphnia magna* were exposed in a flow-through chamber to technical grade hydrogen peroxide (chemical purity 35.4%) at concentrations of 0.0, 0.32, 0.63, 1.25, 2.5 and 5.0 mg/L, concentrations $\geq$ 0.32 mg/L had a negative effect on *Daphnia* growth (Meinertz et al., 2008).

Most of the acute toxicity data for hydrogen peroxide listed in Table 3 is derived from static or semi-static 24-96 hour exposure studies. Due to its high reactivity, hydrogen peroxide applied to water will dissipate fairly quickly (OPP, 2004). In these static and semi-static exposures, constant concentration exposures are not achieved; rather, highest exposures probably occur in the first few hours of experiments or water introduction. While the

standard toxicity tests presented above are somewhat useful, they do not provide information on the specific time during which the measured effect or lethality may actually occur within that 24-96-hour observation period. It is possible that these effects may actually be occurring very early in the observation period. Duration and intensities of exposure and knowledge of when effects or mortalities occur have import for inferring the potential non-target impacts of hydrogen peroxide based products in aquatic environments. In order to address this issue, a search of the literature was conducted to identify short-term "pulse" acute exposure studies with *Daphnia*. Such data was not found in the published literature. However, limited pulse sampling toxicity studies with *Daphnia* obtained from Environment Canada (unpublished data, 2010) were used to more clearly define the actual exposure period. The Environment Canada tests include static 1-hour and 4-hour *Daphnia* pulse exposure studies with a follow-up observation period up to 48 hours including exposure time. For comparison, a standard 48-hour static exposure study was also conducted. The results of these tests are summarized in Table 4.

**Table 4. Hydrogen Peroxide Studies in *Daphnia magna* from Environment Canada (unpublished data, 2010)**

| Test Type | Exposure Duration (hours) | Value (mg/L) |
|---|---|---|
| Static EC50 24-hr | 1 | high control response |
| Static LC50 48-hr | 1 | 10.7 |
| Static EC50 24-hr | 4 | between 3.00 and 9.60 |
| Static LC50 48-hr | 4 | 5.37 |
| Static EC50 24-hr | 48 | 5.37 |
| Static LC50 48-hr | 48 | 5.37 |

These results indicate similar toxicities/lethalities in the 4-hr pulse and 48-hour studies, indicating that most of the effects of hydrogen peroxide occur quickly. The 1-hr pulse study shows somewhat higher EC50 and LC50 values indicating that with reduced exposure duration the effects occur at slightly higher concentrations and the exposure-response curve is somewhat less steep.

**Table 5. Peracetic Acid Acute Toxicity Data – Invertebrates**

| Species | Duration | Percent | | | Endpoint, result EC50 or LC50 (mg peracetic acid/L) | NOEC | Reference |
|---|---|---|---|---|---|---|---|
| | | peracetic acid | $H_2O_2$ | HOAc | | | |
| **Immobility EC50** | | | | | | | |
| *Daphnia magna* | 48 | 15 | 14 | 28 | 0.50 | 0.15 | Douglas and Pell, 1986 |
| *Daphnia magna* | 48 | 4.5 | 27.5 | NS | 1.1 | 0.45 | Burgess and Forbis, 1983 |
| *Daphnia magna* | 48 | 15.5 | 22 | 15 | 0.69 | 0.16 | Terrell, 1987 |
| *Daphnia magna* | 48 | 5.2 | 20 | NS | 0.73 | 0.56 | Gardner and Bucksath, 1996 |
| *Daphnia magna* | 48 | 18.0 | 0.3 | NS | <1.0 | <1.0 | Lamy et al., 1997 |
| *Daphnia magna* | 48 | 0.35 | 7 | NS | 0.135-0.350 | >0.035 | Licata-Messana, 1995 |
| **Lethality LC50** | | | | | | | |
| *Crangon crangon* | 96 | 12 | 20 | 8 | 15 | 6.7 | Tinsley and Sims, 1987 |
| *Mytilus edulis* embryo | 48 | 12.5 | 19 | 18 | 0.27 | 0.13 | Fairhurst, 1987 |
| *Crassostrea gigas* embryo | 48 | 12.5 | 19 | 18 | 0.28 | 0.13 | Butler, 1987 |

**Table 6. Peracetic Acid Acute Toxicity Data – Fish**

| Species | Duration (hr) | Percent | | | Endpoint, result EC50 or LC50 (mg peracetic acid/L) | NOEC | Reference |
|---|---|---|---|---|---|---|---|
| | | Peracetic acid | $H_2O_2$ | HOAc | | | |
| *Oncorhyncus mykiss*[b] | 96 | **15** | 14 | 28 | 2.0 | 1.5 | Douglas and Pell, 1986 |
| *Oncorhyncus mykiss* | 96 | **15.5** | 22 | 15 | 0.91 | 0.16 | Terrell, 1987 |
| *Oncorhyncus mykiss* | 96 | **4.5** | 27.5 | NS | 1.0 | 0.45 | Cohle and McAllister, 1983 |
| *Oncorhyncus mykiss* | 96 | **5.2** | 20 | NS | 1.6 | 0.82 | Gardner and Bucksath, 1996 |
| *Lepomis macrochirus* | 96 | **4.5** | 27.5 | NS | 1.2 | 0.45 | McAllister and Cohle, 1983 |
| *Lepomis macrochirus* | 96 | **15.5** | 22 | 15 | 3.3 | 2.7 | Terrell, 1987 |
| *Lepomis macrochirus* | 96 | **5.2** | 20 | NS | 1.1 | 0.47 | Gardner and Bucksath, 1996 |
| *Brachydanio rerio* | 96 | **18.0** | 0.3 | NS | 1.0 | < 1.0 | Bazzon *et al*., 1997[a] |
| *Brachydanio rerio* | 96 | **0.35** | 7 | NS | ≈ 0.35 | >0.035 | Licata-Messana, 1995 |
| *Pluoronectes platessa*[c] | 96 | **12** | 20 | 8 | 11 | 6.7 | Tinsley and Sims, 1987 |

[a] Analytical methods following Gouges and Teral, 1997 NS Not Stated (UCETC, 2001)
[b] Previous name*: Salmo gairdneri*
[c] Saltwater species

**Table 7. Percarbonate Acute Toxicity Data: Acute Toxicity Comparison of Sodium Percarbonate, Hydrogen Peroxide and Sodium Carbonate**

| Test substance | Species | EC50 (mg/L) | | | References |
|---|---|---|---|---|---|
| | | SPC [A] | $H_2O_2$ [A] | SC [A] | |
| Sodium percarbonate | Fathead minnow | 50-100 | 16-33 | 34-68 | Shurtleff, 1989a |
| Hydrogen peroxide | Fathead minnow | | 13-21 | | Shurtleff, 1989a |
| Sodium carbonate | Freshwater fish | | | 300-740 | HERA (2002) |
| Sodium percarbonate | Daphnia pulex | 2-12 | 0.7-3.8 | 1.4-8.0 | Shurtleff,1989b |
| Hydrogen peroxide | Daphnia pulex | | 1.0-5.5 | | Shurtleff, 1989b |
| Sodium carbonate | Ceriodaphnia dubia | | | 200-227 | HERA (2002) |

[A] LC50 values are expressed as 95% confidence intervals (HERA, 2002)
SPC = sodium percarbonate, $H_2O_2$ = hydrogen peroxide and SC = sodium carbonate

An interesting perspective on the toxicity data presented above with regards to fish comes from the field of fish farming and hatcheries. Formalin has traditionally been used for the control of fungal and parasitic infections but there has been increasing concern regarding its safety to users and the environment. Several papers from the literature (Arndt and Wagner, 1997; Kiemer and Black, 1997; Rach et al., 2000; Rach et al., 2005; Tort et al, 2002) report on the efficacy and relatively low toxicity of hydrogen peroxide when used at concentrations up to several orders of magnitude higher than those presented in this review to treat parasites in farmed or hatchery fish for very short time periods (i.e., typically one hour or less). It can be drawn from these papers however, that toxicity of hydrogen peroxide appears to be temperature-related. One study (Kiemer and Black, 1997) concludes that hydrogen peroxide at these high concentrations should not be applied to waters at water temperatures higher than about 14 $^{o}$C (i.e., 52 $^{o}$F) due to potentially much-increased toxicity, though the basis for this statement is not clear. The paper recommends that treatment of water with hydrogen peroxide best be conducted in winter for this reason. Given that Massachusetts ponds and lakes typically experience their algae problems in summer when these waterbodies often reach temperatures of 21$^{o}$C (70 $^{o}$F) or more, it appears that application of very high concentrations of hydrogen peroxide-based products during warmer weather would not be prudent, even for very short periods of time. Nevertheless, hydrogen peroxide (as well as formalin) have both been found to increase survival in channel catfish infected with fungi or parasites.

**PLANTS**

Several fumigation studies with hydrogen peroxide in plants (i.e., wheat, Norway spruce and red beech) indicated reversible effects on assimilation and photosynthesis in wheat plants. Effects on trees were more severe and included effects on internal needle and leaf structure. However, there were no EC50s or NOECs determined in these studies (ECJRC, 2003).

A study conducted with hydrogen peroxide and the algae *Chlorella vulgaris* indicated an EC50 of 2.5 mg/L and a NOEC of 0.1 mg/L (UCETC, 2001; HERA, 2002). Another study conducted with sodium percarbonate in *C. vulgaris* yielded an EC50 of 7.7 mg/L and a NOEC of 0.3 mg/L (HERA, 2002).

Given that herbicide products that contain these active ingredients are formulated to treat algae, the effect levels cited above are consistent within the range of application levels for these products.

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# APPENDIX

**PROPERTIES OF HYDROGEN PEROXIDE, SODIUM PERCARBONATE AND PERACETIC ACID**

**Table A-1 Properties of Hydrogen Peroxide**

| Property | Value | Reference |
|---|---|---|
| CAS # | 7722-84-1 | |
| Synonyms Property | Dihydrogen dioxide; hydrogen dioxide; hydroperoxide | ECJRC, 2003; Merck Index, 1996 |
| Molecular formula | $H_2O_2$ | Merck Index, 1996 |
| Molecular weight | 34.01 g/mol | Merck Index, 1996 |
| Physical properties | Colorless liquid | Merck Index, 1996 |
| Melting point | -0.43 | Merck Index, 1996 |
| Boiling point | 152 | Merck Index, 1996 |
| Density | 1.463 | Merck Index, 1996 |
| Vapor pressure | 1.97 mm Hg | SRC, 2009 |
| Photolysis half-life (in $H_2O$) | negligible | ECJRC, 2003 |
| Biodegradation half life | Readily biodegradable (i.e., < 10 days) | ECJRC, 2003 |
| Log $K_{ow}$ | -1.57 | ECJRC, 2003; SRC, 2009 |
| BCF | Negligible (i.e., 1.4 in fish) | ECJRC, 2003 |
| Water solubility | $1 \times 10^6$ | SRC, 2009 |

**Table A- 2. Properties of Sodium Percarbonate**

| Property | Value | Source |
|---|---|---|
| CAS # | 15630-89-4 | |
| Synonyms Property | PCS; solid hydrogen peroxide; sodium carbonate hydrogen peroxide; sodium carbonate peroxyhydrate; | Wikipedia, 2009 |
| Molecular formula | $2Na_2CO_3 \cdot 3H_2O_2$ | HERA, 2002 |
| Molecular weight | 314.06 | HERA, 2002 |
| Physical properties | white, crystalline solid | Wikipedia, 2009 |
| Melting point | NA; decomposes when heated | HERA, 2002 |
| Boiling point | NA | --- |
| Density | 2.14 g/cm$^3$ | HERA, 2002 |
| Vapor pressure | negligible | HERA, 2002 |
| Water solubility | 140 g/L | HERA, 2002 |

**Table A-3. Properties of Peracetic Acid**

| Property | | Value | Source |
|---|---|---|---|
| CAS # | | 79-21-0 | UCETC, 2001 |
| Synonyms | | Acetyl hydroperoxide; ethaneperoxoic acid; peroxyacetic acid | UCETC, 2001 |
| Molecular formula | | $CH_3COOOH$ | UCETC, 2001 |
| Molecular weight | | 76.05 | UCETC, 2001 |
| Physical properties | | Colorless liquid; acrid odor | Wikipedia, 2009 |
| Melting point | (5%) | -26 to -30 $^oC$ | UCETC, 2001 |
| | (15%) | -30 to -50 $^oC$ | UCETC, 2001 |
| | (35%) | -44 $^oC$ | UCETC, 2001 |
| Boiling point | (5%) | 99 to 105 $^oC$ | UCETC, 2001 |
| | (15%) | > 100 $^oC$ | UCETC, 2001 |
| | (35%) | > 105 $^oC$ | UCETC, 2001 |
| Density at 20$^o$ C | (5%) | 1120 kg/m$^3$ | UCETC, 2001 |
| | (15%) | 1150 kg/m$^3$ | UCETC, 2001 |
| | (35%) | 1130 kg/m$^3$ | UCETC, 2001 |
| Vapor pressure at 20$^o$ C | (5%) | 21 to 27 hPa | UCETC, 2001 |
| | (15%) | 25 hPA | UCETC, 2001 |
| | (35%) | 17 hPA | UCETC, 2001 |
| Photolysis half-life (in $H_2O$) | | -- | -- |
| Biodegradation half life | | -- | -- |
| Log $K_{ow}$ at 25$^o$C | | -0.25 (measured); -1.25 (calculated) | UCETC, 2001 |
| BCF | | 1 | HSDB, 2002 |
| Water solubility at 20 $^o$C | | 1000 g/kg | UCETC, 2001 |