Review of Chemical Disinfectants Registered in Maine 2006 – 2007

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Acronyms

ADBAC	**alkyl dimethyl benzyl ammonium chloride**
CFR	**Code of Federal Regulations**
CPO	**Chlorine Produced Oxidants**
DCI	**Data Call In**
DDAC	**didecyl dimethyl ammonium chloride**
EPA	**Environmental Protection Agency**
EPP	**Environmentally Preferable Purchasing**
FQPA	**Food Quality Protection Act**
FR	**Federal Register**
kg	**Kilograms**
L	**Liter**
LC_{50}	**Median lethal concentration; units mg/L or ppm; ug/L or ppb**
LD_{50}	**Median lethal dose; units mg/kg body weight**
LOAEL	**Lowest Observable Adverse Effect Level (mg/kg/day)**
mg	**Milligrams**
MSDS	**Material Safety Data Sheets**
NOAEL	**No Observable Adverse Effect Level (mg/kg/day)**
NSPIRS	**National State Pesticide Information Retrieval System**
OSHA	**Occupational Safety and Health Administration**
ppb	**parts per billion**
ppm	**parts per million**
RED	**Re-registration Eligibility Document**
RPI	**Rennsalaer Polytechnical Institute**
SPIRS	**Silver Platter Pesticide Information Retrieval System**
TRC	**Total Residual Chlorine**

BACKGROUND: Disinfectants and Pesticide Registration

Before we begin the discussion some definitions are necessary. The disinfectants and sanitizers are defined on the EPA Antimicrobials webpage:

> ***"Disinfectants:*** Used on hard, inanimate surfaces and objects to destroy or irreversibly inactivate infectious fungi and bacteria, but not necessarily their spores. Disinfectant products are divided into two major types: hospital and general use. Hospital type disinfectants are the most critical to infection control and are used on medical and dental instruments, floors, walls, bed linens, toilet seats, and other surfaces. General disinfectants are the major source of products used in households, swimming pools, and water purifiers (EPA 2007a)."
>
> ***"Sanitizers***: Used to reduce, but not necessarily eliminate, microorganisms from the inanimate environment to levels considered safe, as determined by public health codes or regulations. Sanitizers include food contact and non-food contact products. Sanitizing rinses for surfaces such as dishes and cooking utensils, as well as equipment and utensils found in dairies, food-processing plants, and eating and drinking establishments comprise the food contact Sanitizers. These products are important because they are used on sites where consumable food products are placed and stored. Non-food contact surface sanitizers include carpet sanitizers, air sanitizers, laundry additives, and in-tank toilet bowl sanitizers (EPA 2007a)."

Disinfectants and sanitizers utilize the same set of compounds with different contact times and end-use dilutions. One hundred and twenty-four of the 292 institutional disinfectants registered in Maine 2006/2007 are also sanitizers (NSPIRS 2007).

Establishing guidelines for Environmentally Preferable Purchasing (EPP) of disinfectants for the State of Maine requires some understanding of pesticide products and the EPA registration process. Pesticide products are comprised of 1 or more "active" ingredients and "inert" or "other" ingredients. By definition, the active ingredients are active on the labeled target pests. The "inert" or "other" ingredients may be fillers, solvents (including water), baiting materials, propellants or wetting agents, emulsifiers or surfactants, etc.

Technical products are concentrated active ingredients which are formulated into end-use products. The end-use products are what are bought and used. The pesticide formulation refers to the chemical (% active ingredients) and the physical nature of the product (liquid, pressurized liquid, emulsifiable or soluble concentrates, impregnated materials, etc.). To further complicate the issue, especially for the disinfectants, a parent product may be sold by a variety of distributers with multiple brand names.

There are 51 active ingredients formulated into 292 parent products (with 1204 brand names) registered in Maine with "Institutional"as the site and "Disinfectants" as the type (SPIRS 2007, NSPIRS 2007). In their review process, EPA grouped these compounds

into chemical class “case” groups. The majority of ME-2006/2007 anti-microbial products contain one or more of the five groups of active ingredients listed in Table 1. The cases for the quaternary ammonium compounds have been combined in Table 1, as have the cases for the substituted phenols. The reason for this is that individual compounds within these two groups are rarely found as solo active ingredients in products. The second, third or fourth, etc., active ingredient may or may not be of the same chemical class. The number of products registered in Maine and co-occurrence of multiple active ingredients is summarized in Appendix A. Re-registration Eligibility Decisions (REDs) may be available for only one component of the product.

Table 1. Active Ingredient Groups

Active Ingredient Chemical Classes	EPA Case #	# Parent Products
Quaternary Ammonium Compounds	3003; 0350	183
Aliphatic alcohols	4003	34
Substituted Phenols	2575; 2045; 3016	25
Peroxides	4072	15
Sodium hypochlorite	0029	14

EPA Review

In their review process, EPA requires a battery of toxicological testing dependent on the use patterns (indoor vs outdoor; food vs non-food). These include acute (short term) and chronic (long term or lifetime) studies. Reproductive and developmental studies are also required. The data from these studies are used in conjunction with exposure studies (or assumptions) to assess risks. In certain instances when EPA requires more data a "data call in" (DCI) will be issued. In other cases where the compounds have a history of use, both as pesticides and as non-pesticide uses EPA will grant a waiver for a data requirement. Both of these EPA judgment calls were made for various disinfectants discussed below.

From the pesticide (disinfectant) perspective there are two important sources of health/risk assessment information, the label and the EPA REDs. EPA has established “cases” for the active ingredients. These may be single active ingredients or groups of similar active ingredients. REDs are then issued for a “case” which may be a single compound or the group of compounds. The third set of easily obtainable documents for health and risk assessment information are the Material Safety Data Sheets (MSDSs) which are generated under Occupational Safety and Health Administration (OSHA) rules. The number of products and brands available preclude an MSDS review at this time. EPA

uses acute hazard indicators (Table 2) to assign signal words (Table 3) to technical active ingredients and end-use products (40CFR156 2006).

EPA routinely publishes RED for pesticide active ingredient "cases" both single and groups of active ingredients. These decisions include EPA peer-reviewed toxicity and environmental fate studies and a variety of exposure scenarios and risk assessments for those scenarios. In 1996, the Food Quality Protection Act (FQPA) was enacted and EPA changed the manner in which risk assessments were done. This is reflected in the types of studies and risk assessment values found in the disinfectant REDs. One of the major changes was the inclusion of the FQPA safety factor of 10X when there is evidence that the developing fetus is more sensitive to exposure than the adult animal.

Some of the disinfectant active ingredients have post FQPA REDs (dated after 1996), most notably the quaternary ammonium disinfectants; didecyl dimethyl ammonium chloride (DDAC; case 3003), EPA 2006c) and the alkyl dimethyl benzyl ammonium chloride (ADBAC; case 0350), EPA 2006d) and o-phenylphenol and its potassium and sodium salts (case 2575, EPA 2006a). Older REDs (pre 1996) have been made available for some of the other active ingredients.

Table 2. EPA Hazard Indicators and Toxicity Categories (40CFR156 2006)

Hazard indicators	Toxicity Categories			
	I	II	III	IV
Oral LD_{50}	≤ 50 mg/kg	50 to 500 mg/kg	500 to 5,000 mg/kg	> 5,000 mg/kg
Dermal LD_{50}	≤ 200 mg/kg	200 to 2,000 mg/kg	2,000 to 20,000 mg/kg	> 20,000 mg/kg
Inhalation LC_{50}	≤ 0.2 mg/L	0.2 to 2 mg/L	2 to 20 mg/L	> 20 mg/L
Eye Effects	Corrosive; corneal opacity not reversible within 7 days	Corneal opacity reversible within 7 days; Irritation persisting for 7 days	No corneal opacity; Irritation reversible within 7 days	No irritation
Skin Effects	Corrosive	Severe irritation at 72 hrs	Moderate irritation at 72 hrs	Mild or slight irritation at 72 hrs

Table 3. Signal Words;and EPA Toxicity Categories (40CFR156 2006)	
DANGER	Toxicity Category I
DANGER Skull & Crossbones	Toxicity Category I based on lethality as opposed to local effects; skin and eye "Poison" with the skull and crossbones
WARNING	Toxicity Category II
CAUTION	Toxicity Category III or IV

Environmental fate characteristics presented here are summarized from the EPA REDs or supporting documents used by EPA in developing the REDs. The sites discussed are those EPA has decided to re-register. In the re-registration process, EPA requires a battery of tests on birds and aquatic organisms based on use patterns and the environmental chemistry of the compound in question. Environmental fate and toxicity tests may not be required for certain groups of active ingredients having the following characteristics:

- Primarily indoor uses
- Short half lives in water, such as peroxide compounds
- Not likely to get into water supplies, such as quaternary ammonium compounds

In addition, EPA issues DCI notices for required studies that have not yet been done. When DCI occurs, it will be so noted. While EPA's current system of providing information is a major improvement over "the good old days" one of the drawbacks is that a DCI issued in 1995 may have been responded to, but the EPA analysis of that study may not be available until a new RED is issued.

The toxicity studies required by EPA registration guidelines include studies in birds, acute LD_{50} in mg/kg body weight (Median Lethal Dose) and chronic 8 day feeding, LC_{50} ppm diet. EPA peer-reviewed studies are presented individually. EPA ranks studies for registration purposes. The data ranks used by EPA are "core", "supplemental" or "invalid". Core studies satisfy data requirements, supplemental studies support the registration and may be updated to fill the data requirement. If the RED indicated that a study satisfied a data requirement, it was assumed to have a "core" ranking. Older REDs usually did not include the data ranking.

Signal words and disinfectants

As discussed earlier, many disinfectants present skin and eye effects as a major toxicological endpoint (Table 4). EPA requires testing for skin and eye effects on end use products as well as the technical active ingredients. In the case of corrosive skin and eye effects, the toxicity category is I and the signal is "danger" A toxicity category I technical compound may be diluted into an end-use product with a "warning" or "caution" label.

On the other hand, technical materials which are not classified as toxicity category I, may be in "danger" products due to the presence of an "inert" ingredient. For example: the three phenol products registered in Maine as institutional disinfectants, trade name: Sporicidin[tm] contain 1.56 % phenol and 0.06% sodium phenate. The signal words for the "towelettes" and "solution ready to use" products are "caution" and the aerosol product has a signal word of "warning" most likely due to the presence of the propellant.

Because of the relationship between concentration and hazard, sets of labels have been summarized in the report. The details of the labels reviews are found in Appendix B, Tables 1, 2, 3, and 4. For ease of comparison, summaries of the acute and chronic mammalian toxicity of the active ingredients are presented in Appendix C. EPA's cancer classification systems are described in Appendix D. At the request of the Bureau of Purchases, an individual product review can be performed.

The environmental fate data and avian and aquatic toxicity testing are discussed in the text. Detailed results from the aquatic toxicity studies submitted to EPA in support of registration for quaternary ammonium compounds and the substituted phenols are presented in Appendix E. Due to the complex nature of the sodium hypochlorite review, that information is presented in the text.

Table 4. Technical Active Ingredient Chemical Groups; Skin and Eye Effects

AI Chemical Classes	Skin	Eyes
Quaternary Ammonium Compounds	corrosive I "danger"	corrosive I "danger"
Aliphatic Alcohols	negative IV "caution"	slight IV to moderate III "caution"
Peroxy Compounds	corrosive I "danger"	severe I "danger"
Substitutes Phenols	slight IV "caution" to severe I "danger"	severe I "danger" to data-call- in
Sodium hypochlorite	corrosive I "danger"	corrosive I "danger"

Toxicity of Caustic Substances

Many of the compounds included in the chemical classes of disinfectants listed in Table 1 are considered caustic depending on the concentration. The toxic effects of caustic agents is dependent on the concentration, volume, acidity (pH), ability to penetrate tissues and duration of contact of the solution, rather than mass per unit body weight (mg/kg). Quaternary ammonium compounds, peroxides (depending on concentration) and sodium

hypochlorite fit this category (Goldfranck *et al.*, 1998). The substituted phenols may also have caustic properties. With caustic agents, toxicity is due to complications following severe tissue damage. These complications may include toxemia, shock, perforation, hemorrhage, infection and obstruction (Gosselin *et al.* 1984*)*. These attributes of caustic agents make interpretation of the classic toxicology tests (oral and dermal LD_{50}s; inhalation LC_{50}) difficult. However, the acute toxicity testing on the end-use product and the resultant signal words will be extremely important. The EPA standard battery of acute toxicity data is found in Appendix C, Table 1.

REVIEW OF CHEMICALS BY GROUP

Information will be provided for each of the chemical groups (Table 1) and the summaries will include:

- Products; formulations and signal words
- Acute and chronic mammalian toxicity
- Environmental fate
- Ecological toxicity studies

Quaternary Ammonium Compound; Products

The chemical class, quaternary ammonium disinfectants includes 63 quaternary ammonium chloride salts. Nineteen of these are currently registered in Maine and 14 are registered in institutional products (NSPIRS). EPA divided these compounds into four groups in 1988. Two of these major groups are the aliphatic alkyl quaternaries, prototype didecyl dimethyl ammonium chloride (DDAC) and the alkyl dimethyl benzyl ammonium chloride (ADBAC) (EPA 1988). EPA completed re-registration decisions for these two major groups of quaternary ammonium disinfectants in 2006.

These active ingredients are made into a variety of formulated products (Table 5). The lower concentrations in these products may result in a lower hazard rating; caution or warning. To add some perspective to these signal words, Table 6 summarizes the signal words for the quaternary ammonium products registered for use in institutional and institutional/ household settings. In addition mitigation of these effects may be accomplished through the use of appropriate protective clothing; goggles, face shields, etc.

The number of soluble concentrate products is the highest, 117, for the quaternary ammonium products (Table 5). Within this subgroup there are four “caution” labeled products, four “warning” labeled products and 99 “danger” labeled products. Six of the seven products submitted in response to the Maine 2007 bid “Q200701497" contain quaternary ammonium chloride as their active ingredients. All six of those products have “danger” as signal words (Maine 2007).

Table 5. Quaternary Ammonium Formulations (NSPIRS 2007 and SPIRS 2007)	
Formulation	**Number of Products**
Soluble Concentrates	117
Ready to use	28
Pressurized liquids (foams and sprays)	24
Impregnated Materials (including disinfectant wipes)	11
Formulation Intermediates (used to make other products)	2
Water Soluble Packets	1
Total	183

Table 6. Label Hazards for Quaternary Ammonium Disinfectants Institutional verses Institutional and Household Uses (NSPIRS 2007 and SPIRS 2007)		
Uses	**Signal Word**	**# Products**
Institutional	danger	115
	warning	22
	caution	46
Institutional and Household	danger	44
	warning	14
	caution	29

Some of the quaternary ammonium products are registered for both disinfection and sanitizing. A label review of selected quaternary ammonium compound pressurized liquids indicates that a major difference between the disinfectants and sanitizers is contact time. The contact times are 20 to 30 seconds for sanitizing and 10 minutes for disinfection (Appendix B, Table 1).

Quaternary Ammonium Compounds; Mammalian Toxicity

Undiluted quaternary ammonium compounds, both didecyl dimethyl ammonium chloride (DDAC) and alkyl dimethyl benzyl ammonium chloride (ADBAC) are not skin sensitizers in the guinea pig and are EPA toxicity category II or III for exposure via the

oral, dermal and inhalation routes. However, both groups exhibit corrosiveness to both eyes and skin EPA toxicity category I (EPA 2006c and 2006d) (see Appendix C Table 1).

With regard to chronic toxicity, both DDAC and ADBAC type active ingredients have similar profiles. The EPA cancer classifications are DDAC "not likely human carcinogen" (EPA 2006c) and ADBAC "negative" (EPA 2006d). The FQPA safety factor has been reduced to 1X for both groups, indicating a lack of sensitivity in the developing fetus compared to adults in teratology and reproductive studies (EPA 2006c and 2006d).

In chronic rat feeding studies the no observable adverse effect level (NOAEL) for DDAC was 10 mg/kg/day, the lowest observable effect level (LOAEL) was 20 mg/kg/day and the effect observed at the LOAEL was a decrease in total cholesterol (EPA 2006c). For the ADBAC group, the NOAEL was 44 mg/kg/day and the LOAEL was 88 mg/kg/day. The effects seen at the LOAEL was a decrease in body weight and a decrease in body weight gain (EPA 2006d) (see Appendix C, Table 2).

One issue that the EPP Committee discussed was that of foaming aerosols verses spray aerosols with regard to hazard. A label review was done on the 24 pressurized liquid formulations containing quaternary ammonium compounds. The details of the label review are found in Appendix B, Table 1. The products, signal words and personal protective equipment (PPE) requirements from the label are summarized in Table 7. The likelihood of bystander exposure will be less for the foam products than the sprays.

Table 7. Summary of Label Hazards for Quaternary Ammonium Disinfectant Pressurized Liquid Formulations (Label Review)

Foam/Spray	Signal Word	# Products	PPE Requirements
Foams	Caution	6	one product with warning label requires: goggles and face shield; safety glasses
	Warning	2	
Sprays	Caution	8	one product with warning label requires: goggles and face shield
	Warning	8	

Quaternary Ammonium Compounds Environmental Fate

DDAC is stabile to hydrolysis in the absence of microbes (buffered pH 5 - 9), with exposure to sunlight, and when exposed to microbes with or without oxygen (EPA 2006c). ADBAC is also stabile to hydrolysis under in the absence of microbes (buffered pH 5 - 9) and with exposure to sunlight. However, ADBAC is degraded in the presence of microbes (EPA 2006d). Both DDAC and ADBAC are immobile in soil and not expected to contaminate surface or ground waters (EPA 2006c, EPA 2006d).

The primary uses of DDAC and ADBAC disinfectants are spray applications to indoor surfaces. These sites include: truck interiors, kennels, institutional areas, household areas, re-circulating cooling towers, evaporative condensers, swimming pools and spas, pulp/paper mills (ADBAC only) and oil field mud treatments.

Quaternary Ammonium Compounds Ecological Toxicity

With regard to ecological toxicity testing, most of the toxicity information reviewed by EPA for the quaternary ammonium compounds concern ADBAC. ADBAC is considered moderately toxic to birds based on an oral LD_{50} of 136 mg/kg/ body weight in the Bobwhite quail. EPA has issued a DCI for a reproductive study in the Bobwhite quail (EPA 2006d).

ADBAC is considered moderate to highly toxic in freshwater fish (LC_{50}s range from 0.5 to 1 mg/L), very highly toxic to freshwater invertebrates with and LC_{50} of 0.02 mg/L in *Daphnia magna* and highly to very highly toxic to marine organisms with acute LC_{50}s ranging from 0.055 to 0.86 mg/L (EPA 2006d, EPA 2006b).

Chronic toxicity studies for ADBAC included a fish early life stage study in the fathead minnow and an invertebrate life cycle in *Daphnia*. The NOEC for the fathead minnow study was 0.032 mg/L, with a LOEC of 0.0759 mg/L, specific effects at the LOEC were not reported. The NOEC in the *Daphnia* study was 0.00415 mg/L. There was no LOEC determined making this study supplemental for support of registration (EPA 2006b). EPA intends to issue a DCI for a chronic study in freshwater invertebrates for ADBAC (EPA 2006d) and there will be a DCI for chronic studies in freshwater fish and invertebrates for DDAC (EPA 2006c).

EPA concluded that for the indoor uses of DDAC or ADBAC, it is unlikely that any appreciable exposure to terrestrial or aquatic organisms would occur. However, industrial facilities releasing large quantities of DDAC or ADBAC for indoor applications are required to have National Pollutant Discharge Elimination System (NPDES) permits prior to discharging effluents into receiving water (EPA 2006c, EPA 2006d).

Aliphatic alcohol; Products

The alcohol group of active ingredients includes ethanol (as in alcoholic beverages; and bio-diesel) and isopropyl alcohol (as in rubbing alcohol). There are 34 institutional disinfectant products containing one of the alcohols as an active ingredient (SPIRS 2007).

Ethanol and isopropanol are highly volatile compounds which are stable in water. The use sites are primarily indoors and EPA does not expect significant exposure organisms in the environment (EPA 1995b). There were no data regarding toxicity in birds for these two alcohols. EPA considers, ethanol and isopropanol as practically non-toxic to freshwater fish and invertebrates as well as saltwater species with LC greater than 250 mg/L (EPA

1995b). Because of their prevalence and common uses they will not be discussed in detail here.

Phenols and Substituted Phenols; Products

Substituted phenol derivatives comprise the next largest class of institutional disinfectants (Table 1). There are 25 parent products containing the substituted phenols; o-phenyl phenol, o-benzyl-p-chlorophenol and, p-tert-amylphenol (and their salts) registered as institutional disinfectants in Maine (SPIRS 2007). Substituted phenols are usually found in combination with each other in multiple 2 or 3 active ingredient products (Appendix A). If there is a non-substituted phenolic active ingredient in one of these products it is likely to be ethanol (4 products) or pine oil (1 product). The exception is a pressurized liquid with six active ingredients; 3 substituted phenols, ethanol and two quaternary ammonium compounds. The formulations and signal words for substituted phenol products are summarized in Table 8 (NSPIRS 2007 and SPIRS 2007).

Table 8. Substituted Phenol Products Formulations and Signal Words (NSPIRS 2007 and SPIRS 2007)

Formulation	Signal Words			Total
	Danger	Warning	Caution	
Soluble Concentrates	17	0	0	17
Pressurized liquids (foams and sprays)	0	3	2	5
Ready to use	0	0	1	1
Emulsifiable Concentrates	0	1	0	1
Impregnated Materials (including disinfectant wipes)	0	0	1	1
Total	17	4	4	25

Substituted Phenols; Mammalian Toxicity

The EPA toxicity classifications for the undiluted substituted phenols are category III or IV for oral, dermal, and inhalation exposure. There are EPA DCIs for dermal and inhalation toxicity for o-phenyl phenol (EPA 2006a) and p-tert-amylphenol (EPA 2005) and their salts. Technical (undiluted) o-benzyl-p-chlorophenol; potassium and sodium salts exhibit slight skin effects, but severe eye effects (EPA 1995a). Technical o-phenyl phenol and p-tert-amylphenol and their salts demonstrate moderate (potassium salt of o-phenyl phenol) or severe/corrosive skin effects (EPA 2006a and EPA 2005).

There are limited positive cancer data in animal studies for o-phenyl phenol (and its salts) as indicated by the "not likely at doses lower than 200 mg/kg/day" ranking assigned by EPA (EPA 2006a). Similarly, o-benzyl-p-chlorophenol received a "C" ranking suggestive animal evidence by EPA (EPA 1995a) There were no cancer data provided for p-tert-amylphenol and the salts (EPA 2005) (Appendix C, Table 2).

With regard to sensitivity in the developing fetus, as of 1996 EPA began using the FQPA Safety Factor of 10X when there is evidence of an increase in sensitivity in the developing fetus to the toxic insult. The RED for o-benzyl-p-chlorophenol and the salts was issued in 1995, prior to FQPA. Review of the developmental studies in that report indicates a slight increase in sensitivity in the fetal response to o-benzyl-p-chlorophenol exposure in the rabbit but not the rat. This effect was reported but was not statistically significant and EPA did not require further studies to confirm the effect. The FQPA Safety Factor was reduced to 1X for o-phenyl phenol (and the salts) (EPA 2006a) and was retained at 10X for p-tert-amylphenol and the salts (EPA 2005) indicating development toxicity concerns.

Substituted Phenols: Environmental Fate

The environmental fate and toxicity of the substituted phenols is summarized below. o-phenylphenol and its potassium and sodium salts are stable in water in the absence of microbes and sunlight. The aquatic half-life in the presence of microbes ranges from 3 hrs and 3 days depending on the type of water system (holding pond to running river). The half-life when aqueous solutions compounds are exposed to sunlight is 14 days. These compounds are unstable in air and immobile in soil.

o-benzyl-p-chlorophenol salts in water, readily degrade to the acid. The acid is stable to hydrolysis in the presence of microbes. Microbial bio-degradation is the major route of degradation. Because of this, o-benzyl-p-chlorophenol is unstable in sludge (EPA 1995a).

p-tert-Amylphenol is volatile with a half life in air of 3 hrs, may bio-accumulate (log K_{ow} = 3.91), has slight mobility in soil (K_{oc} = 3799) and is readily bio-degraded by microbes. The potassium and sodium salts are not expected to bio-accumulate (log K_{ow} = 1.23), may be mobile in soil (estimated K_{oc} comparable to that of p-tert-Amylphenol) and have the same tendency to be degraded by microbes as p-tert-Amylphenol (EPA 2005).

Substituted Phenols; Ecological Toxicity

o-Phenylphenol and its salts are considered by EPA to be slightly to practically non-toxic to birds. The acute LD_{50} is 1,000 mg/kg body weight in Bobwhite quail and the 8-day dietary $LC_{50}$is greater than 5,620 ppm diet for both Bobwhite quail and the Mallard duck (EPA 2006a).

The toxic effects of o-Phenylphenol to aquatic organisms are summarized in Table 4. According to EPAs scale, o-Phenylphenol is moderately toxic to freshwater fish and invertebrates with LC_{50}s between 2.5 and 4.6 mg/L. It is considered moderately toxic to marine organisms with an LC50 of 0.89 mg/L in mysid shrimp. EPA issued a DCI for acute toxicity in marine fish (EPA 2006a).

In the 1995 RED, EPA reported an oral LD_{50} of greater than 2,510 mg/kg body weight in the Bobwhite quail and 8-day LC_{50}s of greater than 5,620 ppm (diet), in both the Bobwhite quail and the Mallard duck, indicating a low level of toxicity in birds.

With regard to freshwater organisms, o-benzyl-p-chlorophenol is considered highly toxic to freshwater fish and invertebrates; (Lc_{50}s between 0.33 and 0.72 mg/L) (EPA 1995a). o-benzyl-p-chlorophenol is consider by EPA to be highly toxic to freshwater fish and invertebrates with LC_{50}s between 0.33 and 0.72 mg/L (EPA 1995a). Toxicity tests for o-benzyl-p-chlorophenol and its salts on marine organisms were waived due to use sites and nature of products (1995b).

Two 1974 invalid acute avian toxicity studies were identified in EPA's database, one in Bobwhite quail and the other in Mallard duck. While unacceptable to support registration, these studies indicated moderate toxicity to birds. EPA issued a DCI for acute bird toxicity studies; the chronic dietary studies were waived because of the indoor uses (EPA 2005).

p-tert-amylphenol is classified as slightly to moderately toxic to freshwater fish by EPA based on two "supplemental" studies (LC_{50}s range from 1.7 to 16 ppm). EPA listed acute studies in freshwater fish and invertebrates for p-tert-amylphenol as data requirements (EPA 2005, EPA 2005 e). Toxicity studies in male carp exposed to p-tert-Amyphenol resulted in endocrine disruption. The 30-day EC_{50} for these effects was 0.063 mg/L. The NOEC for oviduct formation was < 0.036mg/L and the NOEC for vitellogen induction was 0.09 to 0.256 mg/L (EPA 2005).

Similar to the quaternary ammonium compounds, the uses of the substitute phenols are primarily indoors and an NPDES permit are required if significant quantities are being released as the result of an indoor use. EPA concludes that these compounds have a low potential for environmental exposure and has made adjustments in the required toxicity testing for this reason (EPA 2006a, EPA 1995a, EPA 2005).

Peroxy Compounds; hydrogen peroxide and peroxyacetic acid; Products

There are 15 hydrogen-peroxide-containing products registered for institutional use in Maine. This group of products includes 9 products with peroxyacetic acid as the second active ingredient. The other 5 of the 7 products contain hydrogen peroxide as the sole active ingredient. One of the other contains hydrogen peroxide, peroxyacetic acid and octanoic (caprylic acid), and the last product contains hydrogen peroxide and 2 of the

quaternary ammonium compounds. Twelve of these products have "danger" signal words. The other 3 have "caution" signal words and contain hydrogen peroxide below 4% in the sole active ingredient (NSPIRS 2007 and SPIRS 2007). A label review of hydrogen peroxide containing was undertaken. The formulation, signal word and PPE requirements are summarized in Table 9. The details of the label review are found in Appendix B, Table 2.

The "caution" labeled products have no PPE requirements on their labels. The "danger" labeled products require PPE ranging from "safety glasses, goggles, rubber gloves" to "coveralls, over long pants and long sleeve shirt; socks and chemical resistant footwear; goggles; face shield; chemical-resistant gloves, chemical-resistant apron; mask or respirator (Table 9)."

Table 9. Summary Hydrogen Peroxide Containing Product Label Review

Active Ingredients (# Products)	Signal word	Formulations	PPE
4.25 to 7.95 % hydrogen peroxide (2)	Danger	Soluble concentrates	eye, face and gloves
3.95 % hydrogen peroxide (1)	Caution	Soluble concentrate	none
0.5 to 1 % hydrogen peroxide (2)	Caution	Ready to use	none
1.00 to 27.5 % hydrogen peroxide 0.08 to 15 % peroxyacetic acid (8)	Danger	Ready to use or Soluble concentrates	eye, face and gloves
6.9 % hydrogen peroxide 4.4 % peroxyacetic acid 3.3 % octanoic acid (1)	Danger	Soluble concentrate	eye, face and gloves, mask or respirator
6.3 % hydrogen peroxide 6.0 % quats; part 1 of a 2 part system; product must be mixed with activator (1)	Danger	Soluble concentrate	eye, face and gloves

Peroxy Compounds; hydrogen peroxide and peroxyacetic acid; Mammalian Toxicity

To put this in perspective, the over-the-counter product used to cleanse wounds contains 3% hydrogen peroxide and 30% hydrogen peroxide is characterized as a "***Strong oxidizing agent***" and requires rubber gloves and goggles for handling (Merck 1989). Three to 9% hydrogen peroxide is classified as "an irritant" and 27.5 to 70% is classified as "a caustic compound" by Goldfranck *et al*., 1998.

Other than a statement to the effect that peroxides, due to their reactivity are expected to interact with macromolecules the 1993 RED provides no information on chronic toxicity (EPA 1993). In the recent petitions to exempt hydrogen peroxide and peroxyacetic acid from tolerance, EPA has stated that they concur with the registrants that all further data requirements are waived for the following reasons: the "oxygen-oxygen" bond is short lived in mammalian systems and in the environment; the use dilutions are low and are expected to have no residues of concerns on treated commodities and the degradates are oxygen, water and acetic acid (FR 2000 and 2002).

The International Agency for Research on Cancer classifies hydrogen peroxide as a "Group 3", not classifiable as to its carcinogenicity to humans and the American Conference of Industrial Hygienist (ACGIH) has classified hydrogen peroxide as a confirmed animal carcinogen with unknown relevance to humans (HSDB 2007). No carcinogenicity data were identified for peroxyacetic acid and potassium peroxymonosulfate (EPA 2006h and IARC 2007).

Potassium Peroxymonosulfate

There are two potassium peroxymonosulfate and sodium chloride containing products (trade name Virkon and Virkon S) registered in Maine for institutional use. These are included because they are the disinfectants that USDA would recommend in an animal disease outbreak such as foot and mouth disease. The potassium peroxymonosulfate oxidizes the sodium chloride to hypochlorous acid (also known as the hypochlorite ion found as the sodium salt in many household bleaches such as Chlorox^{tm}), the next group of disinfectants. The acute toxic endpoints of concern for potassium peroxymonosulfate are, once again, severe corneal opacity in the eye and corrosive skin effects.

Peroxy Compounds; hydrogen peroxide and peroxyacetic acid, Environmental fate

Peroxy compounds are extremely unstable compounds, to the point that highly concentrated peroxides may explode. Disinfectant products, as well as hydrogen peroxide in the medicine chest, are not nearly that concentrated. Hydrogen peroxide degrades in water to water and oxygen. Peroxyacetic acid decomposes into acetic acid (vinegar) and water and oxygen. Because of this instability in water and the fact that the uses were indoors, EPA waived toxicity tests in freshwater fish tests for hydrogen peroxide and peroxyacetic acid (EPA 1993). To verify that this is still the case, a review of the parent label sites for14 hydrogen peroxide alone or with peroxyacetic acid products currently registered in Maine for institutional uses indicates no change in this use pattern (SPIRS 2007) (Appendix B, Table 2) .

Potassium peroxymonosulfate is used with sodium chloride (table salt) and hypochlorous acid is generated. The product has a strict pH dependency, range of 7.2 to 7.6 (EPA 1993).

The two potassium peroxymonosulfate products, Virkon and Virkon S have label instruction regarding an NPDES permit if effluent releases contain this product.

Peroxy Compounds; hydrogen peroxide and peroxyacetic acid, **Ecological Toxicity**

The results of acute toxicity testing in freshwater fish resulted in 96-hr LC_{50}s of 0.78 mg/L (ppm) in rainbow trout and 1.0 mg/L (ppm) in Bluegill sunfish. Studies in freshwater invertebrates were waived due to indoor uses and there were no data presented for marine organisms in EPA RED (EPA 1993).

Sodium Hypochlorite, Products

The final chemical class of institutional disinfectants discussed here are the sodium hypochlorite bleaches, first registered in 1957. As with other pesticides, the label claims make the product a pesticide. If you had two containers of chemically identical bleaches and one is labeled "whitens and brightens" and the other is labeled other "whitens, brightens and disinfects (or kills bacteria or viruses)" the second is a pesticide and the first is not.

There are 14 sodium hypochlorite products with institutional uses on their master labels. End-use product labels may include some or all of the uses form the master label. The label review of these products identified some obvious "homeowner" labels and some "commercial" labels and some products that are labeled for both sites (Table 10). The soluble concentrates (SC) in Table 10 are the typical "laundry bleaches" with disinfectant uses. Each of those SC products have master labels between 17 and 29 pages in length, containing service bulletins for treating drinking water, bathrooms, poultry plants and seed potatoes. The details of the label review for all 14 hypochlorite products are found in Appendix B, Table 3.

Table 10. Summary of Sodium Hypochlorite Institutional Disinfectants

% Active Ingredients (# products)	**Signal Word**	**Homeowner (# labels) Commercial (# labels)**
SC [(a)] 6.0-6.15 % sodium hypochlorite (5)	Danger	Homeowner (7) Commercial (3)
SC 5.25 % sodium hypochlorite (1)	Warning	Commercial (1)
RTU [(b)] < 0.55 % sodium hypochlorite (3)	Caution	Commercial (3)
RTU 1.1-4 % sodium hypochlorite (5)	Warning	Homeowner (11) Commercial (5)

(a) SC = soluble concentrate
(b) RTU = Ready to use

The Clorox label review exemplifies the complexity of the sodium hypochlorite product registration situation (Table 11). Clorox Clean-up with bleach (EPA# 5813-21) is a ready-to-use 1.84% sodium hypochlorite product with 2 homeowner and 2 commercial labels. In other cases, similar Clorox products; 5.25%, 6.0 % and 6.15% soluble concentrates (SC) are registered by the 2 different Clorox companies "The Clorox Company (EPA company # 5813)" and "The Clorox Professional Products (EPA company # 67619)." The Clorox ready-to-use (RTU) products have "caution"or "warning" signal words on their labels and more protective clothing and warnings than do the higher concentration soluble concentrates Appendix B, Table 4. There is a gap between the current label language on the 6 to 6.15% soluble concentrates with "danger" signal words and the "warning" and "caution" products. The 1992 RED (EPA 1992) and the 1986, *"Guidance for the Re-registration of Pesticide Products Containing Sodium and Calcium Hypochlorite Salts"* (EPA 1986a) addresses several issues specific to the historical use of the sodium hypochlorite for disinfection. If the registrant wants to keep the "danger" signal word, with its associated language, then no further data is required. If the registrant wants to get a "warning" or "caution" label, then product-specific data for eye and skin hazard must be generated. This would explain the different levels of precautions and PPE in the Clorox RTU products in Appendix B, Table 3.

Sodium Hypochlorite Mammalian Toxicity

EPA concluded in the 1986 review that "the existing acute toxicity data (and fish and wildlife data) are sufficient to address acute toxicity risks to humans and has concluded that there is no need for chronic or subchronic data to continue registering sodium and calcium hypochlorite for the registered uses (EPA 1986a)."

Sodium Hypochlorite, Environmental Fate

The chemistry of chlorination of water is extremely complex. The effectiveness of the disinfection depends on the generation of "active oxidants" (RPI 1996). To further complicate the matter, chlorination of freshwater results in a different group of "active oxidants" than saltwater (EPA 1985). Adding chlorine gas (Cl_2) as opposed to sodium hypochlorite (Na^+ClO^-) results in same set of products and the ratio of one product to the other is dependent on the pH of the water (US Army 1986).

Sodium hypochlorite is a unique case. It was first registered as a disinfectant in 1957 (EPA 1986a). The EPA in their most recent REDs cite the 1981 *"Draft Ambient Water Quality Criteria for Chlorine"* as the environmental toxicity database on which they continued registration (EPA 1986a and EPA 1992). The "*Ambient Water Quality Criteria for Chlorine"* was finalized in 1985 (EPA 1985) and the most recent version of the "*National Recommended Water Quality Criteria"* tables (EPA 2006g) contains the same

values. This indicates that chemistry and the toxicity hypochlorite disinfectants and their toxicity to aquatic organisms have not been reviewed by the agency since the mid-1980s. These documents also support the concept that the environmental exposure to sodium hypochlorite is the same as total residue chlorine, in a variety of chemical forms and that these data may be used for risk assessment.

The active oxidants formed with the addition of chlorine to freshwater are the hypochlorite ion (ClO^-) and hypochlorous acid (HClO). If there is ammonia present, then chloramine ($ClNH_2$) and dichloramine (Cl_2NH) are also formed. These four products are considered together as "Total Residual Chlorine" (TRC). Saltwater contains bromine. When chlorine is added to saltwater, in addition to the chlorine and chloramine products above, a series of bromine products are formed. These include the bromite ion (BrO^-), hypobromous acid (HBrO), and brominated amines. These products are referred to as "Chlorine Produced Oxidants" (CPO) (EPA 1985).

Sodium Hypochlorite, Ecological Toxicity

The aquatic toxicity for chlorine and sodium hypochlorite is summarized in Table 11. The EPA Ambient Water Quality Criteria Document for chlorine (EPA 1985) reported on seven aquatic chronic studies, summarized in Table 12.

CONCLUSIONS

Preferences

Preferred product selection would be disinfectants with EPA RED or tolerance actions published after the federal Food Quality Protection Act (FQPA) was adopted in 1996.The exception would be aliphatic alcohols because of their other common household and industrial uses. As post-FQPA reviews of o-benzyl-p-chlorophenol and its salts and sodium hypochlorite become available, these compounds will be revisited.

The substituted phenol containing products would not have preferred status because:

> o-phenylphenol and its salts have been ranked as not likely to cause cancer at doses less than 200 mg/kg/day (Appendix C. Table 2)
> o-benzyl-p-phenol and its salts have been ranked as a "C" possible human carcinogen (Appendix C. Table 2)
> 4-tert-Amylphenol containing products would not be preferred due to endocrine disruption in fish.(Appendix E.)

Disinfectants are available in both concentrated and ready-to-use formulations. The sub-committee recognized the issue of increased transportation cost and the greater amounts of plastic involved when comparing the concentrates with the ready-to-use products. The tradeoff is with the less concentrated disinfectant products the signal word is likely to be

"CAUTION" or "WARNING" rather than DANGER" corrosive to skin and/or eyes for concentrates. In addition, "DANGER"corrosive to skin and/or eyes products will most likely have more PPE requirements than the "CAUTION" or "WARNING" products.

Because of this the subcommittee recommends that dilute products with "CAUTION" or "WARNING" labels will get preference over products with "DANGER" labels. Products with no personal protection equipment (PPE) requirements will be preferred over products requiring PPE. In situations where an aerosol application makes sense, preference would be foams or pump sprays over pressurized liquid sprays.

Due to the fact that the delivery system currently in use by BGS, tends to reduce exposure of the custodial staff to the non-disinfectant products, this system or a similar system should be retained. However, the only disinfectant that is sold by the current vendor for use in that system is a quaternary ammonium product, (EPA # 8155-22) with a "DANGER" label that requires "Goggles or face shield and gloves when handling, (which includes mixing, loading and application)".

Recommendations

This EPP disinfectant subcommittee recommends that when the next bid goes out that, the state consider less concentrated disinfectants which do not require the Gulf South dispenser. If a more preferable product is identified and is practical it will be considered. If not, then use of the current disinfectant (EPA # 8155-22) will be continued and the required PPE, "goggles or face shield and gloves" for mixing, loading and application will be provided to the custodial staff and a training program on proper PPE use and care and the importance of wearing it will be instituted.

Because of the number of products registered for institutional use in Maine, a label review of products submitted for bid will be required to determine, Maine registration status, the signal word and the PPE requirements. At the request of either the Bureau of Purchasing, Department of Environmental Protection (DEP) or the Bureau of General Services (BGS) alternative products, not identified by the bidding process, will also be reviewed.

Table 11. Sodium Hypochlorite/Chlorine; Acute Aquatic Toxicity Studies			
Freshwater Fish			
Compound	**Species**	**96 hr LC50 mg/L (ppm)**	**Reference**
Sodium hypochlorite	Rainbow trout	0.18 to 0.22	EPA 1986b
Sodium hypochlorite	Bluegill sunfish	0.44 to 0.75	EPA 1986b
TRC	Fish [(h)]	0.039 to 0.71	EPA 1985
Freshwater Invertebrates			
Sodium hypochlorite	*Daphnia magna*	0.033 to 0.048	EPA 1986b
TRC	Invertebrates [(f)]	0.017 to 0.96	EPA 1985
Marine Organisms; No Data in EPA RED (1986b)			
CPO	Fish [(f)]	0.032 to 0.27	EPA 1985
CPO	Invertebrates [(g)]	0.026 to 1.418	EPA 1985

Table 12. Chronic Aquatic Toxicology NOECs for Chlorine [mg/kg (ppm)] (EPA 1985)		
Exposure	**Type of study**	**NOEC**
TRC	Freshwater aquatic invertebrates; life cycle study sewage; two species in two studies	0.002 to 0.012
	Freshwater fish; life cycle study; one specie in 2 studies	0.006 to 0.016
CPO	Saltwater fish; early life stage	0.04

References Cited	
1981	EPA 1981 Draft Ambient Water Quality Criteria for Chlorine
1984	Gosselin, R. E., Smith, R. P. and Hodge, H. C. (1984) *Clinical Toxicology of Commercial Products*; fifth edition. Williams & Wilkins, Baltimore, MD
1985	EPA 1985 Ambient Water Quality Criteria for Chlorine
1986a	EPA 1986a Guidance for the Re-registration of Pesticide Products containing Sodium and Calcium Hypochlorite Salts as their Active Ingredients
1986b	EPA 1986b Chemical fact sheet for Sodium and Calcium Hypochlorite
1986	US Army 1986 *"US Army's Technical Manual fro Swimming Pool Operation and Maintenance*" available at: http://www.usace.army.mil/publications/armytm/tm5-662/chap6.pdf
1988	EPA 1988 PR Notice 88-2 Clustering of Quaternary Ammonium Compounds
1989	The Merck Index; 11th edition Merck and Co. Rahway NJ 1989
1992	EPA 1992 Reregistration Eligibility Document for Sodium and Calcium Hypochlorite Salts
1993	EPA 1993 Reregistration Eligibility Decision for Peroxy Compounds List D Case 4072
1995a	EPA 1995a Reregistration Eligibility Decision for ortho-benzyl-para-chlorophenol (List B Case 2045
1995b	EPA 1995b Reregistration Eligibility Decision (RED) Aliphatic Alcohols
1996	RPI 1996 *Chlorination Chemistry* Rennsalaer Polytechnical Institute (RPI) available at: http://www.rpi.edu/dept/chem-eng/Biotech-Environ/DISINFECT/clchem.htm
1998	Goldfranck, L. R., Flomenberg, N.E., Lewin, N.A., Wesiman, R.S., Howland, M.A., and Hoffman, R. S. (1998) *Goldfranck's Toxicological Emergencies*; sixth edition. McGrw-Hill, New York, NY
2000	Federal Register Volume 65 Number 232, page 75168 - 75173; Peroxyacetic acid; Exemption form the requirement of a Tolerance
2002	Federal Register Volume 67 Number 40, page 9214-9218; Hydrogen peroxide; Exemption form the requirement of a Tolerance

References Cited	
2005	EPA 2005 Reregistration Eligibility Decision (RED) for 4-t-Amylphenol
2006a	EPA 2006a Reregistration Eligibility Decision for 2-phenylphenol and salts (Orthophenylphenol or OPP)
2006b	EPA 2006b Ecological Risk Assessment in Support of the Antimicrobials Division's Reregistration of ADBAC and DDAC
2006c	EPA 2006c Reregistration Eligibility Decision Aliphatic Alkyl Quaternaries (DDAC)
2006d	EPA 2006d Reregistration Eligibility Decision Alkyl Dimethyl Benzyl Ammonium Chloride
2006e	EPA 2006e Chemicals Evaluated for Carcinogenic Potential, Health Effects Division of Office of Pesticides Programs
2006f	EPA 2006f Ecological Hazard and Environmental Risk Assessment for 4-tert-Amylphenol and its salts
2006g	EPA 2006g National Recommended Water Quality Criteria available at: http://www.epa.gov/waterscience/criteria/nrwqc-2006.pdf
2006h	EPA 2006h 2006 Edition of Drinking Water Standards and Health Advisories
2006	40CFR156 2006
2007a	EPA 2007a Antimicrobials webpage @ http://www.epa.gov/oppad001/ad_info.htm
2007b	EPA 2007b Pesticide Reregistration Status webpage @ http://www.epa.gov/pesticides/reregistration/status.htm
2007	HSDB 2007 Hazardous Substances Data Base; National Library of Medicine http://toxnet.nlm.nih.gov/cgi-bin/sis/htmlgen?HSDB
2007	IARC 2007 International Agency of Research for Cancer; http://www.iarc.fr/
2007	Maine 2007 Maine Bureau of Purchases; Bid Q200701497
2007	NSPIRS 2007 National State Pesticide Information Retrieval System (2007) Perdue University
2007	SPIRS 2007 Silverplatter Pesticide Information Retrieval System (2007)

Appendix A.
Universe of Active Ingredients found in Institutional Disinfectants Registered in Maine 2006-2007

Appendix A. EPA " Cases" and Combination Products, Sorted by Case and Active Ingredient			
EPACase; Case #; Re-registration Eligibility Decision (RED) Active Ingredient	**CAS #**	**# Products**	**With (# products)**
Aliphatic Alcohols (Case 4003; RED EPA 1995c)			
Ethyl alcohol	64-17-5	21	phenol, substituted [(a)] (10) quats [(b)] (10) phenol, substituted and quats (1)
Isopropanol	67-63-0	13	sole (2) quats (11)
Aliphatic Alkyl Quaternaries (DDAC) (Case 3003; RED 2006c); **Alkyl Dimethyl Benzyl Ammonium Chloride (ADBAC) (Case 0350; RED EPA 2006d) (Quats)**	various	182	See Quat discussion
Bronopol (Case 2770; RED EPA 1995b)	52-51-7	1	sole (1)
Chlorine dioxide and sodium chlorite (Case 4023; RED EPA 2006e)			
Chlorine dioxide	10049-4-4	5	sole (4) quats (2)
Chlorine dioxide generator; Sodium chlorite	7758-19-2	2	sole (2)
Chloroxylenol (Case 3045; RED EPA 1994)	88-4-0	1	sole (1)
Citric acid (Case 4024; RED EPA 1992)	77-92-9	3	sole (1) hydrochloric and phosphoric acids (1) silver (1)

Appendix A. EPA " Cases" and Combination Products, Sorted by Case and Active Ingredient			
EPACase; Case #; Re-registration Eligibility Decision (RED) Active Ingredient	**CAS #**	**# Products**	**With (# products)**
Hypochlorous acid	7790-92-3	1	sodium hypochlorite (1)
Iodine (Case 3080)			
Iodine	7753-56-2	1	sole (1)
Nonylphenoxypolyethoxyethanol, Iodine Complex	11096-42-7 35860-86-7	1	sole (1)
L-Lactic acid	79-33-4	1	sole (1)
Mineral acids (Case 4064; RED EPA 1993a)			
Hydrogen chloride (=hydrochloric acid, anhydrous)	7647-1-0	1	citric and phosphoric acids (1)
Phosphoric acid	1314-56-3 7664-38-2	2	hydrochloric and citric acids (1) quats (1)
Octanoic acid; caprylic acid	124-7-2	3	sole (2) hydrogen peroxide and peroxyacetic acid (1)
Peroxy Compounds (Case 4072; RED EPA 1993b)			
Hydrogen peroxide	7722-84-1	14	sole (4) peroxyacetic acid (9) peroxyacetic and octanoic acids (1)
Peroxyacetic acid	79-21-0	9	hydrogen peroxide (8)

Appendix A. EPA " Cases" and Combination Products, Sorted by Case and Active Ingredient			
EPACase; Case #; Re-registration Eligibility Decision (RED) Active Ingredient	**CAS #**	**# Products**	**With (# products)**
			hydrogen peroxide and octanoic acid (1)
Potassium peroxymonosulfate	10058-23-8	2	sodium chloride (2)
Phenols and Phenols, Phenols (Multiple cases); **Phenol (Case 4074; no RED)**; **o-benzyl-p-chlorophenols (Case 2045; RED EPA 1995a)**; **o-phenylphenol (Case 2575; RED EPA 2006a)**; **p-tert-amylphenol (Case 3016; RED EPA 2005b)**	various	28	See phenol and phenol, substituted Discussion
PHMBs (Case 3122; RED EPA 2004)	32289-58-0	1	silver (1)
Pine oil (Case 3113; RED EPA 2006f)	8002-9-3	9	sole (1) quats (7) phenol, substituted (1)
Propylene glycol (Case 3126; RED EPA 2006g)	57-55-6	1	isopropanol (1)
Silver (Case 4082)	7440-22-4	2	PHMBs (1) citric acid (1)
Sodium chloride (Case 4051)	7647-14-5	2	Potassium peroxymonosulfate (2)
Sodium hypochlorite (Case 0029; EPA Fact Sheet 1986)	7681-52-9	14	sole (1)
s-Triazinetrione and Dichloroisocyanurate (Case 0569)			
Sodium dichloro-s-triazinetrione	2893-78-9	1	sole (2)

Appendix A. EPA " Cases" and Combination Products, Sorted by Case and Active Ingredient			
EPACase; Case #; Re-registration Eligibility Decision (RED) Active Ingredient	**CAS #**	**# Products**	**With (# products)**
Sodium dichloroisocyanurate dihydrate	51580-86-0	2	sole (1)
Trichloro-s-triazinetrione	87-90-1	1	sole (1)
Trichloro melamine (Case 3144; RED EPA 2005c)	7673-9-8	2	sole (3)
Triethylene glycol (Case 3146; RED EPA 2005d)	112-27-6	2	sole (1) isopropanol and quats (1)

(a) Phenol, substituted = o-benzyl-p-chlorophenol and its potassium and sodium salts, o-phenylphenol and its potassium and sodium salts, p-tert-amylphenol and its potassium and sodium salts
Quats = Quaternary ammonium compounds

Appendix B.
Review of Labels for Selected Disinfectants

NOTE: Labels and Material Safety Data Sheets (MSDS) reviewed are identified by their EPA Numbers and are not presented in the reference list; The labels and MSDSs reviewed here are the most current master labels from the EPA's Pesticide Product Label System (PPLS) or specific product labels or MSDSs from the BPC's label files.

Appendix B. Table 1. Label Review of Quaternary Ammonium Containing Pressurized Liquids			
EPA #	**Signal word; PPE**	**Foam or Spray**	**Label claims**
498-62	Caution	Foam	Disinfects in 10 min; cleans and deodorize; removes mold and mildew; HIV directions
498-88	Caution	Foam	Disinfects in 10 min; cleans and deodorizes; removes mold and mildew; HIV directions
498-179	Caution	Spray	Disinfects in 10 min; Sanitizes in 20 sec; space deodorizes and air freshener; removes mold and mildew; HIV directions
498-197	Warning; goggles; face shield	Spray	Disinfects in 10 min; Sanitizes in 20 sec; space deodorizes and air freshener; HIV directions
777-72	Warning	Spray	Disinfects in 10 min; Sanitizes in 30 sec; deodorizes; “kills or reduces odor causing bacteria on soft surfaces”; “eliminates odor” leave on for 15 min; controls mold and mildew; HIV directions
777-99	Caution	Spray	Disinfects in 10 min; Sanitizes in 30 sec; deodorizes; controls mold and mildew; HIV and Hanta virus directions
1769-283	Caution	Foam	Disinfects in 10 min; Sanitizes in 5 min; cleans and deodorizes; soft surfaces; cleans; HIV directions
1839-84	Warning	Spray	Disinfects in 10 min; cleans and deodorizes; controls mold and mildew; cleans and disinfects small air conditioner coils; HIV directions
1839-85	Caution	Spray	Disinfects in 10 min; deodorant; air freshener and deodorizes; controls mold and mildew
5741-14	Caution	Foam	Disinfects in 10 min; cleans and deodorizes; can be used to preclean; controls mold and mildew; disinfects moderate amounts of organic soil; HIV directions
			Disinfects in 10 min; Sanitizes in 60 sec; cleans; disinfects 5% organic matter; controls

Appendix B. Table 1. Label Review of Quaternary Ammonium Containing Pressurized Liquids			
EPA #	**Signal word; PPE**	**Foam or Spray**	**Label claims**
7176-6	Caution	Foam	mold and mildew; HIV directions
10807-21	Warning; goggles face shield safety glasses	Foam	Disinfects in 10 min; cleans and deodorizes; HIV directions
10900-56	Warning	Spray	Disinfects in 10 min; deodorizes; controls mold and mildew; HIV directions
10900-57	Caution	Foam	Disinfects in 10 min; cleans and deodorizes; controls mold and mildew; HIV directions
11525-30	Caution	Spray	Disinfects in 10 min; Sanitizes in 50 sec; cleans and deodorizes; controls mold and mildew; HIV directions
11623-24	Caution	Spray	Disinfects in 10 min; deodorizes; controls mold and mildew; HIV directions
11694-34	Warning	Foam	Disinfects in 10 min; cleans and deodorizes; controls mold and mildew; HIV directions
33176-24	Caution	Spray	Disinfects in 10 min; deodorizes; controls mold and mildew; cools, lubricates, prevents rust on clippers
42964-17	Warning	Spray	Disinfects in 10 min; controls mold and mildew; HIV directions
44446-20	Caution	Spray	Disinfects in 10 min; deodorizes and air freshener; automatic dispenser; controls mold and mildew; HIV directions
67603-4	Warning	Spray	Disinfects in 10 min; deodorizes; controls mold and mildew; HIV directions
67619-3	Warning	Spray	Disinfects in 10 min; Sanitizes in 30 sec; deodorizes; controls mold and mildew; HIV

Appendix B. Table 1. Label Review of Quaternary Ammonium Containing Pressurized Liquids			
EPA #	**Signal word; PPE**	**Foam or Spray**	**Label claims**
			directions
70799-9	Warning	Spray	Disinfects in 10 min; cleans and deodorizes; HIV directions
71245-2	Caution	Spray	Disinfects in 10 min; deodorize

Appendix B. Table 2. Hydrogen Peroxide Containing Product Label Review				
EPA #	**Active Ingredients**	**Signal word**	**Formulation**	**Personal Protective Equipment**
69268-1	7.95 % hydrogen peroxide	Danger	Soluble concentrate	safety glasses, goggles, rubber gloves
69268-2	3.95 % hydrogen peroxide	Caution	Soluble concentrate	none; label states “after product is diluted in accordance with directions for use, safety glasses, or other eye protection are not required”
69268-3	1 % hydrogen peroxide	Caution	Ready to use	none
70627-56	0.5 % hydrogen peroxide	Caution	Ready to use	none
70627-54	4.25 % hydrogen peroxide	Danger	Soluble concentrate	goggles; face shield; rubber gloves protective clothing
1043-119	1.00 % hydrogen peroxide 0.08 % peroxyacetic acid	Danger	Ready to use	goggles; face shield; rubber gloves
1677-129	27.5 % hydrogen peroxide 5.8 % peroxyacetic acid	Danger	Soluble concentrate	coveralls, over long pants and long sleeve shirt; socks and chemical resistant footwear; goggles; face shield; chemical resistant gloves, chemical resistant apron; mask or respirator
63838-1	26.5 % hydrogen peroxide 5.6 % peroxyacetic acid	Danger	Soluble concentrate	goggles; face shield; rubber gloves, mask or respirator
65402-1	21.7 % hydrogen peroxide 5.1 % peroxyacetic acid	Danger	Soluble concentrate	goggles; face shield; chemical resistant gloves, chemical resistant apron
54288-4	22 % hydrogen peroxide 15 % peroxyacetic acid	Danger	Ready to use	goggles; face shield; rubber gloves, mask or respirator

Appendix B. Table 2. Hydrogen Peroxide Containing Product Label Review				
EPA #	**Active Ingredients**	**Signal word**	**Formulation**	**Personal Protective Equipment**
65402-3	10 % hydrogen peroxide 15 % peroxyacetic acid	Danger	Ready to use	goggles; face shield; rubber gloves, mask or respirator
70627-53	13.4 % hydrogen peroxide 5.2 % peroxyacetic acid	Danger	Soluble concentrate	splash proof goggles; face shield; rubber gloves, mask or respirator
1043-120	22 % hydrogen peroxide 4.5 % peroxyacetic acid	Danger	Soluble concentrate	goggles; face shield; rubber gloves
1677-158	6.9 % hydrogen peroxide 4.4 % peroxyacetic acid 3.3 % octanoic acid	Danger	Soluble concentrate	goggles; face shield; rubber gloves, mask or respirator
63761-8	6.3 % hydrogen peroxide 6.0 % quats; part 1 of a 2 part system; product must be mixed with activator	Danger	Soluble concentrate	goggles; face shield; rubber gloves protective clothing

Appendix B. Table 3. Summary of Sodium Hypochlorite Disinfectants					
Product Name	**EPA#**	**% Active Ingredients**	**Signal Word**	**Commercial labels Homeowner labels (# labels) Formulation**	**Comments and PPE**
Ultra Clorox Regular Bleach	5813-50	6.0 % sodium hypochlorite	Danger	Homeowner (3) SC [(a)]	Label 28 pages with service bulletins
Tackle; Clorox Clean-up with Bleach	5813-21	1.84 % sodium hypochlorite	Warning	Homeowner (2) RTU [(b)] Commercial (2) RTU	Not recommended for use by persons with heart conditions or chronic respiratory problems such as asthma, emphysema or obstructive lung disease
Ultra Clorox Fresh Scent	5813-51	6.0 % sodium hypochlorite	Danger	Homeowner (4) SC	Each label has a different scent
CPPC Bleach	67619-1	5.25 % sodium hypochlorite	Warning	Commercial (1) SC	Label 25 pages with service bulletins
CPPC Ultra Bleach	67619-8	6.15 % sodium hypochlorite	Danger	Commercial (1) SC	Label 29 pages with service bulletins
CPPC Tsunami	67619-12	0.55 % sodium hypochlorite	Caution	Commercial (1) RTU	Protective eye wear; gloves if skin is sensitive
CPPC Storm	67619-13	2.4 % sodium hypochlorite	Warning	Commercial (1) RTU	Protective eye wear; Not recommended for use by persons with heart conditions or chronic respiratory problems such as asthma, emphysema or obstructive lung disease

Appendix B. Table 3. Summary of Sodium Hypochlorite Disinfectants					
Product Name	**EPA#**	**% Active Ingredients**	**Signal Word**	**Commercial labels Homeowner labels (# labels) Formulation**	**Comments and PPE**
Lime	67619-14	0.0095 % sodium hypochlorite	Caution	Commercial (1) RTU	
Lysol Brand Disinfectant	777-83	2 % sodium hypochlorite	Warning	Homeowner (6) RTU	Not recommended for use by persons with heart conditions or chronic respiratory problems such as asthma, emphysema or obstructive lung disease
Sysco Reliance Ultra Disinfectant Bleach	29055-3	6.0 % sodium hypochlorite	Danger	Commercial (1) SC	Safety glasses and rubber gloves; vacate poorly ventilated areas; 17 page label
X-14 Mildew Stain	71903-1	4.0 % sodium hypochlorite	Warning	Homeowner and Commercial (1) RTU	For prolonged contact or sensitive skin gloves; vacate poorly ventilated areas Not recommended for use by persons with heart conditions or chronic respiratory problems such as asthma, emphysema or obstructive lung disease
Oculus Microcyn Sanitizer	81206-1	0.00357 % sodium hypochlorite 0.00252% hypochlorous	Caution	Homeowner and Commercial (1) RTU	Primarily a sanitizer

Appendix B. Table 3. Summary of Sodium Hypochlorite Disinfectants					
Product Name	**EPA#**	**% Active Ingredients**	**Signal Word**	**Commercial labels Homeowner labels (# labels) Formulation**	**Comments and PPE**
		acid			
Pure Bright	70271-13	6.0 % sodium hypochlorite	Danger	Commercial (1) SC	Safety glasses and rubber glove; vacate poorly ventilated areas; 25 page label
Soft Scrub with Bleach	64240-44-57125	1.1 % sodium hypochlorite	Warning	Homeowner (2) and Commercial (1) RTU	Sites listed are: hospitals, daycares, hotels, and health clubs; For sensitive or prolonged use wear gloves

SC = Soluble Concentrate
RTU = Ready to use

Appendix B. Table 4. Summary of Clorox Institutional Sodium Hypochlorite (AI) Disinfectants			
Product Name; EPA #	**Form; % AI**	**Signal Word; PPE and comments**	**MSDS Review [a]**
Lime; EPA# 67619-14	RTU [b] 0.0095 %	Caution	< 0.01% Hydrochloric acid
CPPC Tsunami; EPA# 67619-12	RTU 0.55 %	Caution; Protective eye wear; gloves if skin is sensitive	0.01 to 0.1 % Sodium hydroxide
Tackle; EPA# 5813-21	RTU 1.84 %	Warning; Not recommended for use by persons with heart conditions or chronic respiratory problems	0.01 to 0.1 % Sodium hydroxide
CPPC Storm; EPA# 67619-13	RTU 2.4 %	Warning; Protective eye wear; Not recommended for use by persons with heart conditions or chronic respiratory problems	0.01 to 0.1 % Sodium hydroxide
CPPC Bleach; EPA# 67619-1	SC [c] 5.25 %	Warning	None listed
Ultra Clorox Fresh Scent EPA# 5813-51	SC 6.0 %	Danger; Corrosive May cause severe irritation or damage to eyes and skin. Protect eyes when handling. For prolonged use wear gloves. Wash after contact with product. Avoid breathing vapors and use only in a well ventilated area.	< 1 % Sodium hydroxide
Ultra Clorox Regular Bleach; EPA# 5813-50	SC 6.0 %	Danger; Corrosive May cause severe irritation or damage to eyes and skin. Protect eyes when handling. For prolonged use wear gloves. Wash after contact with product. Avoid breathing vapors and use only in a well ventilated area.	< 1 % Sodium hydroxide

Appendix B. Table 4. Summary of Clorox Institutional Sodium Hypochlorite (AI) Disinfectants			
Product Name; EPA #	**Form; % AI**	**Signal Word; PPE and comments**	**MSDS Review [(a)]**
CPPC Ultra Bleach EPA# 67619-8	SC 6.15 %	Danger; Corrosive May cause severe irritation or damage to eyes and skin. Protect eyes when handling. For prolonged use wear gloves. Wash after contact with product. Avoid breathing vapors and use only in a well ventilated area.	< 1 % Sodium hydroxide

MSDS review = other OSHA hazardous compounds in the formulation
SC = soluble concentrate
RTU = Ready to use

Appendix C.
Mammalian Toxicity Studies for Disinfectants by Group

Appendix C. Table 1. Acute Mammalian Toxicological Summaries						
Active Ingredient	**LD_{50} [a]**		**LC_{50} [b]**	**Irritant effects [c]**		**sensitizer**
	oral	**skin**	**Inh**	**skin**	**eye**	
Quaternary Ammonium Compounds						
DDAC	238	2, 900	0.07	corrosive I	corrosive I	negative
ADBAC	304.5	930	II	corrosive I	corrosive I	negative
Aliphatic Alcohols						
Ethyl alcohol	7, 060		39	negative IV	mild IV	not expected
Isopropanol	4, 384	16.37	68.5	negative IV	slight- moderate III - IV	ND
Substituted Phenols						
o-Phenylphenol and its potassium salt	2, 733	DCI [d]	DCI [d]	severe I	DCI	negative
o-Phenylphenol, sodium salt	591	DCI [d]	DCI [d]	moderate to severe II	DCI	negative
o-benzyl-p-chlorphenol, salts	4, 147	> 2, 000	2.50	slight IV	severe I	waived
p-tert-Amylphenol, salts	>2, 000	DCI	DCI	corrosive I	?	DCI
Peroxides						

Appendix C. Table 1. Acute Mammalian Toxicological Summaries						
Active Ingredient	**LD_{50} [a]**		**LC_{50} [b]**	**Irritant effects [c]**		**sensitizer**
	oral	**skin**	**Inh**	**skin**	**eye**	
Hydrogen peroxide	2, 000	4, 060	227	corrosive	severe	ND
Peroxyacetic acid	1, 540	1, 410	0.45	corrosive	severe	ND
Potassium peroxymonosulfate	1, 129	> 2, 000	> 5, 000	corrosive	severe corneal opacity	negative
Hypochlorite, sodium						
Sodium hypochlorite [e]	192	> 3, 000		corrosive	corrosive I	ND

(a) LD_{50} = lethal oral or dermal dose killing 50% of the population; units mg/kg body weight
LC_{50} = lethal inhalation concentration killing 50% of the population; units mg/L
Roman numerals refer to EPA's toxicity categories; text Table 1.
For o-Phenylphenol and its sodium salt, the 21 day dermal NOAEL was 100 mg/kg/day; LOAEL of 500 mg/kg/day, this NOAEL was used to evaluate inhalation risks
Toxicity data for sodium hypochlorite is from the 1986 EPA fact sheet

Appendix C. Table 2. Chronic Mammalian Toxicological Summaries			
Active Ingredient	**Cancer [a]**	**FQPA SF [b]**	**NOEL [c]**
Quaternary Ammonium Compounds			
DDAC	not likely	1	10
ADBAC	negative	1	44
Aliphatic Alcohols			
Ethyl alcohol	not expected	pre 1996	
Isopropanol	No RED		
Substituted Phenols			
o-Phenylphenol and salts	not likely < 200 mg/kg/day	1	39
o-benzyl-p-chlorphenol and salts	C	pre 1996	30
p-tert-Amylphenol and salts	ND	10	50
Peroxides; No data, RED pre 1996			
Sodium hypochlorite; No data, RED pre 1996			

(a) Cancer rankings are presented in Appendix D.
FQPA SF = Food Quality Protection Act Safety Factor; any number other than 1 indicates that the developing organism is more sensitive than the adult; **Note: FQPA was passed in 1996, RED's prior to this had no FQPA SF**
NOEL = Chronic No Observable Effect Level from animal studies; units are mg/kg body weight/day

Appendix D.
EPA Carcinogenicity Classification Scheme

EPA Carcinogenicity Classification of Pesticides

CLASSIFICATION – 2005

The following descriptors from the 2005 Guidelines for Carcinogen Risk Assessment can be used as an introduction to the weight of evidence narrative in the cancer risk assessment. The examples presented in the discussion of the descriptors are illustrative. The examples are neither a checklist nor a limitation for the descriptor. The complete weight of evidence narrative, rather than the descriptor alone, provides the conclusions and the basis for them.

CARCINOGENIC TO HUMANS. This descriptor indicates strong evidence of human carcinogenicity. It covers different combinations of evidence.

- This descriptor is appropriate when there is convincing epidemiologic evidence of a causal association between human exposure and cancer.
- Exceptionally, this descriptor may be equally appropriate with a lesser weight of epidemiologic evidence that is strengthened by other lines of evidence. It can be used when all of the following conditions are met: (a) there is strong evidence of an association between human exposure and either cancer or the key precursor events of the agent's mode of action but not enough for a causal association, and (b) there is extensive evidence of carcinogenicity in animals, and (c) the mode(s) of carcinogenic action and associated key precursor events have been identified in animals, and (d) there is strong evidence that the key precursor events that precede the cancer response in animals are anticipated to occur in humans and progress to tumors, based on available biological information. In this case, the narrative includes a summary of both the experimental and epidemiologic information on mode of action and also an indication of the relative weight that each source of information carries, e.g., based on human information, based on limited human and extensive animal experiments.

LIKELY TO BE CARCINOGENIC TO HUMANS. This descriptor is appropriate when the weight of the evidence is adequate to demonstrate carcinogenic potential to humans but does not reach the weight of evidence for the descriptor "Carcinogenic to Humans." Adequate evidence consistent with this descriptor covers a broad spectrum. As stated previously, the use of the term "likely"as a weight of evidence descriptor does not correspond to a quantifiable probability. The examples below are meant to represent the broad range of data combinations that are covered by this descriptor; they are illustrative and provide neither a checklist nor a limitation for the data that might support use of this descriptor. Moreover, additional information, e.g., on mode of action, might change the choice of descriptor for the illustrated examples. Supporting data for this descriptor may include:

- an agent demonstrating a plausible (but not definitively causal) association between human exposure and cancer, in most cases with some supporting biological, experimental evidence, though not necessarily carcinogenicity data from animal experiments;
- an agent that has tested positive in animal experiments in more than one species, sex, strain, site, or exposure route, with or without evidence of carcinogenicity in humans;
- a positive tumor study that raises additional biological concerns beyond that of a statistically significant result, for example, a high degree of malignancy, or an early age at onset;
- a rare animal tumor response in a single experiment that is assumed to be relevant to humans; or
- a positive tumor study that is strengthened by other lines of evidence, for example, either plausible (but not definitively causal) association between human exposure and cancer or evidence that the agent or an important metabolite causes events generally known to be associated with tumor formation (such as DNA reactivity or effects on cell growth control) likely to be related to

the tumor response in this case.

SUGGESTIVE EVIDENCE OF CARCINOGENIC POTENTIAL. This descriptor of the database is appropriate when the weight of evidence is suggestive of carcinogenicity; a concern for potential carcinogenic effects in humans is raised, but the data are judged not sufficient for a stronger conclusion. This descriptor covers a spectrum of evidence associated with varying levels of concern for carcinogenicity, ranging from a positive cancer result in the only study on an agent to a single positive cancer result in an extensive database that includes negative studies in other species. Depending on the extent of the database, additional studies may or may not provide further insights. Some examples include:

- a small, and possibly not statistically significant, increase in tumor incidence observed in a single animal or human study that does not reach the weight of evidence for the descriptor "Likely to Be Carcinogenic to Humans." The study generally would not be contradicted by other studies of equal quality in the same population group or experimental system (see discussions of *conflicting evidence* and *differing results*, below);
- a small increase in a tumor with a high background rate in that sex and strain, when there is some but insufficient evidence that the observed tumors may be due to intrinsic factors that cause background tumors and not due to the agent being assessed. (When there is a high background rate of a specific tumor in animals of a particular sex and strain, then there may be biological factors operating independently of the agent being assessed that could be responsible for the development of the observed tumors.) In this case, the reasons for determining that the tumors are not due to the agent are explained;
- evidence of a positive response in a study whose power, design, or conduct limits the ability to draw a confident conclusion (but does not make the study fatally flawed), but where the carcinogenic potential is strengthened by other lines of evidence (such as structure-activity relationships); or
- a statistically significant increase at one dose only, but no significant response at the other doses and no overall trend.

INADEQUATE INFORMATION TO ASSESS CARCINOGENIC POTENTIAL. This descriptor of the database is appropriate when available data are judged inadequate for applying one of the other descriptors. Additional studies generally would be expected to provide further insights. Some examples include:

- little or no pertinent information;
- conflicting evidence, that is, some studies provide evidence of carcinogenicity but other studies of equal quality in the same sex and strain are negative. Differing results, that is, positive results in some studies and negative results in one or more different experimental systems, do not constitute *conflicting evidence,* as the term is used here. Depending on the overall weight of evidence, differing results can be considered either suggestive evidence or likely evidence; or
- negative results that are not sufficiently robust for the descriptor, “Not Likely to Be Carcinogenic to Humans.”

NOT LIKELY TO BE CARCINOGENIC TO HUMANS. This descriptor is appropriate when the available data are considered robust for deciding that there is no basis for human hazard concern. In some instances, there can be positive results in experimental animals when there is strong, consistent evidence that each mode of action in experimental animals does not operate in humans. In other cases, there can be convincing evidence in both humans and animals that the agent is not carcinogenic. The judgment may be based on data such as:

- animal evidence that demonstrates lack of carcinogenic effect in both sexes in well-designed and well-conducted studies in at least two appropriate animal species (in the absence of other animal or human data suggesting a potential for cancer effects),
- convincing and extensive experimental evidence showing that the only carcinogenic effects observed in animals are not relevant to humans,
- convincing evidence that carcinogenic effects are not likely by a particular exposure route (see Section 2.3), or
- convincing evidence that carcinogenic effects are not likely below a defined dose range.

A descriptor of "not likely" applies only to the circumstances supported by the data. For example, an agent may be "Not Likely to Be Carcinogenic" by one route but not necessarily by another. In those cases that have positive animal experiment(s) but the results are judged to be not relevant to humans, the narrative discusses why the results are not relevant.

MULTIPLE DESCRIPTORS. More than one descriptor can be used when an agent's effects differ by dose or exposure route. For example, an agent may be "Carcinogenic to Humans" by one exposure route but "Not Likely to Be Carcinogenic" by a route by which it is not absorbed. Also, an agent could be "Likely to Be Carcinogenic" above a specified dose but "Not Likely to Be Carcinogenic" below that dose because a key event in tumor formation does not occur below that dose.

CLASSIFICATION – 1999 Draft

The terms used to describe carcinogenic potential in the July 1999 Review Draft of the Guidelines for Carcinogen Risk Assessment.@ are listed and defined as follows:

CARCINOGENIC TO HUMANS. This descriptor is appropriate when there is convincing epidemiologic evidence demonstrating causality between human exposure and cancer. This descriptor is also appropriate when there is an absence of conclusive epidemiologic evidence to clearly establish a cause and effect relationship between human exposure and cancer, but there is compelling evidence of carcinogenicity in animals and mechanistic information in animals and humans demonstrating similar mode(s) of carcinogenic action. It is used when all of the following conditions are met:

- There is evidence in a human population(s) of association of exposure to the agent with cancer, but not enough to show a causal association, and
- There is extensive evidence of carcinogenicity, and
- The mode(s) of carcinogenic action and associated key events have been identified in animals, and
- The keys events that precede the cancer response in animals have been observed in the human population(s) that also shows evidence of an association of exposure to the agent with cancer.

LIKELY TO BE CARCINOGENIC TO HUMANS. This descriptor is appropriate when the available tumor effects and other key data are adequate to demonstrate carcinogenic potential to humans. Adequate data are within a spectrum. At one end is evidence for an association between human exposure to the agent and cancer and strong experimental evidence of carcinogenicity in animals; at the other, with no human data, the weight of experimental evidence shows animal carcinogenicity by a mode or modes of action that are relevant or assumed to be relevant to humans.

SUGGESTIVE EVIDENCE OF CARCINOGENICITY, BUT NOT SUFFICIENT TO ASSESS

HUMAN CARCINOGENIC POTENTIAL. This descriptor is appropriate when the evidence from human or animal data is suggestive of carcinogenicity, which raises a concern for carcinogenic effects but is judged not sufficient for a conclusion as to human carcinogenic potential. Examples of such evidence may include: a marginal increase in tumors that may be exposure-related, or evidence is observed only in a single study, or the only evidence is limited to certain high background tumors in one sex of one species. Dose-response assessment is not indicated for these agents. Further studies would be needed to determine human carcinogenic potential.

DATA ARE INADEQUATE FOR AN ASSESSMENT OF HUMAN CARCINOGENIC POTENTIAL. This descriptor is used when available data are judged inadequate to perform an assessment. This includes a case when there is a lack of pertinent or useful data or when existing evidence is conflicting, e.g., some evidence is suggestive of carcinogenic effects, but other equally pertinent evidence does not confirm a concern.

NOT LIKELY TO BE CARCINOGENIC TO HUMANS. This descriptor is used when the available data are considered robust for deciding that there is no basis for human hazard concern. The judgment may be based on:

- Extensive human experience that demonstrates lack of carcinogenic effect (e.g., phenobarbital).
- Animal evidence that demonstrates lack of carcinogenic effect in at least two well- designed and well-conducted studies in two appropriate animal species (in the absence of human data suggesting a potential for cancer effects).
- Extensive experimental evidence showing that the only carcinogenic effects observed in animals are not considered relevant to humans (e.g., showing only effects in the male rat kidney due to accumulation of "2u-globulin).
- Evidence that carcinogenic effects are not likely by a particular route of exposure
- Evidence that carcinogenic effects are not anticipated below a defined dose range.

CLASSIFICATION – 1996
In April 1996, EPA released the Proposed Guidelines for Carcinogen Risk Assessment.@ This scheme varied from the earlier 1986 scheme in that it used descriptors rather than letters to classify carcinogenic potential. The descriptors are:

KNOWN/LIKELY. This category of descriptors is appropriate when the available tumor effects and other key data are adequate to convincingly demonstrate carcinogenic potential for humans.

CANNOT BE DETERMINED. This category of descriptors is appropriate when available tumor effects or other key data are suggestive or conflicting or limited in quantity and, thus, are not adequate to convincingly demonstrate carcinogenic potential for humans. In general, further agent specific and generic research and testing are needed to be able to describe human carcinogenic potential.

NOT LIKELY. This is the appropriate descriptor when experimental evidence is satisfactory for deciding that there is no basis for human hazard concern, as follows (in the absence of human data suggesting a potential for cancer effects).

1986 CLASSIFICATION
The following cancer classification scheme was first introduced in 1986. It was used until 1996.

GROUP A – HUMAN CARCINOGEN. This group is used only when there is sufficient evidence from

epidemiologic studies to support a causal association between exposure to the agents and cancer.

GROUP B – PROBABLE HUMAN CARCINOGEN. This group includes agents for which the weight of evidence of human carcinogenicity based on epidemiologic studies is "limited" and also includes agents for which the weight of evidence of carcinogenicity based on animal studies is "sufficient." The group is divided into two subgroups. **Group B1** is reserved for agents for which there is limited evidence of carcinogenicity from epidemiologic studies. **Group B2** is used for Agents for which there is "sufficient: evidence from animal studies and for which there is “inadequate evidence" or "no data" from epidemiologic studies.

GROUP C – POSSIBLE HUMAN CARCINOGEN. This group is used for agents with limited evidence of carcinogenicity in animals in the absence of human data.

GROUP D – NOT CLASSIFIABLE AS TO HUMAN CARCINOGENICITY. This group is generally used for agents with inadequate human and animal evidence of carcinogenicity or for which no data are available.

GROUP E – EVIDENCE OF NON-CARCINOGENICITY FOR HUMANS. This group is used for agents that show no evidence for carcinogenicity in at least two adequate animal tests in different species or in both adequate epidemiologic and animal studies.

Appendix E.
Aquatic Toxicity Studies Disinfectants by Group

Appendix E. Aquatic Toxicity				
Quaternary Ammonium Compounds (ADBAC) (EPA 2006 i); Freshwater Fish				
Species	**%**	**LC_{50}(96 hr) [a] mg/L (ppm)**	**NOEC[b] mg/L (ppm)**	**EPA rank [c]**
Bluegill sunfish	30	0.515	0.456	core
Fathead minnow	80	0.28	ND	core
Rainbow trout	30	0.923	0.619	core
Rainbow trout	50	1.01	ND [d]	NA [e]
Quaternary Ammonium Compounds (ADBAC) (EPA 2006 i); Freshwater Invertebrates				
Species	**%**	**LC_{50}(96 hr) [a] mg/L (ppm)**	**NOEC[b] mg/L (ppm)**	**EPA rank [c]**
Daphnia magna	30	0.0059 (EC50)	ND	core
Daphnia magna	50	0.02	ND	core
Quaternary Ammonium Compounds (ADBAC) (EPA 2006 i); Marine Fish				
Species	**%**	**LC_{50}(96 hr) [a] mg/L (ppm)**	**NOEC[b] mg/L (ppm)**	**EPA rank [c]**
Sheepshead minnow	80	0.86	0.68	core
Inland silverside	50	0.31	ND	NA
Quaternary Ammonium Compounds (ADBAC) (EPA 2006 i); Marine Invertebrates				
Species	**%**	**LC_{50}(96 hr) [a] mg/L (ppm)**	**NOEC[b] mg/L (ppm)**	**EPA rank [c]**
Mysid shrimp	80	0.092	0.047	core

Appendix E. Aquatic Toxicity				
Mysid shrimp	50	0.08	ND	supplemental
Eastern oyster	80	0.055	ND	supplemental
o-Phenylphenol (EPA 2006 a); Freshwater Fish				
Species	**%**	**LC_{50}(96 hr) [(a)] mg/L (ppm)**	**NOEC[(b)] mg/L (ppm)**	**EPA rank [(c)]**
Rainbow trout		4	ND	core
Bluegill sunfish		4.6	ND	core
o-Phenylphenol (EPA 2006 a); Freshwater Invertebrates				
Species	**%**	**LC_{50}(96 hr) [(a)] mg/L (ppm)**	**NOEC[(b)] mg/L (ppm)**	**EPA rank [(c)]**
Daphnia magna		2.51	ND	core
o-Phenylphenol (EPA 2006 a); Marine and Estuarine Organisms				
Species	**%**	**LC_{50}(96 hr) [(a)] mg/L (ppm)**	**NOEC[(b)] mg/L (ppm)**	**EPA rank [(c)]**
Mysid shrimp		0.89	ND	core
Eastern oyster		0.32 (EC_{50})	ND	core
o-benzyl-p-chlorophenol and its salts (EPA 1995 a); Freshwater Fish				
Species	**%**	**LC_{50}(96 hr) [(a)] mg/L (ppm)**	**NOEC[(b)] mg/L (ppm)**	**EPA rank [(c)]**
Rainbow trout		0.72	ND	core
Bluegill sunfish		0.33	ND	core

Appendix E. Aquatic Toxicity				
o-benzyl-p-chlorophenol and its salts (EPA 1995 a); Freshwater Invertebrates				
Species	**%**	**LC_{50}(96 hr) [a] mg/L (ppm)**	**NOEC[b] mg/L (ppm)**	**EPA rank [c]**
Daphnia magna		0.59	ND	core
p-tert-Amylphenol and its salts (EPA 2005 b) [d]; Freshwater Fish				
Species	**%**	**LC_{50}(96 hr) [a] mg/L (ppm)**	**NOEC[b] mg/L (ppm)**	**EPA rank [c]**
Fathead minnow		2.5	ND	supplemental
Fathead minnow		16	ND	supplemental
p-tert-Amylphenol and its salts (EPA 2005 b); Marine Organisms				
Species	**%**	**LC_{50}(96 hr) [a] mg/L (ppm)**	**NOEC[b] mg/L (ppm)**	**EPA rank [c]**
Shrimp		1.7	ND	supplemental

a LC_{50}(96 hr) = 96 hr median lethal concentration in mg/L (ppm)
b NOEC = No Observable Effect Concentration in mg/L (ppm)
c EPA rank = "core", "supplemental" or "invalid". A core study satisfies the data requirement, supplemental studies support the registration and may be up dated to fill the data requirement
d Toxicity studies in male carp exposed to p-tert-Amyphenol resulted in endocrine disruption. The 30 day EC_{50} for these effects was 0.063 mg/L. The NOEC for oviduct formation was < 0.036mg/L and the NOEC for vitellogen induction was 0.09 to 0.256 mg/L (EPA 2005).