SAN FRANCISCO ESTUARY INSTITUTE

AQUATIC PESTICIDES MONITORING PROGRAM

Aquatic Pesticides Monitoring Program Literature Review

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List of Acronyms

AchE - acetylcholinesterase

AI - active ingredient

ALL - Altosid Liquid Larvicide

AMPA - aminomethylphosphonic Acid

bw - body weight

CAS - Chemical Abstract Service

cfs - cubic feet squared

DPR - Department of Pesticide Regulation

EC_{50} - effective concentration of the pesticide in mg/L that produce a specific measurable effect in 50% of test organisms within the stated study time.

EPSP - 5-anolpyruvylshikimic acid-3-phosphate synthase

FAO - U.N. Food and Agricultural Organization

FIFRA - Federal Insecticide, Fungicide, and Rodenticide Act

GIFAP - Groupement des Industriels francais d`Articles de Peche

GIT - Gastrointestinal tract

GUP - General Use Pesticide

ha - hectare

HDT - highest dose tested

IARC - International Agency for Research on Cancer

IGR - Insect Growth Regulator

IPCS - International Programme on Chemical Safety

JH - juvenile hormone

JPMR - Joint Meetings on Pesticide Residues Monographs and Evaluations

LC_{50} - amount of pesticide present per liter of aqueous solution that is lethal to 50% of test organisms within the stated time.

LCL_{O} - Lethal Concentration Low, the minimum amount of a chemical which tests have shown will be lethal to a specified type of animal (in mg/L).

LD_{50} - dose of pesticide in mg, µg, ng, per Kg of body weight that is lethal to 50% of test organisms within the stated study time.

LDL_{O} - Lethal Dose Low, the minimum amount of a chemical which tests have whown will be lethal to a specified type of animal (in mg/kg body weight).

LOAEL - lowest observed adverse effect limit

LOEC - lowest observed effect concentration, lowest level at which adverse effects are observed.

MATC - Maximum Acceptable Toxicant Concentration, a hypothetical threshold concentration that is the geoemtric mean between NOEC and LOEC concentrations.

NOAEL - no observed adverse affect level

NOEC - level at which no adverse effects are observed.

NTP - U.S. National Toxicology Program

PAN - Pesticide Action Network

PC - Pesticide Chemical

PDS - Pesticide Data Sheet

ppb - part per billion = mg/kg = mg/l

ppm - part per million = mg/kg = mg/l

ppt - part per trillion = mg/kg = mg/l

Rfc- fererence concentration

Rfd - Reference dose

SIDS - Screening Information Data Sheet

TDLo - Lowest Published toxic dose

TIE - Toxicity Identification Evaluations

USEPA - United States Environmental Protection Agency

WHO - World Health Organization

Executive Summary

Chemical pesticides can be effective tools to help control dangerous, damaging, or otherwise unwanted organisms, but their use imposes significant responsibilities on applicators and regulators to ensure that no significant detrimental impacts to public health or the environment results from their use.

One important mechanism to help ensure that pesticide use for aquatic pest control poses no significant negative impacts is a detailed review of the published scientific literature on the pesticide products used, interpreted in light of the agencies' pesticide use practices. Together, this information on toxicology and exposure allows for evaluation of the potential health and environmental consequences of the pesticide applications. This report is such a review.

This report is not intended to be an exhaustive review of all literature related to aquatic pesticides. It is a summary of relevant chemical and toxicity data for use by scientists, regulators, and practitioners when planning studies and interpreting results. More exhaustive information can be found at the Pesticide Action Network's website <pesticideinfo.org> and the Washington State Department of Ecology Supplemental Environmental Impact Statement reports.

Section I. Evaluation of Health and Environmental Risks Associated with Pesticides and other Chemicals in the Environment

Evaluating and describing the potential health and environmental risks of the millions of chemicals that are present in the environment is the basis for the science of toxicology, and this section briefly introduces the primary theoretical principles, research methods, and descriptive tools of this discipline, with a particular focus on the sub-set of potentially toxic materials known as "pesticides."

Chemical Abstracts lists some two million specific chemical compounds described in the scientific literature, and undoubtedly there are millions more chemicals existing in nature and/or potentially synthesized in chemical laboratories that have not yet been named and characterized. Of the vast assortment of presently existing chemicals, several hundred thousand compounds, both natural and synthetic, are known to cause toxicity to humans or other organisms under some circumstances.

Registered pesticides are often differentiated from other potentially toxic materials in law and in public perception because their toxicity is intentionally used to cause harm to undesired organisms ("pests"), including those that spread human disease. Because the application of any potentially toxic materials to the environment inevitably involves some degree of risk to the applicator, the general public, and to organisms other than the target pests, there is properly a high degree of regulation of these materials, their toxicity, and their use. However, evaluating the risks associated with registered pesticide, and therefore the appropriate level of regulation of them, is challenging for a number of reasons. First, the risk posed by any potentially toxic material is a function both of its toxicity (relatively easy to evaluate in a laboratory) and its exposure to sensitive organisms (a much more difficult variable to measure or predict). Second, a very large number of common household products are also toxic to some organisms under some conditions, and many of these, including some medicines (such as antibiotics) and common cleansers (ammonia, bleach, etc.) are intentionally used, like registered pesticides, to harm undesired organisms. Third, most pesticides found in the environment or ingested by humans are not registered synthetic products, but are natural chemicals that occur in plants (potatoes, beans, coffee, etc.) and which protect the growing plants from damage by insects, fungi, rodents, etc. Therefore, it is critical to understand some basic principles of toxicology to reasonably evaluate pesticide-associated risks.

Toxicology, the study of the biological hazards associated with chemicals and the effects on living organisms, is a well-developed field of science, and this section will provide only a brief and preliminary review of its extensive literature on principles, methods, and interpretation of results. A short bibliography is provided for those desiring more discussion of these topics.

A number of basic principles are discussed in this section. First is the importance of careful identification and characterization of the material in question, together with the

allied principle of chemical analogy – the observation that materials can be classified by their toxicological properties into groups, and that some toxic effects can be predicted from observations on similar materials.

A. Chemical Identification and Characterization

I. Chemical Description and Type

The first requirement of a meaningful evaluation of the toxicity or potential toxicity of any substance is an unambiguous identification of the substance. The identification process starts with a determination of whether the substance is comprised of a single chemical "species" or compound or is a mixture of distinct chemicals, the properties of which together determine its effects on living organisms. Next, the potentially active chemical or chemicals must be identified clearly and unambiguously, regardless of trade names and other synonyms. In addition, the formulation(s) of the material, including the presence of "inert" ingredients, can influence the accessibility of potentially toxic chemicals to organisms as well as their persistence and mode(s) of movement within the environment, and should be specified. Finally, because few potentially toxic materials have undergone complete toxic screenings, it is important to identify the chemical "class" or "family" of the material, to help identify materials with more extensive toxicology information and potentially similar toxic profiles.

II. Chemical Identification

The chemical name listed for each pesticide in Section III is the most common name used for the particular active ingredient. Synonyms are other names that may be used for the active ingredient. Synonyms include technical chemical names, common product names, common chemical names and trade names as well as chemical identification codes from the USEPA, California Department of Pesticide Regulation (DPR) and Chemical Abstract Service.

The Chemical Abstract Service (CAS) Registry Number is a unique identifier assigned to each chemical and to some mixtures of chemicals by the Chemical Abstracts Service, a division of the American Chemical Society. This number is used worldwide. The CAS registry number includes up to nine digits which are separated into three groups by hyphens (xxxxxx-xx-x). The first part of the number, starting from the left, has up to six digits; the second part has two digits. The final part consists of a single check digit or checksum that makes it easy to determine whether a CAS number is valid or not. The CAS numbers reported in Section III were taken from recent pesticide labels and verified in November 2001 on the USEPA and California DPR websites.

The U.S. Environmental Protection Agency (USEPA) assigns a unique chemical code number to a particular pesticide active ingredient or mixture of active ingredients. This USEPA PC (Pesticide Chemical) Code, sometimes referred to as the Shaugnessy Number, is available online on the USEPA Pesticide Product Information System at www.opp.epa.gov. The values reported in Section III were verified in the USEPA website on November 12,

2001. The California DPR also assigns a unique chemical code number to serve as an identifier for a particular pesticide active ingredient or mixture of active ingredients. The values reported in Section III were verified in the DPR website on November 12, 2001.

In addition to the active ingredients, pesticide products also contain "inert" ingredients or "adjuvants" used to increase the effectiveness of the active ingredients, make the product easier to apply, or to allow several active ingredients to mix in one solution. Solvents, emulsifiers, and spreaders fall in this category. Assigning CAS numbers to these materials can be difficult because the pesticide manufacturers are not required to list them on the pesticide label, as a measure to protect intellectual property rights.

III. Chemical Class/Group/Family

Because the number of potential interactions between chemicals and organisms vastly exceeds the analytical capacities of toxicologists and toxicology laboratories, many evaluations of potential toxicity are based on analogies between materials with similar chemical properties. While this is a pragmatic and necessary response to a condition of limited resources, especially for materials with relatively small markets and therefore little financial backing, it has often been observed that materials with similar chemical traits can have substantially different toxicity profiles. Thus, it is important to understand the uses and limitations of chemical "classes", "groups", "families", and "proxies" as concepts invoked to assist predictions of the potential toxicity of incompletely tested materials.

When the specific mode of toxic action is not known, evaluating whether two materials are similar enough chemically to demonstrate essentially similar toxic effects can rarely be accomplished with certainty. Nonetheless, enough is known of many physiological mechanisms of toxicity and of the environmental fates of materials that many chemicals can be placed with some confidence into chemical "classes" or "families" with predictably similar outcomes in toxicity trials or epidemiological studies.

The Chemical Classification used by USEPA (e.g. organophosphorus compounds, chlorophenoxy acids or esters, etc.) is one way of broadly categorizing chemicals, but not all chemicals can easily be placed into a chemical class and pesticides within a class can be quite diverse in their toxicity profiles. Thus, some toxicologists have taken this classification scheme to a finer level of detail. For example, the Pesticide Action Network (PAN) database uses a "Parent/Related Chemical" scheme to make it easier to find similar chemicals. This system is based on identifying chemical groups based on one or more of the following eight criteria of chemical composition, properties and/or structure (PAN 2003):

1. Parent chemicals and their salts and esters, e.g., glyphosate and glyphosate, isopropylamine salt or 2,4-D and 2,4-D, butoxyethyl ester.
2. Parent chemicals and derivatives other than esters made by substitution of a functional group or groups.
3. Compounds of highly toxic metals, with distinct groupings for different types of arsenic, mercury, cadmium, tin, lead, and hexavalent chromium compounds.
4. Compounds of less-toxic transition metals, with distinct groupings for different types of copper, zinc, iron, and silver compounds.

5a. Parent chemicals and their transformation products, e.g. DDT and its transformation products DDE and DDD.

5b. Phosphorothioates and their oxygen analogs are a special sub-category of parent chemicals and their transformation products.[1]

6. Optical, geometric, and structural isomers of compounds.

7. Strong acids, weak acids, strong bases, and weak bases.

8. California DPR's "other related" chemicals, such as "DDVP" and "DDVP, other related".

B. Dose-Response Relationship

The dose-response relationship is the fundamental principle behind toxicity. Toxicity is very dependent on the amount and time of exposure of an organism to the chemical agent (Crosby 1998). In general, the higher the dose, the higher the toxic response will be. The dose-response relationship is established by the scientific data collected from experimental animal, human clinical, or cell studies (National Library of Medicine 2001). In addition to dosage, the mechanisms by which an organism can remove the toxic from their system will determine the toxicity effect (i.e. excretion, degradation of the toxic, physiological absorption capacity) (Crosby 1998). The degree of dosage, removal mechanisms, and sensitivity level of an organism all determine whether a response will be acute or chronic. Acute toxicity is the immediate response to an exposure, while chronic refers to the effects from long-term exposure of an agent. Acute and chronic toxicity are usually expressed through different toxic mechanisms and target organs, and toxicity studies differentiate between the two response types.

I. Toxicity Measurement and Endpoints

Toxicity testing attempts to determine the harmful effects of agents and the cellular, biochemical, and molecular mechanisms responsible for the effects (National Library of Medicine 2001). Toxicity is investigated in humans and the environment through quantitative measurement of an organisms' tolerance level to exposure of a given toxicant. In order to measure the observable effect of a toxin on a test organism, toxicity endpoints are determined, such as death, growth inhibition, behavioral effects, and genetic effects.

Standardized endpoints have been established and are the most commonly used in toxicity testing (Crosby 1998). These are the LD_{50}, LC_{50}, EC_{50}, LDLo, LCLo, NOEC, LOEC, and MATC, which are further defined as:

LD_{50} is the dose of the pesticide in milligram (mg), microgram (µg), or nanogram (ng) of pesticide per kilogram (kg) of body weight that is lethal to 50% of the test organisms. This designation is used for routes of exposure where a known dose is administered (oral, dermal, intravenous, etc). Units used are: ppm (mg/kg), ppb (µg/kg), and ppt (ng/kg).

[1]The phosphorothioates and their byproducts are separated by PAN because their metabolism results in the formation of the oxygen analogs, which are more toxic than the parent phosphorothioates themselves (PAN 2003).

LC_{50} is the concentration of pesticide in air or aqueous solution that is lethal to 50% of the test organisms within the stated study time. Units used are parts per million (ppm)(mg/L), or parts per billion (ppb)(ug/L).

EC_{50} is the effective concentration of the pesticide that produces a specific measurable effect in 50% of the test organisms. Units in mg/L or ug/L.

LDLo is the lowest dose of pesticide that produces a lethal response in any test animal. Because the LDLo study type is not strictly defined as to the percentage of test animals affected, it is less useful for comparison purposes than LD50.

LCLo is the lowest concentration of pesticide that produces a lethal response in any test animal. As with LDLo, because the LCLo study type is not strictly defined as to the percentage of test animals affected, it is not highly useful for comparing the acute toxicities of different materials.

NOEC is the "no observed effect concentration", or the level below which no adverse effects are observed. This endpoint depends strongly on the sensitivity of the techniques used to measure the effects.

LOEC is the "lowest observed effect concentration", or the lowest level below which adverse effects are observed. This endpoint depends strongly on the sensitivity of the techniques used to measure the effects.

MATC is the "maximum acceptable toxicant concentration" and is a hypothetical threshold concentration that is the geometric mean between the NOEC and the LOEC concentration.

The most common type of toxicity measurements for pesticides are acute and chronic toxicity (Crosby 1998). Acute toxicity refers to the immediate effects (typically 0-7 days) of exposure to a pesticide or other substance. Highly acutely toxic substances can be lethal at very low doses, while other materials may have no detectible toxicity at the highest plausible exposure levels. The most commonly used measure of acute toxicity is acute lethality (LD_{50}, LC_{50}) (Crosby 1998). Chronic toxicity refers to the effects from long-term exposure for a substantial portion of an organism's life to a pesticide or other agent. Endpoints can include $LD_{50}$and LC_{50}, but usually focus on physiological, biochemical, and reproductive effects (Crosby 1998).

C. Evaluation of Human Health Risks

I. Types of Toxicity Investigations

Human toxicity information is primarily obtained through human clinical trials, epidemiological studies, and experimental animal studies. Clinical investigations involve deriving toxicological data from clinical trials where humans are administered the target chemical or agent. For pesticides, human testing is rarely conducted. Epidemiological studies observe humans that have been exposed to chemicals by accident or through the normal

course of their life or occupation (i.e. pesticide applicators). Reliable epidemiological studies are rarely available due to incomplete exposure histories or the presence of confounding environmental factors. Experimental animal tests for pesticides are more commonly conducted in order to determine potential toxic effects in humans prior to conducting human clinical investigations. Animal test results are acceptable proxies by which toxicity in humans can be effectively predicted at comparable dose levels. However, response differences between animals and humans can occur, particularly in relation to metabolism interpretation (National Library of Medicine 2001).

II. Common Toxicity Effects

Toxicity testing can be very specific for a particular effect, such as dermal irritation, or it may be general, such as testing for chronic effects (National Library of Medicine 2001). Standardized tests have been developed for the following effects:

Table 1. Common Toxicity Effects.

Acute Toxicity	Immediate effects (typically 0-7 days) of exposure
Chronic Toxicity	Long-term effects (typically 21-28 days) of exposure
Neurotoxicity	Effects on cells of the central nervous system *(brain and spinal cord)* and the peripheral nervous system *(nerves outside the CNS)*
Carcinogenicity	Effects on the potential for cancer development
Reproductive Toxicity	Effects on gonad function, conception, birth, growth and development of the offspring
Teratogenic and Developmental Toxicity	Effects on the potential for physical defects in the developing embryo and for birth defects
Mutagenic Toxicity	Effects on the potential to induce or increase genetic mutations by causing changes in DNA
Endocrine Toxicity	Effects on hormone production
Dermal Toxicity	Effects that cause irritation and inflammation of the skin, either by direct contact or as an indirect response due to sensitization from prior exposure

III. Exposure Route

The exposure route is the route by which experimental test animals are exposed to a chemical, and this should be denoted within a study in order to accurately infer causality from the study results for humans. The most common exposure routes are oral (by mouth), dermal (applied to the skin), and inhalation (by breathing the chemical). Other exposure routes include:

Implant = Chemical is time-released from an implanted device,

Intraperitoneal = Chemical is injected into the abdominal cavity,

Intravenous = Chemical is injected into a vein,

Intraarterial = Chemical is injected into an artery,

Intraaural = Chemical is placed in the ear,

Intracerebral = Chemical is injected into the brain,

Intracervical = Chemical is placed in the cervix,

Intraduodenal = Chemical is injected into the small intestine,

Intramuscular = Chemical is injected into a muscle,

Intratracheal = Chemical is injected into the trachea,

Ocular = Chemical is placed in the eye,

Parenteral = A general term meaning the chemical was not administered orally (usally this means an intramuscular or intravenous route was used),

Rectal = Chemical is administered through the rectum, and

Subcutaneous = Chemical is injected in the upper layers of the skin.

D. Evaluation of Environmental Risks

I. Types of Toxicity Investigations

Environmental toxicity focuses on the quantitative measurement of toxic responses in common groups of organisms (small mammals, fish, birds, and insect communities) present in the environments on which pesticides might be applied, including terrestrial and aquatic ecosystems. Information is primarily obtained through experimental studies on these organisms at the individual or small population level, as these studies are relatively faster and cheaper than larger population and ecosystem investigations (Crosby 1998). The tests are designed to determine effects such as acute lethality, chronic response in the physiological, biochemical, and reproductive phases of the organisms, behavioral change, and tolerance levels for populations to pesticides. For pesticides applied in aquatic environments, both target (i.e. weed plants and mosquitoes) and non-target (i.e. fish, non-weedy plants) aquatic organisms are studied. Common, standardized tests include the following:

Table 2. Types of Toxicity Testing.

Acute Toxicity	Immediate effects of exposure (typically 0-7 days; 24-96h for smaller organisms)
Chronic Toxicity	Long-term effects of exposure (typically 21-28 days)
Life Cycle Tests	Exposure from embryo through one complete reproductive cycle to determine effects to the reproduction or other physiological and behavioral patterns (Crosby 1998)
Toxicity Identification Evaluations (TIE)	Acute bioassays are performed, and if toxicity is detected, the sample is run through other chemical procedures to isolate and determine the responsible toxin
Phytotoxicity	Effects on plants, i.e. growth rate, chlorophyll loss, deformities, vigor, seed germination
Bioaccumulation Tests	Evaluating the potential for pesticide accumulation in the tissue of organisms, particularly with regard to higher food-chain organisms (fish, mammals, birds)

For aquatic organisms, the shorter acute and chronic toxicity testing are conducted initially within the sediment and water column, and then followed by the other extensive toxicity tests if necessary. Standardized toxicity endpoints such as LD_{50}, LC_{50}, EC_{50}, LDLo, LCLo, NOEC, and LOEC are used for the acute and chronic testing. The common species used for these tests include ducks, quail, trout, sunfish, salmon, minnow, shrimp/amphipod, oyster, snail, insect larvae, water flea, and algal cells.

II. Aquatic Toxicity Table

M. A. Kamrin, in *Pesticide Profiles: Toxicity, Environmental Impact, and Fate* (1997), proposed a narrative system to describe the acute toxicity of pesticides in aquatic systems. Her table is reproduced here because it is used by the Pesticide Action Network and some other groups to characterize the aquatic toxicity profiles of pesticide constituents.

Table 3. Toxicity Categories.

Toxicity Category	**LC_{50} (µg/L)**
Very highly toxic	<100
Highly toxic	100-1,000
Moderately toxic	1,000-10,000
Slightly toxic	10,000-100,000
Not acutely toxic	>100,000

E. Toxic Chemical Regulatory Evaluation and Registration

I. Registration of Pesticides

Pesticides are subject to stringent government requirements for safety testing and cannot be marketed until the U.S. Environmental Protection Agency (USEPA), in accordance with the Federal Insecticide, Fungicide, and Rodenticide Act (FIFRA), has registered them.† In order to obtain registration, a pesticide must undergo an extensive battery of toxicity tests, chemistry analyses, and environmental fate tests.

Per the USEPA website "the EPA evaluates the pesticide to ensure that it will not have unreasonable adverse effects on humans, the environment and non-target species. A pesticide cannot be legally used if it has not been registered with EPA's Office of Pesticide Programs." For further information, visit www.epa.gov/pesticides/regulating/data.htm.

II. Information on Pesticides and Other Toxic Chemicals

The International Programme on Chemical Safety (IPCS) maintains a central information hub called INCHEM for chemicals of international interest, often because of their potential for detrimental impacts to human health or the environment. Some of the documents and data links are specific to labeled pesticide ingredients and products, while others more broadly address potentially hazardous chemicals. The pesticide-specific documents currently available through INCHEM include: Pesticide Data Sheets (PDSs) and Joint Meeting on Pesticide Residues Monographs and Evaluations (JPMR). The Pesticide Data Sheets (PDS's) are a primary source of information on pesticide active ingredients from reliable international sources, although some of them are quite dated. According to the IPCS website (IPCS 2002), the PDS's "contain basic information for safe use of pesticides. The Pesticide Data Sheets are prepared by WHO (World Health Organization) in collaboration with FAO (U.N. Food and Agriculture Organization) and give basic toxicological information on individual pesticides. Priority for issue of PDSs is given to substances having a wide use in public health programmes and/or in agriculture, or having a high or an unusual toxicity record. The data sheets are prepared by scientific experts and peer reviewed. The comments of industry are provided through the industrial association, GIFAP. The data sheets are revised from time to time as required..."

A broader series of documents which cover both some pesticides and some other potentially toxic materials include:

- CIS Chemical Information (ILO/CIS),
- Concise International Chemical Assessment Documents (CICADS),
- Environmental Health Criteria (EHC) Monographs,
- Health and Safety Guides (HSGs),
- International Agency for Research on Cancer (IARC) Summaries and Evaluations,
- International Chemical Safety Cards (ICSCs),
- IPCS/EC Evaluation of Antidotes Series,
- Joint Expert Committee on Food Additives (JECFA) Monographs and Evaluations,
- Poisons Information Monographs (PIMs), and
- UNEP Screening Information Data Set (SIDS) for High Production Volume Chemicals.

III. Toxicity Classifications and Rankings

Narrative toxicity categories (Danger, Warning, Caution)[2] are applied to many substances, and these are generally based exclusively or primarily on their acute toxicity as reflected by LD_{50}. This, for example, is how the USEPA develops narrative warning labels for pesticide products (See Table 4 for LD_{50} narrative equivalents).

There are several organizations that formally evaluate and rank chemicals for their acute toxicity. Active ingredients of pesticides are ranked by the World Health Organization. Information on LD50s for many chemicals, including pesticide product ingredients, can be obtained from materials safety data sheets (MSDS's) or from the U.S. National Toxicology Program (NTP) databases. As noted above, USEPA gives overall toxicity ratings, as warning numbers and words on the pesticide product label, for formulated pesticide products, which generally include inert ingredients as well as the active ingredients.

World Health Organization (WHO) Acute Hazard Classification

The World Health Organization has compiled a dataset (*The WHO Recommended Classification of Pesticides by Hazard and Guidelines to Classification 1998-1999*, World Health Organization, 1998), which includes acute toxicity ratings for 575 pesticide chemicals ("active ingredients"). WHO does not evaluate the fumigants, a class of gaseous pesticides that are often extremely hazardous, nor does it evaluate pesticides believed obsolete or discontinued, even though some of these "obsolete" pesticides are currently registered for use in the U.S. This list is updated biennially and was last published by WHO in July 2001[3], although the table below is from the 1998-99 publication.

The WHO bases its ratings of the acute toxicity of pesticide active ingredients primarily on the lowest credible published rat oral LD_{50} in a standard assay (Table 4 from PAN 2003). While the WHO ratings generally reflect acute toxicity, they also take into account other toxic effects such as acute dermal toxicity (which influences toxicity class at higher LD_{50}'s than oral exposure), and reproductive and developmental toxicity. The specific LD_{50} that defines a toxicity class varies between solid and liquid materials. WHO gives hazard rankings that range from Ia (Extremely Hazardous) for the most hazardous pesticide active ingredients to III for the least acutely hazardous.

[2]"Poison" has a broad set of historical definitions. USEPA uses it specifically for acute systemic toxins, and not for materials with toxicity limited to localized skin or eye damage (PAN 2003).

[3]There is a new version of this list, released in July 2001, that is not yet included in PAN database, but can be downloaded from the IPCS web site (PAN 2003).

Table 4. WHO Pesticide Active Ingredient Acute Toxicity Classification (PAN 2003).

WHO Toxicity Classification		**Rat LD50 (mg of chemical per kg of body weight)**			
Class	**Description**	**Solids (oral)**	**Liquids (oral)**	**Solids (dermal)**	**Liquids (dermal)**
Ia	**Extremely hazardous**	< 5	< 20	< 10	< 40
Ib	**Highly hazardous**	5-50	20-200	10-100	40-400
II	**Moderately hazardous**	50-500	200-2,000	100-1,000	400-4,000
III	**Slightly hazardous**	> 500	> 2,000	> 1,000	> 4,000
Table 5	**Unlikely to present acute hazard in normal use**	> 2,000	> 3,000	---	---
Table 6	**Not classified: believed obsolete**				
Table 7	**Fumigants not classified by WHO**				

United Nations Environmental Programme (UNEP)

The United Nations Environmental Programme maintains an online database of information on potentially toxic chemicals that can be found at http://irptc.unep.ch. The site offers publications, registrations, legal files, inventories, code of ethics, and screening information data sets (SIDS) on internationally used chemicals, particularly persistent organic pollutants and toxic substances.

USEPA Acute Toxicity Rankings

All pesticide products registered for use in the U.S. are required to have an acute toxicity rating on the label. The acute toxicities of formulated pesticide products, which generally include "inert ingredients" (those that are not acutely toxic in themselves to the target organism) in addition to one or more active ingredients, are characterized by the USEPA using both toxicity categories (1 = most acutely toxic to 4 = least acutely toxic) and standardized warning words; both the category and warning word must be prominently posted on the pesticide container label. The USEPA toxicity category of a pesticide product is based on the LD_{50}'s and, for inhalation exposures, the LC_{50} is used (see Table 5)[4].

Table 5. USEPA Pesticide Product Toxicity and Toxicity Categories.

USEPA Categories & Warning Labels		**Acute Toxicity to Rats**				
Category	**Warning Label**	Oral LD50 (mg/kg)	Dermal LD50 (mg/kg)	Inhalation LC50 (mg/L)	Eye Effects	Skin Effects
1	**Danger-Poison***	< 50	< 200	< 0.05	-----	-----
1	**Danger**	< 50	< 200	< 0.05	Corrosive (irreversible destruction of ocular tissue) or corneal involvement or irritation persisting for more than 21 days.	Corrosive (tissue destruction into the dermis and/or scarring)
2	**Warning**	50-500	200-2,000	0.05-0.5	Corneal involvement or irritation clearing in 8-21 days	Severe irritation at 72 hours (severe erythema or edema)
3	**Caution**	500-5,000	2,000-5,000	0.5-2	Corneal involvement or irritation clearing in 7 days or less	Moderate irritation at 72 hours (moderate erythema)
4	**None**	> 5,000	> 5,000	> 2	Minimal effects clearing in less than 24 hours	Mild or slight irritation (no irritation or slight erythema)

The relationship between the acute toxicity of pesticide ingredients and formulated products is influenced by the concentrations of active and inert ingredients, the specific materials in each of these categories, and any potential interactions or formulation effects on toxicity. For example, warning labels for single-active-ingredient pesticide products containing technical grade active ingredients over 90% pure can serve as a reasonable proxy for the toxicity of the active ingredient, but most other products are not so straightforward. In addition, many of these warning labels are not internally consistent, and different pesticide products containing essentially the same concentration of active ingredient are labeled with two or more different toxicity ratings (PAN 2003). In this situation, the USEPA acute toxicity rating for the chemical is not clear (PAN uses "No Consensus Value" in these cases).

[4]References include 1) USEPA Health Effects Test Guidelines: Acute Toxicity Background, USEPA; 2) 40 Code of Federal Regulations, Part 156.10. (Note: The toxicity guidelines given here are different than those given in reference 1. Those in reference 1 were used, since it was published as official guidance from USEPA.); 3) USEPA Pesticide Product Information System (PPIS); and 4) CA DPR Pesticide Product Database.

U.S. National Toxicology Program (NTP) Acute Hazard Rankings

The U.S. National Toxicology Program (NTP) has a database of acute toxicity data for 1,581 chemicals, only some of which are pesticides[5] (PAN 2003). This dataset was compiled by NTP from a variety of peer-reviewed sources, and includes a number of toxicity endpoints in addition to LD_{50} and LC_{50}, and other exposure pathways besides oral, dermal, and inhalation. The NTP does not assign narrative toxicity descriptions. The LC_{50} is only used for inhalation studies in the NTP data and is expressed in milligrams of pesticide per liter of air (mg/L), milligrams of pesticide per cubic meter (mg/m^3), and grams of pesticide per cubic meter (g/m^3). For inhalation studies, the time of exposure is also noted, where H = hours and M = minutes. The LCLo is only used for inhalation studies in the NTP data and is given in milligrams of pesticide per liter of air (mg/L), milligrams of pesticide per cubic meter (mg/m^3), parts per million (ppm), parts per billion (ppb).

Pesticide Action Network (PAN) Acute Toxicity Description

The PAN database assigns narrative Toxicity Ratings (see Table 6) derived from LD_{50} or LC_{50} results according to USEPA guidelines in Table 5. These ratings are derived only from those NTP studies with LD_{50} or LC_{50} endpoints and oral, dermal and inhalation exposure routes for mammals that are reasonable analogs for humans (rats, mice, rabbits, monkeys, dogs, cats, gerbils, and guinea pigs). PAN uses the term "No Rating" for all other studies, including those reporting LDLo and LCLo endpoints.

Because toxicity designations from different sources sometimes conflict with each other, PAN created a summary acute toxicity designation that reflects the most toxic ranking assigned by any organization. In addition, the different terms used by different organizations to describe acute toxicity were translated into a consistent set of terms. For example, if WHO determined a pesticide to be "Highly Hazardous", we used the label "Highly Toxic." The equivalences between the different ranking systems are shown in the table below.

For a chemical to be classified as a PAN "Bad Actor" pesticide on the basis of acute toxicity, it must either be labeled as either Extremely Toxic or Highly Toxic in the PAN summary category.

[5]References include Chemical Health and Safety Data, U.S. National Toxicology Program (12/10/00; PAN 2003); & USEPA Health Effects Test Guidelines: Acute Toxicity Background, USEPA Program (12/10/00; PAN 2003).

Table 6. PAN Acute Toxicity Categories and Equivalences.

PAN category	Equivalence in other ranking systems
Extremely toxic	WHO: Extremely hazardous USEPA: Category I, DANGER U.S. NTP: no parallel category MSDS: no parallel category
Highly toxic	WHO: Highly hazardous USEPA: Category I, DANGER U.S. NTP: based on USEPA's LD50 guidelines MSDS: based on USEPA's LD50 guidelines
Moderately toxic	WHO: Moderately hazardous USEPA: Category II, WARNING U.S. NTP: based on USEPA's LD50 guidelines MSDS: based on USEPA's LD50 guidelines
Slightly toxic	WHO: Slightly hazardous USEPA: Category III, CAUTION U.S. NTP: based on USEPA's LD50 guidelines MSDS: based on USEPA's LD50 guidelines
Not acutely toxic	WHO: Unlikely to be hazardous USEPA: Category IV, CAUTION U.S. NTP: based on USEPA's LD50 guidelines MSDS: based on USEPA's LD50 guidelines

Section II. Aquatic Pesticides

The properties of specific aquatic pesticides are presented and discussed in the following chapters. These aquatic pesticides were selected for review based on fact that they were the aquatic pesticides most often used (in terms of weight) in the State of California during 1999 and 2000. Additional compounds were included in the review on suggestion from several steering committee members. The pesticides that will be reviewed here are 1) Acrolein, 2) Copper sulfate, 3) Diquat dibromide, 4) Endothall, 5)Fluridone, 6) Glyphosate-based herbicides, 7) Malathion, 8) Methoprene, and 9) 2,4-D.

The information in these pesticide profiles does not in any way replace or supersede the information on the pesticide product labeling or other regulatory requirements. Please refer to the pesticide product labeling.

A. Acrolein

I. Introduction

Acrolein is an algaecide and aquatic herbicide, which breaks down cell walls. When used as an aquatic herbicide, acrolein is used to control submersed and floating vegetation in irrigation canals and drainage ditches. It is extremely water soluble and application is made by injecting the chemical into flowing water at a point of good mixing, such as downstream of a weir or siphon. Once mixed, the acrolein travels downstream as a wave of treated water, bathing unwanted aquatic vegetation with herbicide. All typical submersed aquatic weed species and algae are susceptible. Floating weeds are controlled only if herbicide concentration is maintained for extended periods and it has little effect on emergent weeds at the recommended application rates.

Acrolein is a general cell toxicant that reacts with various vital proteins. The dead plant tissues gradually disintegrate and float downstream, with the disintegration taking from three days to two weeks.

Additionally, acrolein is used in manufacture of colloidal forms of metals; making plastics, perfumes; as a warning agent in methyl chloride refrigerant; and has been used in military poison gas mixtures. It is also used as an intermediate in the production of glycerin, methionine, acrylic acid, and esters. Acrolein is also an intermediate for glycerol, polyurethane, polyester resins, and pharmaceuticals.

II. Active Ingredient ID

Synonyms

2-Propenal, Acrolein, Acrylaldehyde, Allyl aldehyde, Acrylic aldehyde, Prop-2-en-1-al, 2-Propen-1-one, Aqualin, Crolean, Magnacide H, Acquinite, NSC 8819, 107028

IUPAC name: prop-2-enal, acrylaldehyde

Structural Formula

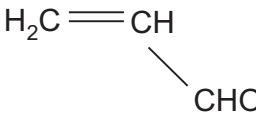


Table 7. Acrolein Active Ingredient Identification Summary Table.

Characteristic	Value	Source
CAS Number	107-02-8	Tomlin 2000
Molecular Weight	56.1	Tomlin 2000
Molecular Formula	C_3H_4O	Tomlin 2000
USEPA PC Code	000701	PAN 2003
CA DPR Chemical Code	3	PAN 2003
USEPA Chemical Class	aldehyde	PAN 2003

III. Physical Properties

Appearance

Technical grade acrolein is a water-white or yellow liquid. It has a disagreeable odor and an odor threshold of 0.2 ppm.

Stability

Acrolein is highly reactive chemically, burns easily, and is easily volatized. It may polymerize if exposed to light and polymerizes violently in the presence of concentrated acids, alkalis and amines. Hydroquinone is added to acrolein as a stabilizer, however polymerization will still occur slowly during storage. To limit polymerization acrolein must be stored in the dark, under nitrogen, and transported in oxygen-free atmosphere. Hydrolysis DT_{50}= 3.5 days at pH=5; 1.5 days at pH=7; 4 hours at pH=10.

Table 8. Acrolein Physical Properties Summary Table.

Characteristic	**Value**	**Source**
Specific Gravity	0.841 at 20°C	Tomlin 2000
Melting Point	-87°C	Tomlin 2000
Boiling Point	52.5°C	Tomlin 2000
Vapor Pressure	59 kPa at 38°C	Tomlin 2000
Water Solubility	208g/kg at 20°C	Tomlin 2000
Solubility in Other Solvents	Miscible in organic solvents	Tomlin 2000
Partition Coefficient (K_{ow})	Log P = 1.08	Tomlin 2000
Adsorption Coefficient (K_{oc})	0.7625 Koc	PAN 2001
Henryís Constant (K_h)	7.0 (calc)	Tomlin 2000
Half-Life	7.5 hrs in non-weed canal, 10 hrs in weeded canal	Baker Petrolite Corporation 1994
Dissipation Rate	Dissipation half-life= 7 hours	Nordone et al. 1998
Hydrolysis DT_{50}	3.5d (pH 5), 1.5d (pH 7), 4 h (pH 10)	Tomlin 2000

IV. Active Ingredient Regulatory Status

The safety and specificity of acrolein are confirmed by their regulatory status at all levels of government.

Table 9. Acrolein Regulatory Status.

Agency/ Regulatory Category	Regulatory Status	Source
UNEP Persistent Organic Pollutant	Not Listed	PAN 2003
UNEP Prior Informed Consent Chemical	Not Listed	PAN 2003
USEPA Registered Pesticide Active Ingredient	Yes	PAN 2003
USEPA Pesticide Use Type	Algaecide	PAN 2003
USEPA Toxicity Class (Pesticide Products)	Highly toxic	PAN 2003
USEPA Hazardous Air Pollutant	Yes	PAN 2003
USEPA Minimum Risk Pesticide (25b list)	No	PAN 2003
CA Registered Pesticide Active Ingredient	Yes	PAN 2003
CA Toxic Air Contaminant	HAPTAC	PAN 2003
CA Groundwater Contaminant	Potential	PAN 2003
PAN Bad Actor	Yes	PAN 2003
PAN Dirty Dozen	Not Listed	PAN 2003

V. Pesticide Status

Pests Controlled

Acrolein-based products are registered for use to control algal and aquatic plant growth.

Pesticide Trade and Other Names

Magnacide H.

Formulations and Dosages

The amount of Magnacide H to be used depends on the weed growth condition of the canal. Concentrations of Magnacide H should not exceed 15ppm per application.

Table 10. Condition and Acrolein Application Rate.

Condition Code (water temp 65 F+)	Magnacide H Herbicide per cfs
A. Little algae and pondweed Less than 6 inches long	0.17 gallons per cfs (for preventive maintenance)
B. Algae (non-floating) and pondweed pondweed less than 12 inches long	0.25 gallons per cfs (for preventive maintenance)
C. Algae (some floating) and pondweed 12-24 inches	0.50 gallons per cfs
D. Algae (some floating) and mature Pondweed	1.0 gallons per cfs
E. Choked conditions	1.5 gallons per cfs

Water temperature affects the amount of Magnacide H needed for effective treatment. Magnacide H is less soluble in cooler water and plant reactivity is lowered. To compensate, adjust amount of Magnacide H used according to chart on product label. Application is done with the use of cylinders and skid tanks.

VI. Toxicity to Humans and Other Mammals

Absorption Route

Acrolein can be absorbed through inhalation, ingestion, and through the skin.

Fate in mammals and excretion products

In hen and goat, no acrolein was detected in tissues or excreta, or in goat milk or hen eggs, following the administration of high doses.

Mode of action

Inhalation of sufficient concentrations can lead to death from cardiac failure accompanied by hyperemia and hemorrhage of the lungs and degeneration of the bronchial epithelium is possible. Exposure can also cause severe gastrointestinal distress with slowly developing pulmonary edema.

Acute toxicity

The EPA Office of Air Quality Planning and Standard considers acrolein to be a "high concern" pollutant based on acute toxicity standard. This hazard ranking was made in accordance with Section 112(g) of the Clean Air Act Amendments.

It is estimated that a probable lethal dose is between 5 to 50 mg/kg. Effects on the lung, such as upper respiratory tract irritation and congestion have been noted at acrolein levels ranging from 0.17 ppm to 0.43 ppm (ATSDR 1999, DHHS 1993).

Acrolein is considered to have high acute toxicity, based on short-term animal tests such as the LC_{50} test in rats. (ATSDR 1999, DHHS 1993).

Neurotoxicity

None documented.

Chronic toxicity

The major effects from chronic inhalation exposure to acrolein in humans consist of general respiratory congestion and eye, nose, and throat irritation. Acrolein is a strong dermal irritant, causing skin burns in humans. Animal studies have reported that the respiratory system is the major target organ for acrolein toxicity (ATSDR 1999, DHHS 1993, Calabrese and Kenyon 1991).

The Reference Concentration (RfC) for acrolein is 0.00002 mg/m^3 based on squamous metaplasia and neutrophilic infiltration of nasal epithelium in rats (US EPA 2003).

EPA has high confidence in the studies on which the RfC was based because adequate numbers of animals were used, careful attention was paid to experimental protocol, and together they demonstrated a consistent profile of histopathological changes in the respiratory system.

EPA has calculated a provisional Reference Dose (RfD) of 0.02 mg/kg/d for acrolein (US EPA 2003).

Carcinogenic effects

Limited animal cancer data are available; one inhalation study in rats reported no evidence of tumors in the respiratory tract or in other tissues and organs, while another study reported an increased incidence of adrenocortical tumors in female rats exposed to acrolein in drinking water (ATSDR 1999, US EPA 2003).

EPA has classified acrolein as a Group C, possible human carcinogen based on limited evidence of carcinogenicity in animals, the structural similarity of acrolein to substances possibly carcinogenic to humans, the carcinogenic potential of one of its metabolites, and the lack of human data (US EPA 2003).

Reproductive effects

No information is available on the reproductive or developmental effects of acrolein in humans. In the one available reproductive animal study, rats were exposed to acrolein by inhalation, with no effects observed on the number of pregnancies or the number and weights of the fetuses.

Teratogenic and developmental effects

Acrolein has been reported to cause birth defects in rats when injected directly into the embryonic tissue (ATSDR 1999).

Mutagenic effects

Acrolein is mutagenic in bacteria and is structurally related to probable or known human carcinogens (US EPA 1994).

Endocrine effects

No information available.

Skin sensitization

Acrolein has shown to be a skin and eye irritant. An acute percutaneous LD_{50} for rabbits was detected at 231 mg/kg (Tomlin 2000).

VII. Routes of Human Exposure

The substance can be absorbed into the body by inhalation of its vapor and by ingestion but information regarding the chronic toxicity of acrolein to humans is scarce (IPCS 1992). Acutely acrolein acts primarily as an irritant to the eyes and respiratory tract. The Lowest Observed Adverse Effect Limit (LOAEL) for eye irritation is 0.06 ppm (0.14 mg/m^3) acrolein for five minutes (Darley et al. 1960). In this study, 36 healthy human volunteers were exposed to 0.06 ppm (0.14 mg/m^3) for 5 minutes. Only volunteers without a prior

history of chronic upper respiratory or eye problems were included in the study. Subjects wore carbon-filter respirators during exposure, so that only the eyes were exposed to the test mixture. Subjects reported a significant incidence of eye irritation in a questionnaire following the exposure.

Kane et al. (1979) proposed the highest concentration suitable for a human air quality standard was 0.002 ppm (0.005 mg/m^3).

VIII. Environmental Toxicological and Ecological Effects

Birds

The acute oral LD_{50} for bobwhite quail is 19 mg/kg and for mallard ducks is 30.2 mg/kg. These studies were for technical grade material, however the maximum rate indicated for use is 15mg/l water so the potential exposure is substantially reduced under normal conditions.

Fish

Acrolein is lethal to fish at concentrations of 1-5 mg/l. The LC_{50} at 24 hours exposure for rainbow trout is 0.15 mg/l, bluegill sunfish 0.079 mg/l, shiners 0.04 mg/l and mosquito fish 0.39 mg/l (Tomlin 2000).

Amphibians

A toxic dose (observed effects) for the frog and toad order anura was reported at 4-6 ppm (PAN 2003).

Non-target aquatic organisms

It is known that the half-life of acrolein in the environment is temperature and concentration dependent, with a dissipation half-life of approximately seven hours (Nordone et al. 1996, Bowmer and Higgins 1976). Nordone (1998) was unable to detect acrolein or its major metabolites in the tissues of crayfish, channel catfish, bluegill, and freshwater clam and suggested that the rapid biodegradation of acrolein in natural waters is followed by the rapid and complete metabolism of the parent and water-borne metabolites in the tissues of all four species tested.

The LC_{50} (48 h) for Daphnia is 22 ppb, 0.01 mg/l for shrimp and 0.46 mg/l in oysters.

IX. Environmental Fate

Transport and Degradation Pathways

Degradation of acrolein in natural water-sediment and sterile water-sediment aquatic conditions has indicated that microbial degradation plays a significant role in the transformation of acrolein in aquatic systems, with a reduction in half-life being associated with the presence of viable microbial populations (Smith et al. 1995). In a Californian Field Dissipa-

tion Study, the half-life of acrolein was measured to be 7.5 hrs in a non-weed canal, and 10 hrs in a weeded canal. (Baker Petrolite Corporation 1999).

Both sterile and non-sterile systems resulted in the production of the primary hydrolytic degradation product, 3-hydroxypropanal. Several metabolic products that were ephemeral in nature were also found, including acrylic acid, allyl alcohol, propionic acid, propanol, and 3-hydroxypropionic acid. The terminal metabolites were oxalic acid and carbon dioxide.

Following high application rates to water lettuce (*Pistia stratiotes*), no acrolein was detected one day following the last applications. The degradation half life (DT_{50}) in water is 150 hours at pH 5, 120-180 hours at pH 7, and 5-40 hours at pH 9. Acrolein is easily metabolized in soil, being mineralized to CO_2. In field dissipation studies, DT_{50} is 7.5-10.2 hours. Oxidation, reduction and hydration have all been proposed as metabolic pathways.

DT_{50} in water is 150 hours (pH 5), 120-180 hours (pH 7), 5-40 hours (pH 9). Acrolein is metabolized easily in soil, being mineralized to CO_2. In field dissipation studies, a DT_{50} of 7.5-10.2 hours was detected. Metabolic pathways involving oxidation, reduction, and hydration have been proposed (Tomlin 2000).

Mode of Action on Target Organism

Acrolein is a general cell toxicant that reacts with various vital proteins. The dead plant tissues gradually disintegrate and float downstream, with the disintegration taking from three days to two weeks.

X. Toxicity Values of Acrolein on Select Aquatic Species

Table 11. Acrolein LC_{50} values for Bluegill Sunfish.

Duration	Effect	Result(µg/l)	Reference
24h	LC_{50}	22.4	Baker Petrolite 1990
48h	LC_{50}	22.4	Baker Petrolite 1990
72h	LC_{50}	22.4	Baker Petrolite 1990
96h	LC_{50}	22.4	Baker Petrolite 1990
96h	LC_{50}	24ppb	Baker Petrolite 1990
96h	LC_{50}	90	Macek et al. 1976
96h	LC_{50}	100	Macek et al. 1976

Table 12. Acrolein Exposure Effects for Rainbow Trout.

Duration	Effect	Result(µg/l)	Reference
1h	Avoidance	100	Folmar 1976
4h	Tainted flesh (1 & 4 days Past exposure)	90	Folmar 1980
24h	LC_{50}	65	Bond 1959
48h	32% mortality	48	Bartley and Hattrup 1970
96h	LC_{50}	24	Baker Petrolite 1990

Table 13. Acrolein Exposure Effects for Fathead Minnow.

Duration	Effect	Result(µg/l)	Reference
48h	LC_{50}	115	Louder and McCoy 1962
6d	Incipient LC_{50}	84	Macek et al. 1976

Table 14. LC_{50} Values for Various Aquatic Species.

	Duration	Effect	Result(ppb)	Reference
Water Flea	48h	LC_{50}	83 ppb	LeBlanc 1980
Snail	24h	LC_{50}	200 ppb	Hopf and Miller 1960
Sheephead Minnow	96h	LC_{50}	430 ppb	USEPA
Largemouth Bass (Flow through Conditions)	24h	LC_{50}	1183 ppb	Louder and McCoy 1962

Table 15. US EPA Ambient Water Quality for Acrolein LC_{50}/EC_{50} Values.

	LC_{50} /EC_{50} (µg/l)	Species Mean Acute Value	Reference
Water Flea	57	-	Macek 1976
	80	68	U.S. EPA 198
Bluegill	100	95	Louder and McCoy 1962
Largemouth Bass	160	160	Louder and McCoy 1962

Table 16. NOEC Values for Various Aquatic Species.

	Effect	Result	Reference
Mysid shrimp	NOEC	0.036 ppm	Baker Petrolite 1994
Eastern Oysters	NOEC	0.13 ppm	Baker Petrolite 1994
Goldfish	NOEC	11.4 ppb	Bridie et al. 1979
Sheephead Minnow (Flow through Conditions)	NOEC	0.13 ppb	Baker Petrolite 1994

Table 17. LOEC Values for Various Aquatic Species.

	Duration	Effect	Result	Reference
Algae				
Selenastrum capricornutum	5 days	EC_{50}	0.05 µg/l	Tomlin 2000
Anabaena flos-aquae	5 days	EC_{50}	0.04 µg/l	Tomlin 2000
Navicula pelliculosa	5 days	EC_{50}	0.07 µg/l	Tomlin 2000
Skeletonema costatum	5 days	EC_{50}	0.03 mg/L	Tomlin 2000
Duckweed				
Lemna gibba	14 days	EC_{50}	0.07 mg/L	Tomlin 2000

XI. Method Detection Limits

Table 18. Acrolein Method Detection Limits.

Analytical Method	MDL	Source
603[1]	0.7 µg/L	US EPA 2001
PFPH / GC/ECD[2]	5.0 ppm	Tulelake Irrigation District 1994
Hewlett Packard 5890 GC[3]	05 ppm	Nordone et al. 1996
HPLC-UV [4]	<10 g	Syracuse Research Corp.1990
NMR[5]	5000 ppm	Syracuse Research Corp.1990
Flourescence spectrometer[6]	>20 ppm	Syracuse Research Corp.1990
Differential pulse polarography[7]	>30 ppb	Syracuse Research Corp.1990

[1] US EPA minimum detection limit for acrolein using the purge and trap chromatographic method #603 was found to be 0.7 mg/L. (US EPA 2001)
[2] The minimum detection limit for acrolein using the pentafluorophenylhydrazine (PFPH) gas chromatography/electron capture detector (GC/ECD) method was found to be 5ppb (Tulelake Irrigation District 1994)
[3] A Hewlett Packard 5890 gas chromatograph used with an electron capture detector at 350 °C was found to have a detection limit of of 0.05 ppm (Nordone et al. 1996).
[4] Trap on zeolite ZSM-5 column, elute with acetonitrile, derivatize with 2,4-DNP (Ogawa and Fritz 1985)
[5] Nondirect measurement of aldehyde signal compared to signal for a calibrated sealed external TMS standard (Kissel et al. 1978)
[6] Dilution of sample with deionized water (Kissel et al. 1978)
[7] Dilution of sample with deionized water, addition of phosphate buffer and EDTA (Kissel et al. 1978)

XII. Manufacturer Contact Info.

Baker Petrolite
12645 West Airport Blvd.
Sugar Land, Texas 77478
1-800-231-3606

XIII. Summary Table

Table 19. Acrolein Summary Table.

Primary use	Nonselective contact aquatic herbicide. Used for submerged macrophytes and algae in habitats with rapid flow, such as irrigation canals and drainage ditches.
Mechanism of Toxicity	Reacts with the sulfhydryl component of enzymes. Breaks down cell walls and disrupts cell's ability to inactivate toxins.
Solubility	208,000 ppm at 20^{o}C
Fate	Highly reactive and volatile. Significant microbial degradation typically causes half-life of <1 day to several days. Not retained in sediment. Does not bioaccumulate due to very low log K_{ow} (~1.0).
Confounding Factors	None identified
Data Gaps	Toxicity tests with repeated concentration measurements to account for volatilization. Chronic effects measurements in zooplankton, amphipods, or insects.

B. Copper Sulfate

I. Introduction

Copper sulfate is a naturally occurring inorganic salt. In addition to its' use as a pesticide, copper is also an essential trace element for plant and animal nutrition.

Copper sulfate is a fungicide, algaecide, and molluscicide. As a fungicide it is used to control bacterial and fungal diseases of fruit, vegetable, nut, and field crops. Such diseases include mildew, leaf spots, blights, and apple scab. For leaf application and seed treatment, Bordeaux Mixture is used as a protective fungicide. Bordeaux mixture is a combination of copper sulfate and lime and without the addition of lime the copper sulfate would be toxic to most plants.

Copper sulfate is used as an algaecide in irrigation and municipal water treatment systems. As a molluscicide is it used to repel and kill slugs and snails. Copper sulfate is used as an aquatic pesticide in its basic copper sulfate, copper sulfate pentahydrate, and chelated copper sulfate forms.

Washington State has written an Environmental Impact Statement Report on copper sulfate compounds that is extensive in its review of the scientific literature.

II. Active Ingredient ID

Synonyms

Basic copper sulfate: BSC Copper Fungicide; CP Basic Sulfate; Tri-Basic Copper Sulfate

Pentahydrate copper sulfate: Copper sulfate, Copper sulfate pentahydrate, Bluestone, Cupric sulfate pentahydrate, Sulfuric acid copper (2+) salt, pentahydrate, Copper (II) sulfate, pentahydrate (1:1:5), Blue copperas, Blue vitriol, Triangle, Hi-Chel, Roman Vitrol, Blue Copper AS, 7758998, Sulfato de cobre, Copper sulphate, Copper as elemental, present as copper sulphate, Copper sulphate pentahydrate, cuivre du sulfate, Copper sulfate pentahydrate, Cutrine, Cutrine-Plus.

Bordeaux Mixture: a combination of copper sulfate, hydrated lime and copper sulfate.

Structural Formula

$CuSO_4 \cdot 5H_20$

Active Ingredient Indentification

Table 20. Active Ingredient Identification Summary Table.

Characteristic	Value	Source
CAS Number	7758-98-7 (pentahydrate), 1344-73-6 (basic) 7758-98-7 (anhydrous)	
Molecular Weight	249.7 (pentahydrate form)	
Molecular Formula	$CuSO_4$ (basic form) $CuH_{10}O_9S$ (pentahydrate form)	
USEPA PC Code	024408	US EPA 2001
CA DPR Chemical Code	161	PAN 2003
USEPA Chemical Class	Inorganic-Copper	PAN 2003
WHO/FAO Chemical Group	Not Available	

III. Physical Properties

Appearance

Copper sulfate is available in crystal, dust, wetable powders, and fluid concentrates. All forms are deep blue in color.

Stability

Copper sulfate in both crystal and liquid form are very stable. In dry forms, it is slowly efflorescent in air. When heated, it loses two molecules of water of crystallization at 30°C, two more molecules at 110°C, and becomes anhydrous at 250°C. In liquid form, by reaction with alkalis, copper oxide is produced. With ammonia and amines, colored complexes are formed. With most organic acids, sparingly soluble salts are formed.

Physical Properties

Table 21. Physical Properties Summary Table.

Characteristic Value		Source
Specific Gravity	2.286 at 15.6°C	
Melting Point	147°C	
Boiling Point	653°C	
Vapor Pressure	Non-volatile	Tomlin 2000
Water Solubility	230.5 µg/kg at 25°C	Tomlin 2000
Solubility in Other Solvents	Insoluble	Tomlin 2000
Partition Coefficient (K_{ow})	Not Available	
Adsorption Coefficient (K_{oc})	Not Available	
Henryís Constant (K_h)	Not Available	
Half-Life	Not Available	
Dissipation Rate	Not Available	

IV. Active Ingredient Regulatory Status

Table 22. Regulatory Status.

Agency/ Regulatory Category	Regulatory Status	Source
UNEP Persistent Organic Pollutant	Not Listed	PAN 2003
UNEP Prior Informed Consent Chemical	Not Listed	PAN 2003
WHO/FAO Pesticide Primary Use	Not Available	
USEPA Registered Pesticide Active Ingredient	Not Available	
USEPA Pesticide Use Type	General use pesticide. Algaecide, Fungicide, Insecticide, Water Treatment, Molluscicide, Nematicide	EXTOXNET 1996 PAN 2003
USEPA Toxicity Class (Pesticide Products)	I	EXTOXNET 1996
USEPA Signal Word (Pesticide Products)	Danger-Poison	EXTOXNET 1996
USEPA Reregistration	Yes	PAN 2003
USEPA Hazardous Air Pollutant	Not Listed	PAN 2003
USEPA Minimum Risk Pesticide (25b list)	No	PAN 2003
CA Registered Pesticide Active Ingredient	Yes	PAN 2003
CA Toxic Air Contaminant	Not Listed	PAN 2003
CA Groundwater Contaminant	Not Listed	PAN 2003
PAN "Bad Actor"	Not Listed	PAN 2003
PAN "Dirty Dozen"	Not Listed	PAN 2003

V. Pesticide Status

Pests Controlled

Copper sulfate-base products are registered for use as an algaecide to control algal and aquatic plant growth. As a fungicide it is used to control bacterial and fungal diseases of fruit.

Pesticide Trade and Other Names

There are three hundred and four listed trade names for both active and cancelled products (PAN 2003)

Formulations and Dosages

Cutrine-Plus Algacide/Herbicide is used for the treatment of a wide range of algae and the rooted aquatic plant hydrilla (*Hydrilla verticillata*).

Table 23. Cutrine-Plus Algacide Application Rates (from 1988 Cutrine-Plus product label).

Application Rates
Gallons Per Surface Acre

ALGAE TYPE	PPM COPPER	DEPTH IN FEET 1	2	3	4
Planktonic	0.2	0.6	1.2	1.8	2.4
Filamentous	0.2	0.6	1.2	1.8	2.4
Chara/Nitella	0.4	1.2	2.4	3.6	4.8

Table 24. Cutrine-Plus Herbicide Application Rates (from 1988 Cutrine-Plus product label).

Application Rates
Gallons/Surface Acre*

Growth/Stage Relative Density	PPM Copper	DEPTH IN FEET 1	2	3	4	5	6
Early Season Low Density	0.4 0.5	1.2 1.5	2.4 3.0	3.6 4.5	4.8 6.0	6.0 7.5	7.2 9.0
	--0.6--	--1.8--	--3.6--	--5.4---	---7.2---	--9.0--	--10.8---
Mid-Season Moderate Density	0.7	2.1	4.2	6.3	8.4	10.5	12.6
	--0.8--	--2.4--	--4.8--	--7.3---	---9.6---	--12.0--	--14.4---
Late Season/ High Density	0.9 1.0	2.7 3.0	5.4 6.0	8.1 9.0	10.8 12.0	13.5 15.0	16.2 18.0

* Application rates for depths greater than six feet may be obtained by adding the rates given for the appropriate combination of depths. Application rates should not result in excess of 1.0 ppm copper concentration within treated water.

Application methods: Before applying, dilute the required amount of Cutrine-Plus with enough water to ensure even distribution with the type of equipment being used. Surface spray/injection or drip system application.

Komeen Aquatic Herbicide is used for the removal of a variety of aquatic plant species including Hydrilla, Elodea, Water Lettuce and Water Hyacinth.

VI. Toxicity to Humans and Other Mammals

Absorption Route

The usual routes by which humans receive toxic exposure to copper sulfate are through skin or eye contact, as well as by inhalation of powders and dusts.

Fate in mammals and excretion products

Copper is an essential trace element that is strongly bioaccumulated. It is stored primarily in the liver, brain, heart, kidney and muscles. About one-third of all the copper in the body is contained in the liver and brain. Another third is contained in the muscles. The remaining third is dispersed in other tissues (Gangstad 1986).

Mode of action

Absorption of copper sulfate into the blood occurs primarily under the acidic conditions of the stomach; the mucous membrane lining of the intestines acts to some extent as a barrier to absorption of ingested copper (EXTOXNET 1996).

Acute toxicity

The lowest copper sulfate dose considered toxic when ingested by humans is 11 mg/kg (NIOSH 1986). Ingestion of copper sulfate is often not toxic because vomiting is automatically triggered by its irritating effect on the gastrointestinal tract. Effects are severe, however, if copper sulfate is retained in the stomach (i.e. if the ingestor is unconscious). Some of the signs of poisoning which occur after ingestion of 1-12 grams of copper sulfate include a metallic taste in the mouth, burning pain in the chest and abdomen, intense nausea, vomiting, diarrhea, headache, sweating, shock, discontinued urination leading to yellowing of the skin. Injury to the brain, liver, kidneys, stomach, and intestinal linings may also occur in copper sulfate poisoning (Clayton 1981).

Copper sulfate is classified as a strong irritant (Windholz 1983). It is readily absorbed through the skin and can produce a burning pain, along with the same severe symptoms of poisoning from ingestion. Skin contact may result in itching or eczema (EXTOXNET 1996). Eye contact with this material can cause: conjunctivitis; inflammation of the eyelid lining; excess fluid buildup in the eyelid; cornea tissue deterioration due to breaks, or ulceration in the eye's mucous membrane; and clouding of the cornea (Clayton 1981).

The LD_{50} for copper sulfate is 30 mg/kg in rats. Ingestion by animals of three ounces of a 1% solution of copper sulfate will produce extreme inflammation of the gastrointestinal tract, with symptoms of abdominal pain, vomiting, and diarrhea. When copper sulfate is given intravenously, or injected into the vein, as little as 2 mg/kg copper sulfate is lethal to guinea pigs; and 4 mg/kg is lethal to rabbits (EXTOXNET 1996).

Examinations of copper sulfate-poisoned animals showed signs of acute toxicity in the spleen, liver and kidneys (EXTOXNET 1996). Injury may also occur to the brain, liver, kidneys, and gastrointestinal tract in response to overexposure to this material (Clayton 1981).

Neurotoxicity

A study conducted by the University of Missouri indicated that copper may play an important role in the neurotoxicity of brain lesions that characterize Alzheimer Disease (Yusof 2001).

Chronic toxicity

Vineyard sprayers experienced liver disease after 3 to 15 years of exposure to copper sulfate solution in Bordeaux mixture. Chronic exposure to low levels of copper can lead to anemia (EXTOXNET 1996).

The growth of rats was retarded when 25 mg/kg of copper sulfate was included in their diets. Starvation and death resulted with the addition of 200 mg/kg to the rat's diet (EXTOXNET 1996). Sheep with access to salt licks that contained five to nine percent copper sulfate showed signs of absence of appetite, anemia, and degenerative changes, followed by death within one or two days of exposure (Clayton 1981).

Carcinogenic effects

Ten mg/kg of copper sulfate caused endocrine tumors in chickens given the material parenterally, that is, outside of the gastrointestinal tract through an intravenous or intramuscular injection (NIOSH 1986).

Reproductive effects

Developing embryos were resorbed in pregnant hamsters given copper salts intravenously on the eighth day of gestation. Testicular atrophy increased in birds as they were fed larger amounts of copper sulfate. Sperm production was also interrupted to varying degrees (EXTOXNET 1996). Reproduction and fertility was affected in pregnant rats given this material on the third day of pregnancy (NIOSH 1986).

Teratogenic and developmental effects

Heart disease occurred in the surviving offspring of pregnant hamsters given intravenous copper salts on the eighth day of gestation (EXTOXNET 1996).

Mutagenic effects

At 400 and 1,000 ppm, copper sulfate caused mutations in two types of microorganisms (NIOSH 1986).

Endocrine effects

Seven cases of enlargement of the sella turcica, nonsecretive hypophyseal adenoma, accompanied by obesity, arterial hypertension, and "red facies" were observed in 75–111 workers exposed to 111–434 mg Cu/m^3 as copper dust (Suciu et al. 1981). The study authors noted that there was a possibility that the clinical manifestations of hypophyseal adenoma or of Cushing's syndrome may have been the result of a disturbance of copper metabolism. The significance of this effect and its relationship to copper exposure cannot be determined.

Skin sensitization

Copper sulfate causes severe skin irritations (Tomlin 2000).

VII. Routes of Human Exposure

Copper and its compounds are naturally present in the earth's crust. Natural discharges to air and water, such as windblown dust, volcanic eruptions, etc., may be significant. Therefore, it is important to consider the background levels that are commonly found in order to distinguish these from levels that can be attributed to anthropogenic activity. The

median concentration of copper in natural water is 4–10 ppb.

Copper compounds may also be intentionally applied to water to kill algae. Of special concern is copper that gets into drinking water from the water distribution system. When the system has not been flushed after a period of disuse, the concentration of copper in tap water may exceed 1.3 ppm, the EPA drinking water limit. The general population may be exposed to high concentrations of copper from drinking water that has picked up copper from the distribution system (both from the water treatment plant and in the home). Contact with available copper may also result from using copper fungicides and algicides (ATSDR 2002).

VIII. Environmental Toxicological and Ecological Effects

Birds

Copper sulfate poses less of a threat to birds than to other animals. The oral LD_{50} for Bordeaux mixture in young mallards is 2,000 mg/kg (Tucker 1970).

Fish

Copper sulfate is very toxic to fish. Its toxicity to fish varies with the species and the physical and chemical characteristics of the water. Even at recommended rates of application, this material may be poisonous to trout and other fish, especially in soft or acid waters. Its toxicity to fish generally decreases as water hardness increases (Pimental 1971). Fish eggs are more resistant than young fish fry to the toxic effects of copper sulfate. Very small amounts of this material can have damaging effects on fish (Gangstad 1986).

Amphibians

Frogs died after being given intravenous doses of 25 mg/kg of copper sulfate. The 96-hour LC50 of copper sulfate to pond snails is 0.39 mg/l, at 20°C. Higher concentrations of the material caused some behavioral changes, such as secretion of mucous, and discharge of eggs and embryos (EXTOXNET 1996).

Non-target Aquatic Organisms

Copper sulfate is toxic to aquatic invertebrates, such as crab, shrimp and oysters (US EPA 1986). Hartley (1983) considers bees to be endangered by strong, water-based copper compounds, such as a Bordeaux mixture of copper sulphate, lime and water. Most animal life in soil, including large earthworms, has been eliminated by the extensive use of copper-containing fungicides in orchards (Pimentel 1971).

IX. Environmental Fate

Transport and Degradation Pathways

Three simultaneous processes control the fate of copper sulfate in the environment. It can be: (a) transported to lower soil levels by groundwater percolation; (b) partly bound to

soil components; and (c) partly changed into different metabolites, or breakdown products (Hartley 1983).

Copper is considered to be among the more mobile of the heavy metals in surface environments. Copper is bound, or adsorbed, to organic materials, and to clay and mineral surfaces. The degree of copper adsorption to soils depends on the level of acidity or alkalinity of the soil. The distance that it can travel in soil is limited by its strong adsorption to many types of surfaces. All applied copper will become a part of the soil copper content. Although copper sulfate is highly water soluble, the copper ions are strongly adsorbed or precipitated to soil particles when it is applied to soil (EXTOXNET 1996). The leaching potential of this material is low in all but sandy soils.

Mode of Action in Environment

Copper is an aquatic algaecide and foliar fungicide with protective action. Deposits must be on the crop before fungal spores begin to germinate. The copper ion (Cu^{2+}) is taken up by the spores during germination and accumulates until a sufficiently high concentration is achieved to kill the spore cell.

X. Toxicity Values of Copper Sulfate for Select Aquatic Species

LC_{50} Values for Various Aquatic Species

Table 25. Copper Sulfate LC_{50} Values for Various Aquatic Species.

	Duration	Effect	Result mg/L	Reference
Water Flea	3 week	LC_{50}	0.044	Harrison and Bishop 1984
Water Flea	50% loss of reproduction		0.035	Harrison and Bishop 1984
Water Flea	72hr	LC_{50}	0.068-.087	Harrison and Bishop 1984
Bluegill	96-h	LC_{50}	12.5	Patrick et al. 1968
Bluegill	24-h	LC_{50}	46 ppm	WSSA 1989
Rainbow trout	14-d	LC_{50}	0.87	Calamari and Marchetti 1973
Rainbow trout	48-hr	LC_{50}	0.8	Herbert et al. 1964
Rainbow trout	48-hrs	LC_{50}	0.75(hardwater)	Brown and Dalton 1970
Chinook salmon	42-96 hr	LC_{50}	0.178-0.318	Holland 1960
Golden shiners	96-hr	LC_{50}	630 (hardwater)	Finlayson 1980
Golden shiners	96-hr	LC_{50}	67 (softwater)	Finlayson 1980
Golden shiners	96-hr	LC_{10}	410 (hardwater)	Finlayson 1980
Golden shiners	96-hr	LC_{10}	8 (softwater)	Finlayson 1980

EC_{50} Values for Select Aquatic Species

Table 26. Copper Sulfate EC50 Values for Various Aquatic Species.

	Parameters	**Result mg/L**	**Reference**
Ceriodaphnia dubia	Hardness 50mg/L	0.01249	Belanger et al. 1989
Ceriodaphnia dubia	Hardness 50mg/L	0.02400	Belanger et al. 1989
Daphnia Magna	Hardness 100mg/L	0.01047	Belanger et al. 1989
Daphnia Magna	Hardness 100mg/L	0.02012	Belanger et al.1989

NOEC/LOEC Values for Select Aquatic Species

Table 27. Copper Sulfate NOEC/LOEC Values for Select Aquatic Species.

Ceriodaphnia dubia	4 day	NOEC=0.03 mg/L	Oris et al. 1990
Ceriodaphnia dubia	4 day	LOEC=0.04 mg/L	Oris et al. 1990

Survival/Spawning of Yearling Brook Trout.

Table 28. Survival/Spawning of Yearling Brook Trout after Eight Months' Exposure to Various Concentrations of Copper.

Mean Copper Concentration (ug/L)	**32.5**	**17.4**	**9.5**	**1.9(control)**
Survival (%)	43	93	86	93
Total Viable Eggs Spawned	316	1263	1046	1310

Source: McKim and Benoit 1971

After 8 months' exposure to copper, the highest concentration of copper (32.5 ug/L) significantly decreased survival and egg production was significantly less than at the control concentration.

Toxicity/Chemical Results for Copper and Fathead Minnow Larvae.

Table 29. Toxicity/Chemical Results for Copper and Fathead Minnow Larvae using a Water-Effect Ratio.

Month	Water	LC_{50}(µg/L)
January	Stream	692
	Laboratory	297
April	Stream	1,975
	Laboratory	145.8
June	Laboratory	225

Source: Diamond et al. 1997

LC_{50} Values of Komeen for Select Aquatic Species

Table 30. Komeen LC_{50} Values for Select Aquatic Species.

	Duration	Effect	Result mg/L	Reference
Bluegill	96-hr	LC_{50}	1250	Rodgers et al. 1992
Rainbow Trout	96-hr	LC_{50}	57-574	Rodgers et al. 1992
Largemouth Bass	96-hr	LC_{50}	6970	Rodgers et al. 1992
White perch	96-hr	LC_{50}	6200	Rodgers et al. 1992
Striped bass	96-hr	LC_{50}	4000-4300	Rodgers et al. 1992

XI. Method Detection Limits

Table 31. Copper Method Detection Limits.

Analytical Method	MDL	Reference
AA (graphite furnace atomic absorption spectroscopy)	5 ppb	Oris et al. 1990

XII. Manufacturer Contact Info:

There are numerous chelated copper pesticide manufacturers. Contact information for them can be obtained from the California Department of Pesticide Regulation <www.dpr.ca.gov>.

XIII. Summary Table

Table 32. Copper Sulfate Summary

Primary use	Aquatic herbicide – algaecide. Used extensively in drinking water reservoirs.
Mechanism of Toxicity	Photosynthesis and cell growth inhibitor. Cu^{2+} is primary toxic form.
Solubility	230,550 ppm at 25°C (anhydr ous)
Fate	Highly water soluble with no degradation. Strong particle and DOC affinity causes rapid sediment deposition. Transport occurs between water and sediment (advection/flux).
Confounding Factors	Toxicity is temperature, pH, and hardness dependent, with greater toxicity in softer waters. Bioavailability is influenced by sorption to DOC and particles.
Data Gaps	Toxic effects on amphibian embryos and larvae, and chronic effects to benthic invertebrates.

C. Diquat Dibromide

I. Introduction

Diquat dibromide is an herbicide and plant growth regulator. It is a quick-acting contact herbicide, causing injury only to the parts of the plant to which it is applied. It causes superoxide production during photosynthesis, which damages cell membranes and cytoplasm. As a nonselective desiccant, it causes all vegetative material it contacts to dry out.

Diquat dibromide is naturally broken down in the environment and leaves little residue on or in plants, soil, or water in areas where the compound is applied. It is used for preharvest desiccation of seed crops, control of annual broad-leaved weeds in other crop fields and control of emergent and submerged aquatic weeds. In 1982, the US EPA estimated that 67% of all diquat dibromide was used in commercial/industrial applications and 33% was used for aquatic uses.

Diquat formulations have low acute toxicity (Howe and Wright 1965, Cobb and Grimshaw 1979) and are not persistent in water (Coats et al. 1964, Grezenda et al. 1966, Langeland and Warner 1986). Therefore, the herbicide can be used in waters that are used for swimming, irrigation, and consumption by livestock, and domestic purposes. However, to provide maximum safety, the water cannot be used for consumptive purposes (overhead irrigation, consumption by livestock, or drinking) for 14 days after applications or until an approved analysis shows that the water does not contain more than the established potable water tolerance of 10ppb diquat cation.

II. Active Ingredient ID

Synonyms

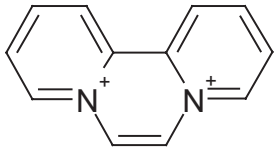
6,7-dihydrodipyrido[1,2-a:2',1'-c] pyrazinediium

1,1'-ethylene-2,2'-bypyridyldiylium

9,10-dihydro-8a,10a-diazoniaphenanthrene

6,7-dihydrodipyrido-[1,2-a:2',1'-c] pyrazine-5,8-di-ium

Structural Formula



Active Ingredient Identification

Table 33. Active Ingredient Characteristics.

Characteristic	Value	Source
CAS Number	85-00-7	PAN 2003
Molecular Weight	344.1	PAN 2003
Molecular Formula	$C_{12}H_{12}Br_2N_2$	PAN 2003
USEPA PC Code	032201	PAN 2003
CA DPR Chemical Code	229	PAN 2003
USEPA Chemical Class	Bipyridylium	PAN 2003

III. Physical Properties

Appearance

Diquat dibromide is an organic solid of colorless to yellow crystals. In water solution the compound is a dark red-brown.

Stability

Stable in neutral and acidic solutions, but readily hydrolyzed in alkaline solutions. DT_{50} at pH=7 in exposure to simulated sunlight is 74 days. DT_{50} under ultraviolet irradiation is less than one week.

Physical Properties

Table 34. Physical Properties Summary Table.

Characteristic	Value	Source
Specific Gravity	1.61 at 25°C	Tomlin 2000
Melting Point	Decomposition above 325°C	Tomlin 2000
Boiling Point	NA	Tomlin 2000
Vapor Pressure	<0.01 mPa	Tomlin 2000
Water Solubility	In water=700g/L at 20°C	Tomlin 2000
Solubility in Other Solvents	In alcohols and hydroxylic solvents=25g/L In non-polar organic solvents= 0.1g/L	Tomlin 2000
Partition Coefficient (K_{ow})	-3.05 to -4.60 (20°C)	EXTOXNET 1996 Tomlin 2000
Adsorption Coefficient	1,000,000 (soil)	EXTOXNET 1996
Henryís Constant (K_h)	5 X 10^9 Pa m^3 mol^{-1} (calc)	Tomlin 2000
Half-Life	<1000 days in soil & ground water, >48 hrs in water column, ~160 days in sediment	EXTOXNET 1996

IV. Active Ingredient Regulatory Status

Table 35. Active Ingredient Regulatory Status.

Agency/ Regulatory Category	Regulatory Status	Source
UNEP Persistent Organic Pollutant	Not Listed	PAN 2003
UNEP Prior Informed Consent Chemical	Not Listed	PAN 2003
USEPA Registered Pesticide Active Ingredient	Yes	PAN 2003
USEPA Pesticide Use Type	General use pesticide	EXTOXNET 1996
USEPA Toxicity Class (Pesticide Products)	II	EXTOXNET 1996
USEPA Signal Word (Pesticide Products)	Warning	PAN 2003
USEPA Hazardous Air Pollutant	Not Listed	PAN 2003
USEPA Minimum Risk Pesticide (25b list)	No	PAN 2003
CA Registered Pesticide Active Ingredient	Yes	PAN 2003
CA Toxic Air Contaminant	Candidate	PAN 2003
CA Groundwater Contaminant	Potential	PAN 2003
PAN "Bad Actor"	Not Listed	PAN 2003
PAN "Dirty Dozen"	Not Listed	PAN 2003

V. Pesticide Status

Pests Controlled

Diquat dibromide-based products are registered for use as herbicides and plant growth regulators. It is a nonselective desiccant and used on crops and for aquatic weed control. It is used to control aquatic weeds such as water milfoils (*Myriophyllum* spp.) and coontail (*Ceratophyllum demersum* spp.) and floating weeds such as duckweeds (*Lemna* spp.), water hyacinth *(Eichhornia crassipes*) and water lettuce (*Pistia stratiotes*).

Pesticide Trade and Other Names

Aquacide, Dextrone, Reglone, Reglox, Weedtrine-D, Aquakill, Vegetrole, Deiquat, Reglon, Tag, Reward, Pathclear, Weedol, and Cleansweep.

Formulations and Dosages (summarized in part from Reward label)

Diquat dibromide is formulated as a liquid and gel. The diquat label requires the application of two gallons/acre to control certain species of aquatic vegetation. The maximum label application rate is 7 kg per hectare when used for aquatic weed control (Peterson et al. 1997).

Reward is used with a mixture of 75% or more nonionic spreader or nonionic surfactant and water. Amount of Reward and water vary according to intended use.

Table 36. Reward (Diquat Dibromide) Application Rate.

Water Depth	Rate of Reward per Treated Surface Area
>2 feet	0.5-1.0 gal
2-4 feet	1.0-2.0 gal
5 feet	1.0-2.5 gal
6 feet	1.0-3.0 gal
7 feet	1.0-3.5 gal
8 feet	1.0-4.0 gal
9 feet	1.0-4.5 gal
10 feet	1.0-5.0 gal
11 feet	1.0-5.5 gal
12 feet	1.0-6.0 gal

Sixty percent of diquat dibromide useage as an aquatic herbicide is in Florida, followed by 13% in Michigan (Ritter et al. 2000). California accounts for approximately 3-4% of total use. The aquatic weed problem is related to the extent of surface water, climate, weed species, and factors affecting dissemination of aquatic plants (e.g. interconnections between waterways and intensity of recreational activities). Application sites include lakes and reservoirs, canals, and ponds that have macrophyte growth (i.e. shallow depths, warm temperatures, low current, and little turbidity). In lake applications, diquat dibromide is typically applied around the shoreline as a spot treatment to less than 5% of the surface area of the lake, however in the West up to 20% of the surface area may be treated (Ritter et al. 2000).

Diquat dibromide is often applied to clear boat trails in the center of a waterway where water depths would be one to four meters deep (Ritter et al. 2000). Canal applications typically occur in bands along the shoreline. The entire surface area of a pond could be treated where weed beds are not dense. Where treatment of dense weed beds is necessary, treatment is restricted to less than one-half the surface area of the water body at one time, with a 14-day delay before subsequent treatments. Applications are generally made from a boat or by hand gun from the water bank, thus minimizing off-target drift. In Florida and California, repeat applications of diquat dibromide may be necessary to control regrowth of aquatic weeds (Ritter et al. 2000). Other states typically have only one application per season.

VI. Toxicity to Humans and Other Mammals

Absorption Route

Absorption routes for diquat are via ingestion or skin contact. Absorption of diquat dibromide from the gut into the bloodstream is low. Oral doses are mainly metabolized within the intestines, with metabolites being excreted in the feces (Stevens and Sumner 1991).

Fate in mammals and excretion products

Rat studies showed only a small percentage of the applied oral dose (6%) was absorbed into the bloodstream and then excreted in the urine. Dermal, inhalation, or intravenous exposure results in little processing and rapid elimination in the urine. Following subcutaneous injection in rats, excretion of about 90% of the dose occurred in the urine on the first day and almost all of the remainder on the next day. Complete elimination of the herbicide was seen in urine and feces of rats within four days of administration of single oral doses of 5 to 10 mg/kg of diquat dibromide (Stevens and Sumner 1991).

Mode of action

Based on records of suicidal ingestion of diquat by humans as well as diquat-feeding studies of monkeys, it has been concluded that diquat is most harmful to the gastrointestinal tract (GIT), kidneys, and liver. Severe congestion and ulceration of the stomach and bowel are produced by the herbicide. After large doses of diquat are given, there is evidence of stretching and irritation of the GIT and thickening of the walls of the alveoli, or air cells of the lungs (Gosselin 1984). When enough diquat is given, the fat in the liver goes through extreme changes. Acute death occurs in the cells of the small glandular tubes that process urine in the kidney. Cataracts are caused when smaller amounts of diquat are given. While diquat dibromide appears to primarily affect the tissue lining of the eye lens and the kidneys, water is apparently removed from other tissues as well. Dehydration can result. The amount of water that is removed depends on how much diquat dibromide is given (Hayes 1982).

Acute toxicity

Diquat dibromide is classified as a moderately toxic chemical. It may be fatal to humans if swallowed, inhaled, or absorbed through the skin. Concentrated solutions may

cause severe irritation of the mouth, throat, esophagus and stomach followed by nausea, vomiting, diarrhea, severe drying out of bodily tissues, gastrointestinal discomfort, chest pain, diarrhea, kidney failure, and liver damage (Occupational Health Service 1986, 1991, WSSA 1989). Very large doses of the herbicide can result in convulsions and tremors (WSSA 1989). Rats given lethal doses of diquat showed few signs of illness during the first 24 hours. They then exhibited lethargy, pupil dilation, respiratory distress, weight loss weakness, and finally death over the course of 2 to 14 days after dosing. Similar patterns of symptoms occurred in mice, guinea pigs, rabbits, dogs, cows, and hens (Hayes 1990).

Diquat dibromide is toxic when it is absorbed through the skin and the possibility for poisoning increases with repeated exposure. Dermal adsorption is higher where the skin is cut or abraded (WSSA 1989). Although absorption is reportedly low following dermal exposure, the demonstrated toxicity of this compound is sufficient to raise serious human health concerns. When absorbed through the skin, some commercial concentrate formulations of diquat can cause symptoms similar to those that occur when it is eaten. There have been reports of workers who have had softening and color changes in one or more fingernails after contact with concentrated diquat dibromide solutions. In some instances, the nail was shed and did not regenerate (Hayes 1982). A single dose of diquat was not irritating to the skin of rabbits. However, repeated dermal doses cause mild redness, thickening, and scabbing (Hayes 1990).

Diquat dibromide also causes eye irritation. Several cases of severe injury to human eyes have been reported after accidental splashings. In each case, initial irritation was mild, but after several days serious burns and sometimes scarring of the cornea developed (Gangstad 1986). Moderate to severe membrane irritation occurred when diquat was put in the eyes of rabbits.

Direct or excessive inhalation of diquat dibromide spray mist or dust may result in oral or nasal irritation, nosebleeds, headache, sore throat, coughing, and symptoms similar to those from ingestion of diquat (Hayes 1982).

The oral LD_{50} for diquat in rats is 120 mg/kg, 233 mg/kg in mice, 188 mg/kg in rabbits, 187 mg/kg in guinea pigs and dogs. Cows appear to be particularly sensitive to this herbicide, with an oral LD_{50} of 30 to 56 mg/kg (American Conference of Governmental Industrial Hygienists 1986, Occupational Health Service 1991). The acute dermal LD_{50} for diquat dibromide is 250-400 mg/kg in rabbits (Worthing 1983).

Neurotoxicity

After evaluating the available database, the Hazard Identification Assessment Review Committee (HIARC) determined that there was no evidence of increased sensitivity to infants and children and that a developmental neurotoxicity study was not required (US EPA 2001).

No indication of abnormalities in the development of the fetal nervous system were observed in the prenatal developmental toxicity studies in rats, rabbits, or mice at maternally toxic oral doses up to 56, 4, or 10 mg/kg/day, respectively. Although in one prenatal study in rats, an increase of expanded lateral ventricle of the brain was observed, this finding was

observed in only one litter, was not supported by findings in the other developmental studies, and was not considered indicative of treatment-related toxicity to the developing nervous system.

In acute and subchronic neurotoxicity studies in rats, no evidence of neuropathology was observed following perfusion of tissues (US EPA 2001).

Chronic toxicity

Cataract formation is the most significant effect of chronic exposure to diquat that is currently recognized. Cataracts occurred in rats and dogs given 2.5 mg/kg and 5 mg/kg of diquat, respectively (Gangstad 1986). The number of cases of cataracts is dose dependent and increased in test animals (cats and dogs) as the amount of diquat was increased in their diets (American Conference of Governmental Industrial Hygienists 1986). However, a single, near-fatal dose will not produce cataracts, chronic exposure is necessary (Hayes 1990).

The effects of repeated, or prolonged, dermal contact with diquat dibromide range from inflammation of the skin, to general bodily ('systemic') poisoning, as evidenced by injury to internal organs, primarily the kidneys. Chronic exposure may damage skin, which allows more absorption of the herbicide. Repeated applications of 42 mg/kg of diquat killed four out of six rabbits tested (Occupational Health Service 1986). While rats fed 50 mg/kg of diquat for two years did not die from testing, their food intake and growth was decreased (American Conference of Governmental Industrial Hygienists 1986).

Repeated inhalation exposure of rats of up to 1.9 mg/m^3 caused inflammatory changes in connective tissues, damage to the kidneys and heart, abnormal levels of several liver enzymes, low white blood cell counts, high red blood cell counts, and depressed cholinesterase activity (Occupational Health Service 1991).

Carcinogenic effects

Diquat dibromide is not classified as a tumor-causing chemical (Clayton 1981, Gosselin 1984). An 80-week feeding study showed that dietary doses of 15 mg/kg/day of diquat did not cause tumors in rats. Likewise, dietary levels of 36 mg/kg/day for two years did not induce tumors in rats (Hayes 1990).

Reproductive effects

Diquat dibromide does not cause reproductive effects. It did not reduce fertility when tested in experimental animals. Rats receiving 25 mg/kg decreased their food intake and showed slowed growth, but had unchanged reproduction. Fertility was reduced in male mice given diquat dibromide during different stages of sperm formation (Hayes 1982). Neither fertility nor reproduction was affected in a three-generation study in rats given dietary doses of 0, 12.5 or 25 mg/kg/day of diquat dibromide, although some growth retardation was seen at the 25 mg/kg/day dose (Hayes 1982).

Teratogenic and developmental effects

The EPA does not consider diquat capable of causing teratogenic effects (US EPA

1997). However, diquat dibromide is thought by other researchers to have the potential to cause birth defects. It is referred to as an experimental teratogen based on a study that showed teratogenic effects in six-day pregnant rats given intravenous injections of diquat. A lowest published toxic dose, or TDLO, of 7 mg/kg resulted from a study by Sax (1984). Growth retardation was seen in test animals given extremely high doses of diquat. No deformities were found in the unborn offspring of pregnant rats that were injected intraperitoneally with 0.5 mg/kg of diquat daily during organogenesis, the stage of fetal development in which organs are formed (Gangstad 1986). Pregnant rats died when they were injected with 14 mg/kg of diquat dibromide. Upon examination of the unborn rats, there was evidence of skeletal defects of the collarbone, as well as little or no ear bone formation (Shepard 1986). While no actual teratogenesis occurred in rats given single abdominal injections during the 7th to 14th days of pregnancy, many rats did not have normal weight gain and bone formation in the unborn was decreased (Sax 1984).

Mutagenic effects

EPA has required more testing on the capability of this herbicide to cause mutations, since available information is contradictory. Diquat dibromide is not known to cause permanent changes in genetic material and is therefore not considered a mutagen. No mutagenic effects were seen in mice given 10 mg/kg of diquat orally for five days (Clayton 1981).

Endocrine effects

EPA is in the process of developing criteria for characterizing and testing endocrine disrupting chemicals and plans to implement an Endocrine Disruptor Screening Program. Diquat dibromide will be reevaluated at that time and additional studies may be required (US EPA 2002).

Skin sensitization

The acute dermal LD_{50} for diquat dibromide is approximately 400 to 500 mg/kg in rabbits, indicating moderate toxicity by this route as well (WSSA 1994, Steven 1991). A single dose of diquat dibromide was not irritating to the skin of rabbits, but repeated dermal dosing did cause mild redness, thickening, and scabbing (WSSA 1994). Moderate to severe eye membrane irritation occurred when diquat dibromide was administered to rabbits (Chevron 1986a). Ingestion of sufficient doses may cause severe irritation of the mouth, throat, esophagus, and stomach, followed by nausea, vomiting, diarrhea, severe dehydration, and alterations in body fluid balances, gastrointestinal discomfort, chest pain, diarrhea, kidney failure, and toxic liver damage (Stevens and Sumner 1991). Skin absorption of high doses may cause symptoms similar to those that occur following ingestion (Chevron 1986b). Very large doses of the herbicide can result in convulsions and tremors (Chevron 1986b).

VII. Routes of Human Exposure

With correct usage, the general population should not be exposed to diquat. However, diquat residues in treated food crops showed to be in between 0.04 mg/kg in potatoes to 4.0 mg/kg in barley (INCHEM 1970).

VIII. Environmental Toxicological and Ecological Effects

Birds

Diquat dibromide ranges from moderately toxic to practically nontoxic to birds, depending on the species. The acute oral LD_{50} in twelve young male mallards was 564 mg/kg. Signs of poisoning in these birds included instability, wing-drop and lack of movement (Hudson 1984). The oral LD_{50} for diquat was 200-400 mg/kg in hens (Clayton 1981).

Fish

Diquat dibromide is slightly toxic to fish. Its toxicity to fish, and food organisms on which fish survive, has been reported in many studies. It appears to be less toxic in hard water. The 8-hour LC_{50} for diquat in rainbow trout is 12.3 ppm, and 28.5 ppm in Chinook salmon (Pimentel 1971). The 96-hour LC_{50} in northern pike is 16 ppm and 20.4 ppm in fingerling trout (Simonin 1977). The shell growth of eastern oysters was not noticeably affected with exposure to 1 ppm of diquat for 96 hours (Pimentel 1971).

Some species of fish may be harmed, but not actually killed, by sublethal levels of diquat dibromide. Oxygen can become depleted in diquat-treated water by decaying aquatic plants. This decreases the amount of oxygen available for fish survival. Research indicates that yellow perch suffer significant respiratory stress when herbicide concentrations in the water are similar to those normally present during aquatic vegetation control programs (Bimber 1976).

There is little or no bioconcentration of diquat dibromide in fish. Pimentel's (1971) investigation into the persistence of diquat in fish showed that one half of the herbicide was lost in less than three weeks.

Paul et al. (1994) felt it possible for diquat applied according to label instructions to be present in concentrations lethal to early life stages of several game fish. The safe use of diquat seems to depend upon the removal of the active ingredient through binding to sediment and/or organic material. However, they felt that, even after accounting for the removal of diquat from the water column by sediment, their data predict that toxic concentrations will exist in shallow regions of the lake. If incomplete mixing occurs, the concentration of diquat in some regions would be even higher that those predicted by the label instructions. Paul et al. (1994) recommended that diquat be applied as a dilute spray to reduce pesticide 'hot spots' and that its use should be discouraged in lakes containing sensitive fish species at times when early life stages will be present. Jones (1985) also felt that bass were sensitive to diquat and that great caution should be exercised in its use.

Amphibians

The most current risk assessments indicate that diquat is not available to most living things when bound to sediment and soil. In addition, diquat is toxic to some invertebrates but less toxic to birds and amphibians (DSEIS 2002).

Non-target aquatic organisms

Since diquat dibromide is a nonselective herbicide, it may present a danger to non-target plant species (US EPA 1986).

Research indicates that yellow perch suffer significant respiratory stress when herbicide concentrations in the water are similar to those normally present during aquatic vegetation control programs (Bimber 1976).

IX. Environmental Fate

Transport and Degradation Pathways

Since diquat is purposely applied to water to control the growth of aquatic weeds, its ability to last as an effective residue has been studied carefully. These studies suggest that diquat is not persistent in water. The fate of diquat residues in the environment following application for weed control are governed by the complex interaction of numerous factors. These factors include: the physicochemical characteristics of the herbicide, application practices, the chemical and biological characteristics of the water column and benthic sediments, and hydrodynamic conditions of the waterbody before and after treatment.

The environmental fate of diquat dibromide is governed primarily by its adsorption to soil and plant matter as evidenced by its high organic carbon coefficients (Ferguson et al. 1994). In the presence of soil and sediment particles, it is rapidly biologically inactivated through its strong binding to the clay minerals. Uptake of diquat dibromide into aquatic macrophytes has been observed (Newman and Way 1966, Cavell and McIntosh 1976, Austin and Calderbank 1964); however, adsorption coefficients are difficult to quantify from these studies because of the simultaneous high adsorption to sediments and the lack of measurable residues in the dissolved phase. Adsorption to minerals is rapid and complete with only trace amounts (less than 0.01%) remaining in solution. However, once adsorbed and no longer available to target organisms, the diquat can remain in the soil environment for an extended period of time. Diquat has been found in pool and pond sediment four years after application (Gangstad 1986).

The diquat dibromide remaining in the water column is degraded by microorganisms (Summers 1980) with a half-life of less than 48 hours in water (EXTOXNET 1996). In addition to microbial degradation, photochemical degradation is important and can be rapid in aqueous solution or on plant surfaces and will be dependent on the characteristics of the aqueous system and the presence of plants exposed to diquat (Tegala and Skidmore, 1987, WHO 1984). Processes such as hydrolysis, volatilization, and oxidation are relatively insignificant with respect to dissipation in the environment.

Mode of Action on Target Organisms

Diquat is a non-selective contact herbicide for emergent and submerged aquatic plants that causes superoxide to be generated during photosynthesis, which damages cell membranes and cytoplasm and eventually leads to desiccation and death.

Table 37. Diquat Toxicity Values for Select Aquatic Species.

Common Name	Species	Age Class	End-Point	Time (days)	NOEC (ppb c.e.)	LOEC (ppb c.e.)	LC_{50} (ppb c.e.)	EC_{50} (ppb c.e.)	Reference**
Daphnid	*Daphnia magna*	life cycle	reproduction and growth	21	36	57			DSEIS 2002
Daphnid	*Daphnia magna*	life cycle	survival	2			32-1620		DSEIS 2002
Daphnid	*Daphnia magna*	first-instar	Immobalization (behavior)	1				3800	DSEIS 2002
Amphipod*	*Hyalella azteca*	4-8 mm	survival	4			48		DSEIS 2002
Amphipod*	*Hyalella azteca*	4-8 mm	survival	2			12-64		DSEIS 2002
Fathead minnow	*Pimephales promelas*	egg to fry	Weight reduction	34	120	320			DSEIS 2002
Fathead minnow	*Pimephales promelas*		survival	4			7600-70,000		DSEIS 2002
Bluegill	*Lepomis macrochirus*	Sac-Fry	survival	12	>10000	>10000			DSEIS 2002
Eastern brook trout	*Salvelinis fontanilis*	eggs to sac-fry	Abnormal sac-fry	NR	2700	5400			DSEIS 2002
Channel catfish	*Ictalurus puntatus*	egg to fry	Weight reduction	NR	>1000	>1000			DSEIS 2002
Killifish	*Fundulus heteroclitus*	egg to fry	Abnormal pigmentation and slow development	32	5.4	5.4			DSEIS 2002
Walleye	*Stizostedion vitreum*	8-10 day fry	survival	4	480	930	750		Paul et al. 1994
Smallmouth Bass	*Micropterus dolomieu*	6-8 d fry	survival	4	1600	3400	3900		Paul et al. 1994
Largemouth Bass	*Micropterus salmoides*	9-13 d fry	survival	4	1800	3600	4900		Paul et al. 1994
Green algae	*Selenastrum capricornutum*		14CO2 uptake	0.9				492	DSEIS 2002
Green algae	*Selenastrum capricornutum*		Cell density	3				96	DSEIS 2002
Green algae	*Selenastrum capricornutum*		Chl levels	3				73	DSEIS 2002
Green algae	*Selenastrum capricornutum*		Growth rate	4				19	DSEIS 2002
Green algae	*Selenastrum capricornutum*		Biomass growth	4	44	88		80	Fairchild et al. 1997
Green algae	*Selenastrum capricornutum*		Growth rate	7				480	DSEIS 2002
Green algae	*Selenastrum capricornutum*		Cell density	7				47	DSEIS 2002
Green algae	*Selenastrum capricornutum*		Chlorophyll levels	7				26	DSEIS 2002
Duckweed	*Lemna minor*		Biomass growth	4	<11	11		18	Fairchild et al. 1997

*Hyalella azteca has been found to be a relatively sensitive invertebrate to diquat.

** DSEIS 2002 compiles many primary references. Refer to that document for specific references cited.

c.e. = a specific chemical form expression of diquat

XI. Method Detection Limits

Table 38. Diquat Method Detection Limits.

Analytical Method	MDL	Reference
HPLC/UV detection	0.72 ug/L (ppb)	Munch and Bashe 1997

XII. Manufacturer Contact Info

Syngenta International AG
P.O. Box CH-4002
Basel, Switzerland
http://www.syngenta.com

XIII. Summary Table

Table 39. Diquat Dibromide Summary Table.

Primary use	Non-selective contact herbicide for emergent and submerged aquatic plants. Surfactant use is recommended.
Mechanism of Toxicity	Causes superoxide to be generated during photosynthesis, which damages cell membranes and cytoplasm. Leads to desiccation.
Solubility	700,000 ppm at 20°C
Fate	Water column concentrations typically drop below detection within days to weeks after application. This results from binding to particles and sediment and retention in plant tissue. Biodegradation and photolysis may be minor loss pathways. Low Kow suggests low bioaccumulation potential.
Confounding Factors	Greater toxicity to fish in soft waters and at low pH. Binds to organic matter (TSS; plant biomass).
Data Gaps	Chronic effects on invertebrates (e.g. *Hyallela azteca*)

D. Endothall

I. Introduction

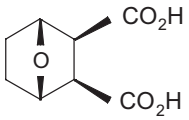
Endothall is a member of the dicarboxylic acid chemical class (Thomson 1993, Bohmont 1981). It is a selective contact herbicide. The potassium and amine salts of endothall are used as aquatic herbicides to control a variety of plants including plankton, pondweed, niad, coontail, milfoil, elodea, and algae in water bodies and rice fields. Endothall is also used to control annual grass and broadleaf weeds in sugar beets, spinach and turf. It reduces sucker branch growth in hops. Endothall is a desiccant to aid the harvest of alfalfa, potatoes, clover, and cotton (Kidd and James 1991). The EPA has classified endothall as Toxicity Class II - moderately toxic. Products containing endothall bear the SIGNAL WORD: WARNING (Meister 1994).

II. Active Ingredient ID

Synonyms

Endothall is endothal in Great Britain. Trade names for the acid form of endothall (technical endothall) include Aquathol, Hydrothal-47 and Hydrothal-191. Trade names for the disodium salt of endothall (disodium endothall) include Accelerate, Des-I-Cate, Tri-endothal, Ripenthol, Hydrothol, and Niagrathol (Kidd and James 1991). The amine salt of endothall is also called Hydrothol (NIOSH 1986).

Structural Formula



Active Ingredient Identification Summary Table

Table 40. Endothall Active Ingredient Identification Summary.

Characteristic	Value	Source
CAS Number	2164-07-0	Crop Data Management Systems MSDS
Molecular Weight	186.2	Tomlin 2000
Molecular Formula	$C_8H_{10}O_5$	Tomlin 2000
USEPA PC Code	038904 (Dipotassium salt)	EPA 2002
CA DPR Chemical Code	1356 (Dipotassium salt)	DPR 2002
USEPA Chemical Class	dicarboxylic acid	EXTOXNET 1995

III. Physical Properties

Appearance

Technical endothall is a colorless or white crystal, which is stable to light, weak acidic media and weak alkaline media. Faint odor (EXTOXNET 1995).

Stability

Stable to light. Stable up to 90°C, above which it undergoes a slow conversion to the anhydride. Endothal is a dibasic acid, and forms water-soluble amine and alkali-metal salts. Completely soluble in water.

Physical Properties Summary Table

Table 41. Endothall Physical Properties Summary Table.

Characteristic	**Value**	**Source**
Specific Gravity	0.739 µg/cm^3	Elf Atochem MSDS 2000
Melting Point	144^{o}C	EXTOXNET 1995
Boiling Point	NA	Elf Atochem MSDS 2000
Vapor Pressure	2.09 X 10^{-5} mPa (24.3^{o}C)	Tomlin 2000
Water Solubility	100 g/kg (20^{o}C)	Tomlin 2000
Solubility in Other Solvents	Methanol 280, dioxane 76, acetone 70, isopropanol 17, diethyl ether 1, benzene 0.1 (all in g/kg (20^{o}C))	Tomlin 2000
Partition Coefficient (K_{ow})	-2.09 (unstated pH)	Tomlin 2000
Adsorption Coefficient (K_{oc})	750.0	PAN 2001
Henryís Constant (K_h)	3.8 X 10^{-13} Pa m^3 mol^{-1} (calc.)	Tomlin 2000
Half-Life	4-7 days	Reinert and Rodgers 1987
Dissipation Rate		

IV. Active Ingredient Regulatory Status

Table 42. Endothall Active Ingredient Regulatory Status.

Agency/ Regulatory Category	Regulatory Status	Source
UNEP Persistent Organic Pollutant	Not listed	UNEP 2002
UNEP Prior Informed Consent Chemical	Not listed	UNEP 2002
WHO/FAO Pesticide Primary Use		
USEPA Registered Pesticide Active Ingredient		
USEPA Pesticide Use Type	General Use Pesticide	EXTOXNET 1995
USEPA Toxicity Class (Pesticide Products)	Toxicity Class II – moderatly toxic	EXTOXNET 1995
USEPA Signal Word (Pesticide Products)	Warning	EXTOXNET 1995
USEPA Reregistration	Yes	PAN 2003
USEPA Hazardous Air Pollutant	Not listed	PAN 2003
USEPA Minimum Risk Pesticide (25b list)	No	PAN 2003
CA Registered Pesticide Active Ingredient	Yes	PAN 2003
CA Toxic Air Contaminant	Not listed	PAN 2003
CA Groundwater Contaminant	Potential	PAN 2003
PAN "Bad Actor"	Not listed	PAN 2003
PAN "Dirty Dozen"	Not listed	PAN 2003

V. Pesticide Status

Pests Controlled

Used in water to control a variety of plants including plankton, pondweed, niad, coontail, milfoil, elodea, and algae.

Pesticide Trade and Other Names

Accelerate (mixture of mono- and di- (N,N-dimethylalkylammonium) salts)

Herbicide 273 (dipotassium salt)

Formulations and Dosages

It is available as granules or as a soluble concentrate (Kidd and James 1991).

VI. Toxicity to Humans and Other Mammals

Absorption Route

Soo et al. (1967) studied the distribution of endothall in nine female rats using the dosing regimen mentioned above. After receiving the radioactive endothall, rats were sacrificed at intervals ranging from 1 to 72 hours for analysis of radioactivity in tissues. The results indicate that the majority was present in the stomach and intestine (95%) with the next highest levels detected in the liver and kidney. Very low levels were measured in other tissues. After 72 hours, all tissue levels had returned to zero and only a trace of the compound remained in the gastrointestinal tract. These results indicate relatively poor absorption of endothall.

In the same report, Soo et al. (1967) administered labeled endothall to two lactating rats to determine whether endothall was secreted in milk The animals received a daily oral dose of 0.2 mg endothall (in 10% sucrose solution) for five consecutive days prior to delivery. After birth, dams received a daily dose of 0.4 mg endothall in 10% sucrose solution for five consecutive days. After sacrifice of the pups, no radioactivity was detected in any of the tissues or stomach contents suggesting that endothall was not secreted into the milk of lactating rats.

Fate in mammals and excretion products

In rats dosed with technical endothall, over 95% of the dose was excreted within 48 hours. Within 72 hours after dosing, 99% of the dose was excreted. Approximately 90% of a dose of technical endothall is excreted in the feces and 7% in urine (US EPA 1987).

Mode of action

Endothall is an inhibition of messenger RNA activity, decreasing the rate of respiration and lipid metabolism, inhibiting protein synthesis and interfering with normal cell division. Endothall tends to kill by contact action (except in aquatic weed control) (CA EPA 1997).

Acute toxicity

The oral LD_{50} for disodium endothall is 51 mg/kg for rats and 250 mg/kg for guinea pigs (Sax 1984, Meister 1992). The LD_{50} is 750 mg/kg for rats and 100 mg/kg for rabbits whose skin is exposed to disodium endothall (Sax 1984, Hayes 1991, Ware 1986). In humans, ingestion of 7 to 8g of disodium endothall causes repeated vomiting, hemorrhages, swelling in the lungs, and bleeding in the gastrointestinal tract (US EPA 1987). The LD_{50} for the amine salt of endothall is 206 mg/kg for rats and 143 mg/kg for rabbits whose skin is exposed to it (Sax 1984, Kidd and James 1991). The oral LD_{50} for technical endothall is 38 mg/kg for rats. Endothall is very irritating to the eyes, skin, and mucous membranes (Sax 1984, Kidd and James 1991, Bohmont 1981).

Neurotoxicity

No information available.

Chronic toxicity

Table 43. Endothall Chronic Toxicity Effects.

	Duration	Effect	Result mg/L	Reference
Walleyes	96 hours	LOEC	11mg/L	Paul et al. 1994
Walleyes	96 hours	NOEC	5.7mg/L	Paul et al. 1994
Smallmouth Bass	96 hours	LOEC	45mg/L	Paul et al. 1994
Smallmouth Bass	96 hours	NOEC	23mg/L	Paul et al. 1994
Largemouth Bass	96 hours	LOEC	100mg/L	Paul et al. 1994
Largemouth Bass	96 hours	NOEC	50mg/L	Paul et al. 1994

Carcinogenic effects

No statistically significant numbers or types of tumors were observed in rats fed as much as 125 mg/kg/day of disodium endothall for two years. Thus, available evidence suggests that endothall does not cause cancer (US EPA 1987).

Reproductive effects

A three-generation study was conducted by feeding male and female rats disodium endothall until they were 100 days old and then mating them. Three successive generations were maintained on the test diet for 100 days and then bred to produce the next generation. When examined at 21 days, rat pups in all three generations whose parents were given 15 mg/kg/day of disodium endothall had decreased body weights. No adverse reproductive effects were observed (NOEL) at 5 mg/kg/day (US EPA 1987). There were no observable signs of developmental toxicity at dose levels that were fatal to the females (US EPA 1987).

Teratogenic and developmental effects

Technical endothall was not teratogenic at the highest dose tested, 30 mg/kg/day (US EPA 1987).

Mutagenic effects

Studies show that technical endothall is not mutagenic in Salmonella bacteria nor in mouse cells. Aquathol K, a formulation of dipotassium endothall, is not mutagenic in fruit flies, mold, or human white blood cells. However, "commercial endothall," with no further description, was mutagenic in fruit flies (US EPA 1987).

Endocrine effects

No information available.

Skin sensitization

Endothall is very irritating to the eyes, skin, and mucous membranes (Sax 1984, Kidd and James 1991, Bohmert 1981). Acute percutaneous LD_{50} for rabbits >2,000 mg/L (acid) (Tomlin 2000).

Organ Toxicity

In male dogs, high doses of 20 mg/kg/day of disodium endothall for 6 weeks caused vomiting, diarrhea, damaged intestinal walls, and hemorrhages in the stomach. In rats, very high doses of 50 mg/kg/day of disodium endothall for four weeks caused liver and kidney damage (US EPA 1987).

VII. Routes of Human Exposure

Based on its limited use in food crops endothall is not monitored for in surveys conducted of residues in fresh produce in California (DPR 1993). Endothall applied to rice paddy fields was not detected in harvested rice (Maini 1992).

VIII. Environmental Toxicological and Ecological Effects

Birds

No information is currently available (EXTOXNET 1995).

Fish

Endothall is toxic to some species of fish (Kidd and James 1991). Inorganic salts of endothall in aquatic formulations are safe to fish in 100-500 ppm concentrations. However, amine salts of endothall are more toxic to fish than the dipotassium endothall (Reinert 1987). Endothall has a low toxicity to crustaceans and a medium toxicity to aquatic insects (Briggs 1992). Long-term ingestion may cause severe damage to the digestive tract, liver and testes in fish (Gosselin 1984).

Amphibians

No information available.

Non-target organisms

Endothall is not toxic to bees (Kidd and James 1991).

IX. Environmental Fate

Transport and Degradation Pathways

Endothall is highly mobile in soil, however rapid degradation limits the extent of leaching. Endothall disappears from soil in 7-21 days (Kidd and James 1991). The half-life of endothall in soil is four to five days in clay soils and nine days in soils with high organic content (Howard 1991).

Endothall is rapidly degraded in water (Kidd and James 1991, USEPA 1994). Its half-life is four to seven days for dipotassium endothall and about seven days for technical endothall in surface water (Reinert 1987). It biodegrades more slowly when air is not present (Howard 1991).

Mode of Action on Target Organisms

The potassium and amine salts of endothall are used as selective, contact aquatic herbicides to control a variety of plants including plankton, pondweed, niad, coontail, milfoil, elodea, and algae in water bodies and rice fields at 2-6kg active ingredient /ha. Endothall inhibits messenger RNA activity, thereby decreasing the rate of respiration and lipid metabolism, inhibiting protein synthesis and interfering with normal cell division.

X. Toxicity Values for Select Aquatic Organisms

Walker (1963) reported a 96-h LC_{50} for largemouth bass of 120 mg/L, which is very similar to the 131 mg/L determined by Paul et al. (1994). Young walleyes are much more sensitive with a 96-h LC_{50} of 16 mg/L (Paul et al. 1994).

Table 44. Endothall Toxicity Values for Select Aquatic Organisms.

	Duration	Effect	Result mg/L	Reference
Midge larvae	72 hours	LC_{50}	120 mg/L	USACE 2002
Amphipod	96 hours	LC_{50}	320 mg/L	USACE 2002
Walleyes	96 hours	LC_{50}	16 mg/L	Paul et al. 1994
Smallmouth Bass	96 hours	LC_{50}	47 mg/L	Paul et al. 1994
Largemouth Bass	96 hours	LC_{50}	130 mg/L	Paul et al. 1994
Bluegill	96 hours	LC_{50}	0.9 mg/L	Helfrich et al. 1996
Rainbow Trout	96 hours	LC_{50}	0.1 mg/L	Helfrich et al. 1996
Chinook Salmon	96 hours	LC_{50}	82 mg/L	USACE 2002
Dimethylalkylamine Endothall				
Largemouth Bass	96 hours	LC_{50}	0.1-0.3 mg/L	USACE 2002
Bluegill	96 hours	LC_{50}	0.06-0.2 mg/L*	USACE 2002
Redear Sunfish	96 hours	LC_{50}	0.1-0.2 mg/L	USACE 2002

*Diamine salt. Dimethylalkylamine salt of endothall is more toxic than the dipotassium salt to fish and other non-target organisms. Increasing water temperature causes a slight increase in toxicity of this formulation (USACE 2002).

XI. Method Detection Limits

The method detection limit for endothall is reported at 0.7 µg/L. The MDL may differ from this value depending upon the nature of interferences in the sample matrix (US EPA 1992). Chemical analysis for endothall is by GLC (Gas-Liquid Chromatography) with FID (Flame Ionization Detector) (Certified EPA method 548.1).

XII. Manufacturer Contact Info

Atofina Chemicals Inc.
2000 Market Street
Philadelphia, PA 19103-3222 United Statea
phone: +1 (215) 419 70 00
fax: +1 (215) 419 75 91
webmaster@ato.com
www.atofinachemicals.com

XIII. Summary Table

Endothall

Table 45. Endothall Summary Table.

Primary use	The potassium and amine salts of endothall are used as selective, contact aquatic herbicides to control a variety of plants including plankton, pondweed, niad, coontail, milfoil, elodea, and algae in water bodies and rice fields at 2-6kg active ingredient /ha.
Mechanism of Toxicity	Inhibition of messenger RNA activity. Decreasing rate of respiration and lipid metabolism, inhibiting protein synthesis and interfering with normal cell division.
Solubility	100 g/L at 20^{o}C
Fate	Endothall is rapidly degraded in water. Its half-life is four to seven days for dipotassium endothall and about seven days for technical endothall in surface water. It biodegrades more slowly in anoxic conditions.
Confounding Factors	Dimethylalkylamine salt of endothall is more toxic than the dipotassium salt to fish and other non-target organisms. Increasing water temperature causes a slight increase in toxicity of this formulation.
Data Gaps	Resident Species. Chronic effects on invertebrates (e.g. *Hyallela azteca* and *Ceriodaphnia*).

E. Fluridone

I. Introduction

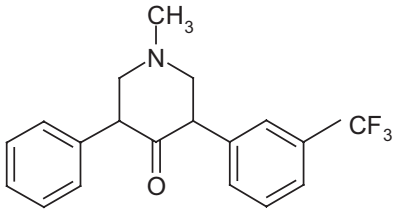
Fluridone is a selective systemic herbicide used to control most submerged and emerged aquatic plants. Fluridone works by reducing carotenoid biosynthesis, by inhibition of phytoene desaturase, which causes chlorophyll depletion and hence inhibition of photosynthesis. Fluridone takes 30-90 days to kill target plants, and should be applied before plants start to grow, or just after they begin to grow (WSDE 2001). Herbicidal symptoms appear in 7-10 days, but 30-90 days are required before weed management is obtained. Advisable application rate is 150 ppb (SePRO Corporation). There is no EPA standard for maximum allowable concentration (MCL) of fluridone in public water supplies (WSDH 2000). The lowest effective application concentration is 10-20 ppb (WSDH 2000). The Sonar label prohibits application to water within one mile of functioning potable water intake, unless treatment is 20 ppb or less.

II. Active Ingredient ID

Synonyms

1-Methyl-3-phenyl-5-(3-(trifluoromethyl)phenyl)-4(1H)-pyridone; 4(1H)-Pyridone, 1-methyl-3-phenyl-5-(3-(trifluoromethyl)phenyl); EL 171, 1-methyl-3-phenyl-5-(a,a,a-trifluoro-m-tolyl)-4-pyridone, Sonar

Structural Formula



Active Ingredient Identification Summary Table

Table 46. Fluridone Active Ingredient Identification Summary Table.

Characteristic	Value	Source
CAS Number	59756-60-4	PAN 2001
Molecular Weight	329.3	PAN 2001
Molecular Formula	$C_{19}H_{14}F_3NO$	PAN 2001
USEPA PC Code	112900	
CA DPR Chemical Code	2279	PAN 2003
USEPA Chemical Class	Not available	PAN 2003
WHO/FAO Chemical Group		

III. Physical Properties

Appearance

In pure form, fluridone is a white to tan crystalline solid. In the form applied as SePRO's Sonar, fluridone is a dark gray or dark brown pellet.

Stability

Fluridone is stable under normal storage conditions, but is decomposed by UV radiation. The half-life of fluridone in sediment in an artificial pond under field conditions was 17 weeks (Muir and Grift 1982b). SONAR half-life with surface application is 11 days. SONAR half-life with bottom application is 24 days (West et al. 1983). Microorganisms are the primary factor responsible for the degradation of fluridone in terrestrial soils. The fluridone molecule rapidly photodegrades to several low molecular weight fragments that dissipate quickly from the water by volatilization, so photoproducts do not accumulate significantly in water (West et al. 1983). Time for fluridone residue to reach no detectable limits in the field range from eight weeks to 12 months (West et al. 1979). Impacts to vegetation persist long after application. Primary fate process is photolysis. Decreased temperatures and low light conditions in the fall can make fluridone persist for months longer (West et al. 1990).

Physical Properties

Table 47. Physical Properties Summary Table.

Characteristic	**Value**	**Source**
Specific Gravity	NA	
Melting Point	154°C	
Boiling Point	NA	
Vapor Pressure	0.013 mPa at 25°C	
Water Solubility	In water=12mg/L at 25°C	
Solubility in Other Solvents	Methanol, chloroform and diethyl ether >10; ethyl acetate >5; hexane <0.5	
Partition Coefficient (K_{ow})	LogP= 1.87 (pH7, 25c)	Tomlin 2000
Adsorption Coefficient (K_{oc})	$3.5X10^5$	
Henryís Constant (K_h)	3.57×10^{-4} Pa m^3 mol^{-1} (calc)	Tomlin 2000
Half-Life	20 days in water; under anaerobic aquatic conditions half-life is nine months	PMEP 1986
Dissipation Rate		

IV. Active Ingredient Regulatory Status

Table 48. Fluridone Active Ingredient Regulatory Status.

Agency/ Regulatory Category	Regulatory Status	Source
UNEP Persistent Organic Pollutant	Not Listed	PAN 2003
UNEP Prior Informed Consent Chemical	Not Listed	PAN 2003
WHO/FAO Pesticide Primary Use	Herbicide	PAN 2003
USEPA Registered Pesticide Active Ingredient		PAN 2003
USEPA Pesticide Use Type	Herbicide	PAN 2003
USEPA Toxicity Class (Pesticide Products)		
USEPA Signal Word (Pestcide Products)		
USEPA Reregistration		
USEPA Hazardous Air Pollutant	Not Listed	PAN 2003
USEPA Minimum Risk Pesticide (25b list)	No	PAN 2003
CA Registered Pesticide Active Ingredient	Yes	PAN 2003
CA Toxic Air Contaminant	Not Listed	PAN 2003

V. Pesticide Status

Pests Controlled

Aquatic vegetation in fresh water ponds, lakes, reservoirs, drainage canals, irrigation canals, and rivers.

Pesticide Trade and Other Names

Sonar

Formulations and Dosages:

Fluridone is applied by aqueous suspension and pellets. Mode of application is through a surface spray, weighted hose dragged near bottom or broadcast (pellet). Application rates are 0.5-4.0 lb active ingredient per surface acre. Additives and surfactants are not used with Sonar.

Application to Ponds

Table 49. Fluridone Application Rates for Ponds (from SePro Sonar product label).

Average Water Depth of Treatment Site (feet)	Pounds of Sonar PR Precision Release per Treated Surface Acre 45 ppb	90 ppb
1	2.5	5
2	5	10
3	7.5	15
4	10	20
5	12.5	25
6	15	30
7	17	34
8	19.5	39
9	22	44
10	24.5	49

Application to Lakes or Reservoirs

Table 50. Fluridone Application Rates for Lakes and Reservoirs (from SePro Sonar product label).

Average Water Depth of Treatment Site (feet)	Pounds of Sonar PR Precision Release Per Treated Surface Acre 16 ppb to	90 ppb
1	0.9	5
2	1.7	10
3	2.6	15
4	3.5	20
5	4.3	25
6	5.2	30
7	6.0	34
8	6.9	39
9	7.8	44
10	8.6	49
11	9.5	54
12	10.4	59
13	11.2	64
14	12.1	68
15	13.0	73
16	13.8	78
17	14.7	83
18	15.6	88
19	16.4	93
20	17.3	98

VI. Toxicity to Humans and Other Mammals

Absorption Route

Systemic absorption (ingestion) and potential risk from direct contact of herbicide with eyes and skin (WSDE 2001).

Fate in mammals and excretion products

No information available.

Mode of action

Fluridone is a systemic herbicide; it is absorbed from water by plant shoots and from hydrosoil by roots. It inhibits carotenoid synthesis, which enhances degradation of chlorophyll, producing white (chlorotic) growing points in susceptible plants.

Acute toxicity

Fluridone was administered to rats and mice as a single dose given either orally or subcutaneously. Dogs and cats received a single oral dose administered in capsules. The acute toxicity of an aqueous suspension formulation containing 45 percent fluridone was evaluated by administering a single application of the material to the skin or eyes of rabbits. Inhalation was evaluated in rats exposed for one hour to an atmosphere containing the compound or formulation. The toxic effects of these treatments are summarized below (WSSA 1983).

DERMAL: LD_{50} >2,000 g/kg (rat, technical); >500 mg/kg (rabbit, technical; no irritation); >2 ml/kg (rabbit, 2 AS; slight irritant); LD50 >2,000 mg/kg (mouse, technical);

ORAL: LD_{50} >10,000 mg/kg (rat, technical); >10,000 mg/kg (mouse, technical); LD50 >0.5 ml/kg (rat, 4 AS); >250 mg/kg (cat, technical); >500 mg/kg (dog, technical);

INHALATION: LC_{0} >2,130 mg/m3 of air (rat, technical); >9.6 ml/m3 of air (rat, 4AS);

EYES: Moderate irritant (rabbit, 44 mg/eye, technical); very slight irritant (rabbit, 0.1 ml/eye, 4 AS).

Neurotoxicity

No information available.

Chronic toxicity

Fluridone has been evaluated for a period of three months in rats, mice and dogs. An increase in liver and kidney weights as well as the histological identification of liver centrilobular hypertrophy occurred in rats fed diets containing 1,400 pm of fluridone. Liver centrilobular hypertrophy was also observed in mice receiving diets containing 560 ppm of fluridone. No treatment-related effects were noted in rats at dietary doses of 330 ppm or noted in mice at dietary doses of 62 ppm. No toxic effects were observed in dogs receiving up to 200 mg/kg/day of fluridone (WSSA 1983).

Carcinogenic effects

Fluridone is not considered to have produced an oncogenic response in the mouse or rat.

Reproductive effects

Fluridone is not considered to be a carcinogen or mutagen and is not associated with reproductive or developmental effects in test animals (WSDH 2000). In a three-generation rat reproduction test, the NOEL was 121 mg/kg daily (Tomlin 2000).

Teratogenic and developmental effects

A valid rabbit teratology study indicates no teratogenic response up to a dose level of 300 mg/kg/day (PMEP 1986).

Mutagenic effects

Mutagenicity assays submitted do not indicate genotoxic potential, gene mutation, or structural chromosomal aberration (PMEP 1986).

Endocrine effects

No information available.

Skin sensitization

Fluridone is was not found to be irritating to the skin, and only minor effects were noted after application of undiluted fluridone to the eyes of rabbits (WSDE 2001).

VII. Routes of Human Exposure

Routes by which the general public can be exposed are ingestion (drinking water and eating aquatic organisms) as well as incidental ingestion and dermal exposure (swimming) (WSDE 2001).

VIII. Environmental Toxicological and Ecological Effects

Birds

Fluridone was administered to one-week old mallard and bobwhite as a component of the diet for four days: avian dietary (bobwhite quail and mallard duck) >5,000 ppm. No impairment on reproduction was found for the above species up to 1,000 ppm dietary exposure. Fluridone was also given to adult bobwhite as a single dose: acute oral (bobwhite quail) >2,000 mg/kg (slightly toxic) (PMEP 1986).

Fish

The Pesticide Action Network (2003) reports that fluridone is moderately toxic to fish (LC_{50} 1,000-10,000 µg/L).

Amphibians

No information available.

Non-target aquatic organisms

The Pesticide Action Network (2003) reports that Fluridone is slightly toxic (LC_{50} 10,000-100,000 µg/L) for crustaceans, moderately toxic to fishes (LC_{50} 1,000-10,000 µg/L) and slightly toxic (LC_{50} 10,000-100,000 µg/L) to zooplankton. Kamarianos et al. (1989) found a drastic reduction of phytoplankton species shortly after fluridone application. The population of one phytoplankton group, Cyanophyceae, disappeared entirely after about 2 months.

IX. Environmental Fate

Transport and Degradation Pathways

Liquid fluridone residues reached a maximum in hydrosoils 14 days after application. No detectable residue (at a test sensitivity of 0.01 ppm) was observed after 62 days (WSDE 2001). West et al. (1990) noted that the dissipation of fluridone from hydrosoils was variable and slow relative to that observed in water. Sonar was applied to two lakes in Florida at a concentration of 0.15 ppm. The concentrations remaining in hydrosoil 324 days after treatment were 0.040 and 0.065 ppm. Low hydrosoil residues indicate that the dissipation of fluridone from pond water was due to degradation rather than adsorption onto hydrosoil. This study also indicated that NMF (N-methylformamide) is not a degradation product of fluridone in natural aquatic environments treated with Sonar (West et al. 1990).

Fluridone is most strongly sorbed to hydrosoils of high organic matter and high silt content. It was found that in all ponds > 50% of the herbicide applied could not be accounted for 10 days after application (Muir et al. 1980). It is also documented that microorganisms are a major factor responsible for the degradation of fluridone in terrestrial soils (PMEP 1986).

No major degradation products of fluridone were identified under field conditions due

to extensive photodegradation of the compound (Muir and Grift 1982b). The fluridone minimum detectable concentration of 0.02 ppb is based on a 90% B/Bo (SePRO Corporation).

Mode of Action on Target Organisms

Fluridone is a selective aquatic herbicide for submersed and emergent vascular plants in bodies of water with little water movement. It is a systemic agent that inhibits production of carotene, which enhances degradation of chlorophyll and inhibits photosynthesis.

X. Toxicity Values for Select Aquatic Species

Table 51. LC_{50} Values for Bluegill Sunfish (mg/L).

9.0-12.5 (96h)	Rodgers et al. 1992
16 (96h)	Helfrich et al. 1996
12-13 (96h)	Hamelink and Buckler 1986
7.4-17.1 (96h)	Hamelink and Buckler 1986
12 (96h)	PMEP 2002

Table 52. LC_{50} Values for Water Flea (*Daphnia magna*) (mg/L).

4.4-6.3 (96h)	Rodgers et al. 1992
2.1-3.9 (96h)	Hamelink and Buckler 1986

Table 53. LC_{50} for Rainbow Trout (mg/L).

4.2-8.1 (96h)	Hamelink and Buckler 1986
7.6-11.7 (96h)	Rodgers et al. 1992
11.7 (96h)	PMEP 2002
12 (96h)	Helfrich et al. 1996
7.1-8.1 (96h)	Hamelink and Buckler 1986

Table 54. LC_{50} for Channel Catfish (mg/L).

8.2-14 (96h)	Hamelink and Buckler 1986
22 (96h)	Rodgers et al. 1992
8.2-13.2 (96h)	Hamelink and Buckler 1986

Table 55. LC_{50} for fathead minnow (mg/L).

>0.5 (96h)	Rodgers et al. 1992
15.0 (96h)	Hamelink and Buckler 1986
6.7-10.2 (96h)	Hamelink and Buckler 1986
6.2 (96h)	CDFG 2002

Table 56. LC_{50} for Sheepshead Minnow (mg/L).

12.5-22.5 (96h)	Hamelink and Buckler 1986
10.91 (96h)	PMEP 2002

Table 57. LC_{50} for Smallmouth Bass (mg/L).

19 (24h)	Paul et al. 1994
11 (48h)	Paul et al. 1994
9.5 (72h)	Paul et al. 1994
7.6 (96h)	Paul et al. 1994
4 (8d)	Paul et al. 1994

Table 58. LC_{50} for Largemouth Bass.

(10-14d)	13 (96h)	Paul et al. 1994
10-14d)	16 (24h)	Paul et al. 1994
(10-14d)	16 (48h)	Paul et al. 1994
(10-14d)	14 (72h)	Paul et al. 1994

Table 59. LC_{50} for Walleye.

(8-12d)	3.6 (24h)	Paul et al. 1994
(8-12d)	2.8 (48h)	Paul et al. 1994
(8-12d)	2.3 (72h)	Paul et al. 1994

Table 60. Acute Toxicity of Fluridone to Invertebrates.

Oyster Embryos	Tech. Grade Fluridone (T)	48h	EC_{50} 16.8 mg/L
Oyster Embryos	Liquid Fluridone (F)	48h	EC_{50} 6.8 mg/L
Daphnids	T	48h	EC_{50} 6.3 mg/L
Daphnids	F	48h	EC_{50} 3.9 mg/L
Crayfish	T	14d	LC_{50}>16.9 mg/L

Table 61. Chronic Toxicity of Technical Grade Fluridone to Water Flea (*Daphnia magna).*

Exposure Concentration (Mg/L)	Survival % of Adults	Total average # of offspring produced in 21 days
Control	100	375
0.06	95	430
0.1	95	652
0.2	80	208
0.4	75	92
0.8	75	18
1.6	75	2
3.4	0	0

Table 62. Growth and Survival of Channel Catfish Continuously Exposed to Technical Fluridone.

Nominal Concentration (Mg/L)	15 day exposure	30 day exposure	45 day exposure	60 day exposure
Control	98% survival	94%	91%	91%
0.12	99%	98%	93%	93%
0.25	98%	98%	98%	98%
0.5	96%	95%	95%	95%
1.0	95%	89%	89%	89%
2.0	98%	70%	68%	68%

Table 63. NOAEC, LOEC, and NOEC for Select Aquatic Species.

Species	Age (d)	NOAEC (24h)	NOAEC (48h)	NOAEC (96h)	Source
Walleye	8-12	1.2 mg/L	1.2 mg/L	0.78 mg/L	Paul et al. 1994
Smallmouth Bass	4-8	8.7 mg/L	6.2 mg/L	4.5 mg/L	Paul et al. 1994
Largemouth Bass	10-14	12 mg/L	12 mg/L	9.6 mg/L	Paul et al. 1994
Species	**Age (d)**	**LOAEC (24h)**	**LOAEC (24h)**	**LOAEC (24)**	**Source**
Walleye	8-12	2.0mg/L	2.0mg/L	1.2mg/L	Paul et al. 1994
Smallmouth Bass	4-8	19mg/L	8.7mg/L	6.2mg/L	Paul et al. 1994
Largemouth Bass	10-14	21mg/L	21mg/L	2mg/L	Paul et al. 1994
Species	**NOEC**		**Source**		
Flathead Minnow	1.88 mg/L		CDFG 2002		
Delta Smelt	1.28 mg/L		CDFG 2002		

XI. Method Detection Limits

Table 64. Fluridone Method Detection Limits.

Analytical Method	MDL	Medium	Reference
LC[1]	1 ppb	Water	West & Turner 1988
HPLC[2]	0.001 ppm	Water	West et al. 1990
HPLC and FasTEST	1.0 µgL-1	Water	Netherland 2000
Reverse phase liquid chromatography[3]	0.06-0.09 ppm	Tissue	West et al 1996
HPLC (Fox et al methods, 1991)	0.05 gL-1	Water	Fox et al. 1994
HPLC (Modified Eli Lilly and Co Method)	-----	Water	Paul et al. 1994
Direct inje ction high pressure LC[4]	~5 ppb	Water	West and Parka 1981
HPLC[4]	0.01 ppm	Hydrosoil	West and Parka 1981
Extraction high-pressure LC[4]	1 ppb	Water	West and Parka 1981
Gas chromatography w/ electron-capture			
Detection (GC- ECD)	1 ppb	Water	West and Parka 1981
GC-ECD	0.5 ppb	Water	West and Parka 1981
GC-ECD	10 ppb	Soil and plant tissue	West and Parka 1981

[1] Fluridone is separated from the water by passing through a SEP-Pak C18 Cartridge. It is then eluted from the cartridge using methanol and concentrated for analysis using liquid chromatography with UV Detection at 313 nm.

[2] Fluridone is separated by passing through a Sep-Pak C18 cartridge, eluted from the cartridge using methanol and then concentrated for analysis using HPLC with UV detection at 313 nm.

[3] Fluridone is purified using liquid partitioning and Florisil Sep-Pak column chromatography. It is separated and measured using reverse phase chromatography with UV detection at 313 nm.

[4]Fluridone residue data generated by reverse-phase high-pressure LC with UV detection at 254 nm. The difference b/t the injection and extraction HPLC assays averaged 0.003ppm. The direct injection technique was more precise than the extraction technique although both methods are more precise and less time consuming than gas chromatography with electron-capture detection (GC-ECD).

XII. Manufacturer Contact Info

SePRO Corporation
11550 North Meridian Street
Carmel, IN 46032-4565
www.sepro.com

XIII. Summary Table

Table 65. Fluridone Summary Table.

Primary use	Selective aquatic herbicide for submersed and emergent vascular plants in bodies of water with little water movement. Recommended application is 0.1 mg/L. Multiple applications necessary to maintain a concentration between 5-20 ppb.
Mechanism of Toxicity	Systemic - inhibits production of carotene, which enhances degradation of chlorophyll and inhibits photosynthesis.
Solubility	12 mg/L at 25°C
Fate	Stable to hydrolysis, but photodegrades; sunlight intensity/penetration are main factors in half-life. Degrades more slowly under anaerobic and low DO conditions. Low K_{OW} and experiments indicated low potential to bioaccumulate or biomagnify. Half-life in water is 20 days under anaerobic aquatic condition up to nine months.
Confounding Factors	Not hardness, temperature, pH or salinity dependent. Binds to organic matter.
Data Gaps	Amphibians and macroinvertebrates.

F. Glyphosate

I. Introduction

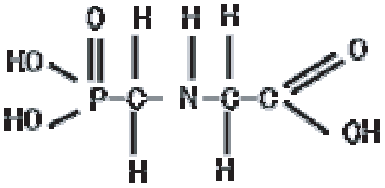
Glyphosate is a non-selective, post-emergent, and systemic herbicide used on agricultural and non-agricultural areas around the world (WHO 1994). It works by inhibiting the synthesis of the enzyme 5-enolpyruvylshikimic acid-3-phosphate synthase (EPSP), which is needed for production of aromatic amino acids tyrosine, tryptophan, and phenylalanine. These amino acids help with the synthesis of proteins that link primary and secondary metabolism (Tu et al. 2001). Glyphosate is not effective on submerged or mostly submerged foliage and therefore is only applied to control emergent foliage (WSDE 2001). Glyphosate, when used to control emergent aquatic plants, is commonly sold as Rodeo or AquaMaster in the formulation of isopropylammonium. Glyphosate is relatively non-toxic to animals because the plant enzymes that are affected when glyphosate is used are not present in animals (Tu et al. 2001). Glyphosate adsorbs strongly to soil particles once it has entered water and this strong adsorbsion prevents excessive movement in the environment (Tu et al. 2001). Glyphosate is readily degraded to aminomethylphosphonic acid (AMPA) by soil microbes and AMPA is then degraded to carbon dioxide (US EPA 1993).

II. Active Ingredient ID

Synonyms

Aquamaster; Rodeo; Roundup; Glycine, N-(phosphonomethys)-, compound with 2-propanamine (1:1); Glyphosate isopropylamine salt; Glyphosate-isopropylammonium; CP 70139; Glifonox; Glycel; Glycine, N-(phosphonomethyl)-, compd. With 2-propanamine (1:1); Glyphosate, isopropylamine salt; isopropylamine glyphosate (N-(phospho nomethyl)glycine); Isopropylamine salt of N-(phosphonomethyl)glycine; MON 139; MON 39; N-(Phosphonomethyl)glycine, isopropylamine salt; Rondo; (USEPA Chemical Registry System [online]).

Structural formula



Active ingredient ID summary table

Table 66. Glyphosate Active Ingredient Identification Summary Table.

Characteristic	Value	Source
CAS Number	38641-94-0	US EPA 1993
Molecular Weight	169.08	EXTOXNET 1996
Molecular Formula	$C_6H_{17}N_2O_5P$	Tomlin 2000
USEPA PC Code	103601	US EPA 1993
CA DPR Chemical Code	1855	PAN 2002
USEPA Chemical Class	Phosphono-glycine	PAN 2002
WHO/FAO Chemical Group		

III. Physical Properties

Appearance

The isopropylamine salt formulation of glyphosate is a colorless and odorless solution.

Stability

Glyphosate is stable for at least 5 years under normal conditions of warehouse storage. Heated facilities are not required (Monsanto 1998). The average soil half-life is 47 days (Tu et al 2001). Reported hydrolysis half-life >35 days, first order half-lives ranged from 1.5-11.2 days in surface water ponds high in suspended sediment (Schuette 1998). US EPA reports a half-life 35-63 days (1993). Washington State Department of Ecology reports the half-life as a minimum of two weeks (2001).

Physical Properties

Table 67. Glyphosate Physical Properties Summary Table.

Characteristic	Value	Source
Specific Gravity	1.22-1.25 (water = 1)	Monsanto 1998
Melting Point	Occurs in 2 steps, 143-164°C and 189-223°C	Tomlin 2000
Boiling Point	Decomposed w/o boiling	Tomlin 2000
Vapor Pressure	2.1 X 10^{-3} mPa	Tomlin 2000
Water Solubility	11.6 g/L	Tomlin 2000
Solubility in Other Solvents	In dichloromethane 0.184 g/l 20°C, in metanol 15.88 g/l 20°C	Tomlin 2000
Partition Coefficient (K_{ow})	5.77+/- 0.03, 2.18+/-0.02 (20+/-2°C)	Tomlin 2000
Adsorption Coefficient (K_{oc})	6922.0 K_{oc}	PAN 2002
Henryís Constant (K_h)	<1.44 X 10 -12 atm-m 3/mole	Schuette 1998
Half Life	Average 47 days in soil	Tu et al. 2001
Dissipation Rate		

IV. Active Ingredient Regulatory Status

Table 68. Glyphosate Regulatory Status.

Agency/Regulatory Category	Regulatory Status	Source
UNEP Persistent Organic Pollutant	Not Listed	PAN 2002
UNEP Prior Informed Consent Chemical	Not Listed	PAN 2002
WHO/FAO Pesticide Primary Use		
USEPA Registered Pesticide Active Ingredient	Yes	PAN 2002
USEPA Pesticide Use Type	General Use Pesticide	EXTOXNET 1996
USEPA Toxicity Class (Pesticide Products)	Class II	EXTOXNET 1996
USEPA Signal Word (Pesticide Products)	WARNING	EXTOXNET 1996
USEPA Registration	Yes	PAN 2002
Agency/Regulatory Category		
USEPA Hazardous Air Pollutant	Yes	PAN 2002
USEPA Minimum Risk Pesticide (25b list)	No	PAN 2002
CA Registered Pesticide Active Ingredient	Yes	PAN 2002
CA Toxic Air Contaminant	Candidate	PAN 2002
CA Groundwater Contaminant	Potential	PAN 2002
PAN Bad Actor	Not Listed	PAN 2002
PAN Dirty Dozen	Not Listed	PAN 2002

V. Pesticide Status

Pests Controlled

Glyphosate based products are used to control woody brush and trees, annual weeds, and perennial weeds. In aquatic environments, glyphosate is commonly used to control emergent plant species such as cattail (*Typha spp*.), cordgrass (*Spartina spp*.), and purple loosestrife (*Lythrum salicaria*). Glyphosate is not effective on totally submerged or mostly submerged foliage.

Pesticide Trade and Other Names

Rodeo and AquaMaster are both manufactured by Monsanto.

Formulation and Dosages

Glyphosate should be mixed with water and a nonionic surfactant.

Table 69. AquaMaster Application Rates.

Desired Volume	**Amount of AquaMaster™**					
	3/4%	1%	11/4%	11/2%	5%	8%
1 Gal	*1oz.*	*11/3 oz.*	*12/3 oz.*	*2oz.*	*6oz.*	*101/4 oz*
25 Gal	11/2 pt.	1qt.	11/4 qt.	11/2 qt.	5qt.	2 gal.
100 Gal	3 qt.	1 gal.	11/4 gal.	11/2 gal.	5 gal.	8 gal.

For each 100 gallons of spray solution mix two or more quarts of a nonionic surfactant. Use only a nonionic surfactant labeled for use with herbicides. The surfactant must contain 50% or more active ingredient. To apply, use spray equipment that has been properly maintained and calibrated to be capable of delivering desired volumes (AquaMaster™ Product label 10/99).

VI. Toxicity to Humans and Mammals

Fate in Mammals and Excretion Products

Glyphosate is poorly absorbed through the digestive tract and is largely excreted unchanged by mammals (EXTOXNET 1996). There was no significant potential for glyphosate to accumulate in animal tissue (EXTOXNET 1996).

Mode of Action

Glyphosate inhibits the EPSP synthase enzyme, which leads to depletion of key amino acids that are necessary for protein synthesis and plant growth.

Acute Toxicity

Studies indicate that glyphosate is practically non-toxic by ingestion. The rat has a reported LD_{50} of 5600 mg/kg. The toxicity of technical glyphosate acid and the formulated product (Roundup) are nearly the same. Mice, rabbits and goats have oral LD_{50} values greater than 10,000 mg/kg. Reported dermal LD_{50} values are greater than 5000 mg/kg for both formulations making it practically nontoxic through skin exposure. A number of human volunteers wore patch tests, which produced no visible skin changes or sensitization (EXTOXNET 1996).

Neurotoxicity

There are no data requirements for acute or subacute neurotoxicity studies since there was no evidence of neurotoxicity in any toxicology studies conducted at very high doses (US EPA 1999).

Chronic Toxicity

No chronic toxicity has been observed to be caused by glyphosate. No toxic effects were seen in rats that had been fed doses as high as 400 mg/kg/day. There were also no toxic effects observed in a chronic feeding study when dogs were fed up to 500 mg/kg/day (EXTOXNET 1996).

Carcinogenic Effects

Glyphosate appears to be non-carcinogenic. Carcinogenicity studies were conducted using rats, mice and beagle dogs. There were no effects based on the parameters examined and resulted in finding that glyphosate was not carcinogenic. Glyphosate was classified as a Group E oncogen in June 1991 based on the lack of convincing evidence of carcinogenicity (US EPA 1993).

Reproductive Effects

Laboratory studies indicate that glyphosate produces reproductive effects very rarely and then only at high doses (over 150 mg/kg/day). Glyphosate is not likely to cause reproductive effects in humans (EXTOXNET 1996).

Teratogenic and Developmental Effects

Glyphosate does not appear to be teratogenic. No developmental toxicity was observed in fetuses of rabbits at the highest doses tested (350 mg/kg/day). Rats given 175 mg/kg/day between days 6-19 of pregnancy had fetuses with no teratogenic effects but other toxic effects were observed in both the mothers and their fetuses. No toxic effects were seen on the fetuses when dosage fed to the mothers was reduced to 50 mg/kg/day (EXTOXNET 1996).

Mutagenic Effects

It appears that glyphosate is not mutagenic. All of the mutagenicity and genotoxicity assays done on glyphosate have been negative. These included the Ames test, other bacteri-

al assays, and the Chinese Hamster Ovary (CHO) cell culture, and mouse dominant lethal assays (EXTOXNET 1996).

Endocrine

An international panel of toxicologists reviewed the extensive data for glyphosate (Williams et al. 2000). They concluded that the normal use of the original Roundup herbicide "does not result in adverse effects on development, reproduction, or endocrine systems in humans and other mammals." The World Health Organization (WHO 1994), the U.S. Environmental Protection Agency (US EPA 1993, 1997), and the European Commission (2002) also have reviewed the data and concluded that the use of glyphosate according to label directions would not result in adverse reproductive or developmental problems or birth defects.

Skin Sensitization

Glyphosate is practically nontoxic by skin exposure. Dermal LD50 values are greater than 5000 mg/kg for both the acid and the isopropylamine salt. Human volunteers wearing patch tests showed no visible skin changes or sensitization (EXTOXNET 1996).

VII. Routes of Human Exposure

Inhalation and skin contact are the most likely routes of human exposure (Monsanto 1998). Ground water and surface water resources are not affected by the use of Glyphosate because the molecules strong sorption to soil limits mobility (Giesy et al. 2000).

VIII. Environmental Toxicology and Ecological Effects

Birds

Glyphosate is slightly toxic to wild birds. Mallards and bobwhite quail have a dietary LC_{50} greater than 4500 ppm (EXTOXNET 1996).

Fish

Glyphosate by itself is moderately toxic to fish. Bluegill sunfish have a 96-hour LC_{50} of 120 mg/L and rainbow trout have a 96-hour LC_{50} of 86 mg/L (Tu et al. 2001). In a flow-through test, bluegill sunfish showed a depuration half-life of 35 days after being exposed for 35 days (Henry et al. 1994). Up to 21 days after continuous exposure to glyphosate, AMPA could still be found in bluegill sunfish (Henry et al. 1994). One experiment found AMPA concentrations in carp up to 21 days after spraying (Henry et al. 1994). Lung damage was found in fish exposed to 5mg/L of glyphosate for two weeks and liver damage was found in fish exposed to 10 mg/L of glyphosate for two weeks (Tu et al. 2001). For fish, technical grade glyphosate is moderately toxic while the toxicity of different formulations can vary significantly (Tu et al. 2001). Rodeo has relatively high LC_{50}s for aquatic species (>900 mg/L) and is approved for use in aquatic applications (Tu et al. 2001). Roundup contains a surfactant and is not approved for use in aquatic applications (Tu et al. 2001). The surfactant X-77 Spreader is often used at the same time as Rodeo. When applications of Rodeo

incorporate X-77, it is ~100 times more toxic to aquatic invertebrates than Rodeo used alone.

Amphibians

Roundup is slightly to moderately toxic to amphibians while glyphosate is practically nontoxic to slightly toxic (Giesy et al. 2000). The higher toxicity of the Roundup formulation is probably due to the addition of a surfactant to the formulation.

In a paper by Perkins et al. (2000) the toxicity of glyphosate was evaluated using the frog embryo teratogenesis assay-Xenopus, commonly referred to as FETAX. Tests were done using two formulations of the herbicide glyphosate, Roundup and Rodeo, manufactured by Mansanto Canada. Roundup contains glyphosate and the surfactant polyoxyethyleneamine (POEA), while Rodeo contains glyphosate without a surfactant.

The results indicated that the Roundup formulation was more than 700 times as toxic as the Rodeo formulation. The difference in toxicity appeared to be from the addition of the surfactant POEA in the Roundup formulation. A limited number of tests found the surfactant POEA to have a lower LC_{50} number than either Rodeo or Roundup indicating that POEA may be the cause of the high toxicity of Roundup. POEA had a 96-h LC_{50} of 6.8 mg/L and Roundup had a 96-h LC_{50} of 9.3 mg AE/L. The 96-hr LC_{50} of Rodeo was 7,296.8 mg/L. The manufacturer is recommending that a surfactant be added to Rodeo sprays and an additional surfactant be added to Roundup to help with the efficiency of the herbicides. Results from this test indicate that adding more surfactant would increase the toxic effects on *X laevis* embryos. More testing needs to be done to determine what surfactants can safely be used in conjunction with glyphosate as an aquatic herbicide or in areas near water. Malformations were very low (<5%). Significant increases were not observed at any concentration of the glyphosate that did not also lead to death at 96-h. Embryo length was a less sensitive indicator of toxicity than embryo mortality.

In a paper by Mann and Bidwell (1999) four species of southwestern Australian tadpoles and one species of southwestern Australian adult frog were looked at to examine the acute toxicity of several formulations of glyphosate. The report prompted the Australian National Registration Authority for Agricultural and Veterinary Chemicals to place restrictions on 84 glyphosate-based products to be used in or over water. The restrictions were for products with the inclusion of a surfactant (polyoxyethylene amine) component in them.

A study by Solberg and Higgins (1993) was conducted on ducks and invertebrates living in South Dakota Wetlands. The ducks were found to have higher breeding rates and over-water nest densities in areas that had been chemically treated with Rodeo. Aquatic invertebrate numbers were greater in untreated cattails contained in Rodeo treated wetlands than in control wetlands. Aquatic invertebrate populations were lower in natural and treated open areas than in untreated areas containing cattails adjacent to the treated sites. The authors were unable to determine if the differences in invertebrate populations were caused by death from the glyphosate treatment or movement from treated areas to non-treated areas.

Non-Target Aquatic Organisms

Technical glyphosate may be slightly toxic to aquatic invertebrates (EXTOXNET 1996). The addition of a surfactant can increase the toxicity of the glyphosate formulation. Studies have indicated that when the surfactant X-77 is used at the same time as Rodeo, toxicity to aquatic invertebrates increased by ~100 times than when Rodeo is used alone (Tu et al. 2001). A study by Henry et al. (1994) involved investigation into the effects of Rodeo, the surfactant X-77 Spreader, and the drift retardant Chem-Trol when used in aerial applications on aquatic invertebrates in wetland settings and in the lab. The laboratory results showed X-77 spreader was about 83-136 times more toxic than Rodeo and Rodeo was >24 times more toxic than Chem-Trol. Daphnids were much more sensitive to X-77 Spreader and Rodeo than other species (Henry et al. 1994). Findings by Simenstad et al. (1996) showed no significant differences between benthic communities of algae and invertebrate species living on untreated mudflats and those living on mudflats treated with Rodeo and X-77 spreader (Tu et al. 2001). Apparently the quick dissipation of glyphosate prevents build-up of levels that would be lethal to most aquatic species.

Monsanto Company conducted a study in a 20-acre test plot in a forest with an application of the herbicide roundup (360 g/l glyphosate acid) (Schuette 1998). The area contained a small stream with fish in it. Fish biomass samples were taken during this study and there were no measurable residues of glyphosate found in the fish samples. Water flea (*Daphnia magna*) underwent chronic toxicity. Twenty *Daphnia* were placed in six different groups and exposed to glyphosate (98.7%) in concentrations of 0, 3.0, 9.4, 30, 94.9, and 300 mg/l for 21 days. All *Daphnia* died that were exposed to the 300 mg/l within 5 days from the start of the exposure. There was no significant mortality found in the other groups. Another study was conducted on five groups of forty daphnids that were less than 24 hours old. They were exposed to glyphosate concentrations of 0, 25, 50, 99, and 397 mg/l for 25 days. The upper three concentration levels (96, 186, 378 mg/l) yielded decreases in the mean number of young/adult/reproductive day (Schuette 1998).

IX. Environmental Fate

Transport and Degradation Pathways

Once glyphosate enters the water column, it is quickly adsorbed to soil particles (Schuette 1998). Microbial degradation begins immediately and glyphosate is broken down to its metabolite amniomethylphosphonic acid (AMPA) and CO_2 (Gardner and Grue 1996). Strong adsorption slows microbial degradation leading to possible persistence for one year (Tu et al. 2001). AMPA is the primary metabolite of glyphosate. It is non-toxic and degrades microbially at a slower rate than the parent compound (Tu et al. 2001).

The amount of time required for glyphosate to break down depends on the type of soil particles present, the adsorption capacity of the soil, and the microbial community present (Glyphosate Pesticide Fact Sheet, Tu et al. 2001). According to Tu et al. (2001), rapid degradation occurs when the molecules are not bound to soil and slower degradation occurs once the molecules become bound. The higher the adsorption capacity, the slower the degradation. Persistance in the environment may last for up to a year. Slow microbial degradation

leads to persistence in the environment and immobility. Increase in clay content, cation exchange capacity, decreasing soil pH and decreasing phosphorous content all increase the ability of glyphosate to adsorb to soil. Adsorption occurs rapidly during the first hour after application and slows down after that. The half-life of glyphosate in soil averages 2 months but can be anywhere between weeks and years. Another source reports a soil half-life between 3-130 days (Glyphosate Pesticide Fact Sheet). Once glyphosate binds to soil, it loses its ability to act as an herbicide.

Glyphosate is highly water-soluble at 11,600 ppm at 25° C (Schuette 1998, Tu et al. 2001). Water stability of glyphosate has been determined with pH 3,5,6, and 9 at temperature 35° C according to experiments conducted for the U.S. EPA's re-registration eligibility decision (RED) (Schuette 1998). The half-life of glyphosate in water ranges from 35-63 days (Glyphosate Pesticide Fact Sheet). The degradation rate of glyphosate in water is generally slower because there are usually fewer microorganisms than in soil (Schuette 1998). Despite having high water solubility, glyphosate has a high ability to bind to soil particles (Tu et al. 2001). Photodegradation may also aid in the break down of glyphosate. The half-life of glyphosate in deionized water under UV light was reported by Lund-Hoie and Friestad (1986) to be four days, degrading into its metabolite AMPA (Tu et al. 2001, Gardner and Grue 1996). Hydrolysis and oxidation do not readily happen to glyphosate in the field (Tu et al. 2001). Glyphosate has a hydrolysis half-life of >35 days with little propensity toward hydrolytic decomposition (Schuette 1998).

Mode of Action

Glyphosate inhibits the EPSP synthase enzyme, which leads to depletion of key amino acids that are necessary for protein synthesis and plant growth. It is a non-selective systematic herbicide, absorbed by the foliage, with rapid translocation throughout the plant. Inactivate on contact with soil.

X. Toxicity values for Select Aquatic Species

Table 70. Glyphosate LC_{50} Values for Rainbow Trout in Different Dilution Water Types (from Wan et al. 1989).

	Glyphosate				**Roundup**			
Water Type	24-h	48-h	72-h	96-h	24-h	48-h	72-h	96-h
Soft (city)	21 mg/L	11	11	10	33	33	33	33
Soft (creek)	32	26	22	22	21	21	17	15
Intermediate (reconstituted)	107	107	103	99	20	18	18	18
Intermediate (well)	115	108	108	93	20	19	19	18
Hard (lake)	220	220	220	197	17	17	15	14

Table 71. Glyphosate LC_{50} Values for Bluegill Sunfish.

120mg/L (96 hrs)	Tu et al. 2001
~ 78ppm (96 hrs)	Schuette 1998
>1000 mg/L (96 hr) Rodeo	WSDE 2001
120 mg/L (96-hr) Glyphosate (tech grade)	WSDE 2001
150 mg/l (24-hr) Glyphosate (tech grade)	WSDE 2001
140 mg/L (96-hr) Glyphosate (tech grade)	WSDE 2001
5.8 mg/L (4 days) Roundup	Giesy et al. 2000
16.1mg RU/L (4 days) Roundup	Giesy et al. 2000, Folmar et al. 1979
34 mg RU/L (4 days) Roundup	Giesy et al. 2000
>24 mg/L (2 days) Acid glyphosate	Giesy et al. 2000
120 mg/L (4 days) Acid Glyphosate	Giesy et al. 2000
140-220 mg/L (4 days) IPA salt	Giesy et al. 2000, Folmar et al. 1979
>1000 mg/L (4 days) IPA salt	Giesy et al. 2000
5.0 mg/L (96h) Roundup	Folmar et al. 1979
150 mg/L (24h) Glyphosate	Folmar et al. 1979
140 mg/L (96h) Glyphoate	Folmar et al. 1979
3.0 mg/L (24h) Surfactant	Folmar et al. 1979
3.0 mg/L (96h) Surfactant	Folmar et al. 1979
140 mg/L (96h) Glyphosate	WHO 1994, Folmar et al. 1979
120 mg/L (96h) Glyphosate	WHO 1994
5.6 mg/L (96h) Glyphosate	LeBlanc 1984
13.2 +or- 0.8 mg/L (48 h) Roundup	Abdelghani 1997
13.0 +or- 0.5 mg/L (96h) Roundup	Abdelghani 1997
3.1 (48h) mg/L Syndet surfactant	Abdelghani 1997
3.1 (48h) mg/L Syndet surfactant	Abdelghani 1997
6.4 mg/L (24h) Roundup	Folmar et al. 1979

Table 72. Glyphosate LC_{50} of *Daphnia magna.*

962 mg/L (96 hrs)	Tu et al. 2001
930 ppm (48 hrs)	Schuette 1998
930 mg/L (48 hr)	WSDE 2001
24 mg/L (2 days) Roundup	Giesy et al. 2000
9.7 mg RU/L (2 days) Roundup	Giesy et al. 2000
12.9 mg RU/L (2 days) Roundup	Giesy et al. 2000
780 mg/L (tested as acid)	Giesy et al. 2000
930 mg/L (IPA salt)	Giesy et al. 2000
3.0 mg/L (48h) Roundup	Folmar et al. 1979
218 mg/L Rodeo	Henry et al. 1999
2.0 mg/L X-77 Spreader	Henry et al. 1999
3.0 mg/L (48h) Glyphosate	LeBlanc 1984

Table 73. Glyphosate LC_{50} for Rainbow Trout.

86mg/L (96 hrs)	Tu et al. 2001
38ppm (96 hrs)	Schuette 1998
140 mg/L (24-hr) glyphosate tech grade	WSDE 2001
>1000 mg/L (96 hr) Rodeo	WSDE 2001
86 mg/L (96-hr) Glyphosate (tech grade)	WSDE 2001
140 mg/L (96-hr) Glyphosate (tech grade)	WSDE 2001
8.2 mg/L (4 days) Roundup	Giesy et al. 2000
22 mg/L	Giesy et al. 2000
27 mg/L (4 days) Roundup	Giesy et al. 2000
27 mg RU/L (4 days) Roundup	Giesy et al. 2000
22 mg/L soft (creek) water (4 days) glyphosate Acid	Giesy et al. 2000
197 mg/L hard (lake) water (4 days) Glyphasate Acid	Giesy et al. 2000
86 mg/L (4 days) Glyphosate Acid	Giesy et al. 2000
>1000 mg/L (4 days) IPA salt	Giesy et al. 2000
140-240 (4 days) IPA salt	Folmar et al. 1979
8.3 mg/L (24 h) Roundup	Folmar et al. 1979
8.3 mg/L (96 h) Roundup	Folmar et al. 1979
140 mg/L (24 h) Glyphosate	Folmar et al. 1979
140 mg/L (96 h) Glyphosate	Folmar et al. 1979
2.1 mg/L (24h) Surfactant	Folmar et al. 1979
2.0 mg/L (96h) Surfactant	Folmar et al. 1979
10-197 mg/L (96h) Glyphosate	WHO 1994, Wan et al. 1989
86 mg/L (96h) Glyphosate	WHO 1994

Table 74. Glyphosate LC_{50} for Carp

>10000 mg/L (96-hr) Rodeo	WSDE 2001
LC_{50} 115 mg/L (96-hr) glyphosate (tech grade)	WSDE 2001
10 mg/L (4 days) Roundup	Gisey et al. 2000
26 mg/L (4 days) Roundup	Gisey et al. 2000
15 mg/L (4 days) Roundup	Gisey et al. 2000
Grass Carp	
26 mg/L (24 h) Roundup	Tooby et al. 1980
24 mg/L (48 h) Roundup	Tooby et al. 1980
15 mg/L (96 h) Roundup	Tooby et al. 1980

Table 75. Glyphosate LC_{50} for Harlequin fish.

>1000 mg/L (96 hr) Rodeo	WSDE 2001
168 mg/L (96-hr) Glyphosate (tech grade)	WSDE 2001
168 mg/L (4 days) acid glyphosate	Gisey et al. 2000
168 mg/L (96h) Glyphosate	WHO 1994

Table 76. Glyphosate LC_{50} for Channel Catfish.

130 mg/L (24-hr) glyphosate tech grade	WSDE 2001
130 mg/L (96-hr) Glyphosate (tech grade)	WSDE 2001
39 mg/L (4 days) Roundup	Gisey et al. 2000
10.6 mg RU/L (4 days) Roundup	Gisey et al. 2000, Folmar et al. 1979
42.0 mg RU/L (4 days) Roundup	Gisey et al. 2000
130 mg/L (4 days) IPA salt	Gisey et al. 2000
16.2mg/L +or- 2.0 (48h) Roundup	Abdelghani 1997
14.5mg/L +or- 1.2 (96h) Roundup	Abdelghani 1997
3.8 +or- 0.2 mg/L (48h) Syndet surfactant	Abdelghani 1997
3.6 +or- 0.2 mg/L (96h) Syndet surfactant	Abdelghani 1997
13 mg/L (24h) Roundup	Folmar et al. 1979
13 mg/L (96h) Roundup	Folmar et al. 1979
130 mg/L (24h) Glyphosate	Folmar et al. 1979
130 mg/L (96h) Glyphosate	Folmar et al. 1979
18 mg/L (24h) Surfactant	Folmar et al. 1979
13 mg/L (96h) Surfactant	Folmar et al. 1979
130 mg/L (96h) Glyphosate	WHO 1994, Folmar et al. 1979

Table 77. Glyphosate LC_{50} for Fathead Minnow.

97 mg/L (24-hr) glyphosate (tech grade)	WSDE 2001
97 mg/L (96-hr) glyphosate (tech grade)	WSDE 2001
7.4 mg RU/L (4 days) Roundup	Gisey et al. 2000, Folmar et al. 1979
23 mg/L (4 days) Roundup	Gisey et al. 2000
97 mg/L (4 days) IPA salt	Gisey et al. 2000, Folmar et al. 1979
>648 mg/L (4 days) IPA salt	Gisey et al. 2000, Byers 1995
730 mg/L (96 hr)	Folmar et al. 1979
LOEC 1000 mg/L	Folmar et al. 1979
2.4 mg/L (24h) Roundup	Folmar et al. 1979
2.3 mg/L (96h) Roundup	Folmar et al. 1979
97 mg/L (24h) Glyphosate	Folmar et al. 1979
97 mg/L (96h) Glyphosate	Folmar et al. 1979
1.4 mg/L (24h) Surfactant	Folmar et al. 1979
1.0 mg/L (96h) Surfactant	Folmar et al. 1979
NOAEC 1000 mg/L Rodeo	Beyers 1995
97 mg/L (96h) Glyphosate	WHO 1994, Folmar et al. 1979

Table 78. Glyphosate LC_{50} for Frog - *Xenopus laevis*.

5,515.5 mg AE/L (96-hr) Rodeo	Perkins et al. 2000
7.7 mg AE/L (96 hr) Round up	Perkins et al. 2000
5.8 mg AE/L (96-hr) surfactant, MONO 0818	Perkins et al. 2000

Table 79. Glyphosate NOEC Values.

NOEC 52 mg AE/L. 21 days Glyphosate	Giesy et al. 2000
NOEC 2.4 mg RU/L. 21 days. Roundup	Giesy et al. 2000
NOEC 26 mg AE/L. Glyphosate. 255 days	Giesy et al. 2000
NOEC 500 mg/L	Folmar et al. 1979
NOAEC 1000 mg/L Rodeo	Beyers 1995.

Table 80. Glyphosate LOEC Values.

LOEC 1000 mg/L	Folmar et al. 1979

XI. Method Detection Limits

Table 81. Glyphosate Method Detection Limits.

Analytical Method	**MDL**	**Reference**
HPLC[1]	0.05mg filter pads	Paveglio et al. 1996
HPLC[1]	0.02mg/g sediment	Paveglio et al. 1996
HPLC[1]	0.5 µg/L seawater	Paveglio et al. 1996
HPLC[1]	0.02 g/g *Spartina*	Paveglio et al. 1996
Liquid Chromatography[2]	0.50-5000 ppb	Oppenhuizen et al. 1991
HPLC[3]	1.755 mg/L	Jones et al. 2000

1 Acidic or basic extraction, cleanup with Chelex 100 resin iron form and anion exchange column chromatographywith BioRad AG 1-x8resin, concentration to 3.0 ml mobile phase, and HPLC analysis with fluorometric detection after post column derivatization with 0-phthalaldehyde.
2 A filtered volume of water is evaporated to dryness, the residue is dissolved in a buffered EDTA solution and the amount of glyphosate is then determined by LC and post column reaction detection.
3 HPLC with post column derivatization and fluorescence.

XII. Manufacturer Contact Info

Monsanto Company
800 North Lindbergh
St. Louis, Mo 63167, U.S.A.
1-800-332-3111
www. monsanto.com

XIII. Summary Table

Table 82. Glyphosate Summary Table.

Primary use	Systemic herbicide for floating and emergent plants (duckweed, loosestrife, cattails, etc.). Recommended application is 4.3 kg/ha as an aquatic herbicide.
Mechanism of Toxicity	Inhibits a key enzyme that plants and bacteria use to make amino acids called EPSP synthase. Structurally, glyphosate resembles the chemical structure of the amino acid glycine. Because of its structural similarity to glycine, glyphosate binds the active site of the EPSP synthase enzyme that is critical for the production of aromatic amino acids. Interruption of biosynthesis of phenylalinine; inhibition of elongation; photosynthetic disruption.
Solubility	11.6 g/L at 25°C
Fate	Once glyphosate enters the water column, it is quickly adsorbed to soil particles. Microbial degradation begins immediately and glyphosate is broken down to its metabolite amniomethylphosphonic acid (AMPA) and CO_2. Not expected to bioconcentrate.
Confounding Factors	Bioavailability influenced by sorption to colloids, DOC, and larger particles.
Data Gaps	Resident amphibian embryos and larvae. Toxicity with and without surfactant.

G. Malathion

I. Introduction

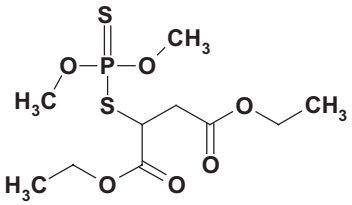
Malathion is a nonsystemic, wide-spectrum organophosphate insecticide. It was one of the earliest organophosphate insecticides developed (introduced in 1950). Malathion is suited for the control of sucking and chewing insects on fruits and vegetables, and is also used to control mosquitoes, flies, household insects, animal parasites (ectoparasites), and head and body lice. Malathion may also be found in formulations with many other pesticides.

II. Active Ingredient ID

Synonyms

Maldison, malathon, mercaptothion, carbofos, mercaptotion. IUPAC name: diethyl (dimethoxythiophosphorylthio)succinate; S-1,2-bis(ethoxycarbonyl)ethyl 0,0-dimethyl phosphorodithioate

Structural formula



Active ingredient ID summary table

Table 83. Malathion Active Ingredient ID Summary Table.

Characteristic	Value	Source
CAS Number	121-75-5	Tomlin 2000
Molecular Weight	330.3	Tomlin 2000
Molecular Formula	$C_{10}H_{19}O_6PS_2$	Tomlin 2000
USEPA PC Code	057701	PAN 2003
CA DPR Chemical Code	367	PAN 2003
USEPA Chemical Class	Organophosphorus	PAN 2003
WHO/FAO Chemical Group	N/A	

III. Physical Properties

Appearance

Technical grade is a clear, amber liquid.

Stability

Relatively stable in neutral, aqueous media. Decomposed by acids and alkalis.

Physical Properties Summary Table

Table 84. Malathion Physical Properties Summary Table.

Characteristic	**Value**	**Source**
Specific Gravity	1.23 at 25°C	Tomlin 2000
Melting Point	2.85°C	Tomlin 2000
Boiling Point	156-157°C/0.7 mmHg	Tomlin 2000
Vapor Pressure	5.3 mPa at 30°C	Tomlin 2000
Water Solubility	145 mg/L at 25°C	Tomlin 2000
Solubility in Other Solvents	Miscible with most organic solvents, e.g. alcohols, esters, ketones, ethers, aromatic hydrocarbons. Slightly soluble in petroleum ether and some types of mineral oil.	Tomlin 2000
Partition Coefficient (K_{ow})	LogP= 2.75	Tomlin 2000
Adsorption Coefficient (K_{oc})	291.0 K_{OC} 1800	PAN 2003 EXTOXNET 1996
Henry's Constant (K_h)	N/A	
Half-Life	Soil & ground water 1-25 days, river water >1 week, distilled water <3 weeks	

IV. Active Ingredient Registration Status

Malathion is a slightly toxic compound in EPA toxicity class III. Labels for products containing it must carry the Signal Word CAUTION. Malathion is a General Use Pesticide (GUP).

Table 85. Malathion Active Ingredient Regulatory Status.

Agency/Regulatory Category	Regulatory Status	Source
UNEP Persistent Organic Pollutant	Not Listed	PAN 2003
UNEP Prior Informed Consent Chemical	Not Listed	PAN 2003
USEPA Registered Pesticide Active Ingredient	Yes	PAN 2003
USEPA Pesticide Use Type	Insecticide	PAN 2003
USEPA Toxicity Class (Pesticide Products)	III	EXTOXNET 1996
USEPA Signal Word (Pesticide Products)	CAUTION	EXTOXNET 1996
USEPA Registration	Yes	PAN 2003
USEPA Hazardous Air Pollutant	Not Listed	PAN 2003
USEPA Minimum Risk Pesticide (25b list)	No	PAN 2003
CA Registered Pesticide Active Ingredient	Yes	PAN 2003
CA Toxic Air Contaminant	Potential	PAN 2003
CA Groundwater Contaminant	Candidate	PAN 2003
PAN "Bad Actor"	Yes	PAN 2003
PAN "Dirty Dozen"	Not Listed	PAN 2003

V. Pesticide Status

Pest Controlled

Used to control Coleoptera, Diptera, Hemiptera, Hymenoptera, and Lepidotera in a wide range of crops, including cotton, pome, soft and stone fruit, potatoes, rice, and vegetables. Used extensively to control major arthropod disease vectors (Culicidae) in public health programs, ectoparasites (Diptera, Acari, Mallophaga) of cattle, poultry, dogs and cats, human head and body lice (Anoplura), household insects (Diptera, Orthoptera), and for the protection of stored grain.

Pesticide Trade and Other Names

Carbophos, maldison and mercaptothion. Trade names for products containing malathion include Celthion, Cythion, Dielathion, El 4049, Emmaton, Exathios, Fyfanon and Hilthion, Karbofos and Maltox.

Formulation and Dosages

Dispersible powder (DP), Emulsifiable concentrate (EC), Ultra-low volume liquid (UL), Wettable powder (WP).

VI. Toxicity to Humans and Mammals

Absorption Route

Malathion is rapidly and effectively absorbed by practically all routes including the gastrointestinal tract, skin, mucous membranes, and lungs (Gallo 1991).

Fate in Mammals and Excretion Products

Malathion undergoes similar detoxification mechanisms to other organophosphates, but it can also be rendered nontoxic via another simple mechanism, splitting of either of the carboxy ester linkages. Animal studies indicate it is very rapidly eliminated though urine, feces and expired air with a reported half-life of approximately eight hours in rats and approximately two days in cows. Autopsy samples from one individual who had ingested large amounts of malathion showed a substantial portion in the stomach and intestines, a small amount in fat tissue, and no detectable levels in the liver. Malathion requires conversion to malaoxon to become an active anticholinesterase agent. Most of the occupational evidence indicates a low chronic toxicity for malathion (Gallo 1991).

Mode of Action

Malathion's mode of action is through acetylcholinesterase (AChE) inhibition, which disrupts nervous system function. AChE is an enzyme made of protein, which cleaves the neurotransmitter acetylcholine in nervous system junctions. Inhibiting this enzyme leads to accumulation of the neurotransmitter thus causing signals in the nervous system to persist longer than normal. Typical symptoms for pesticides, which act in this manner are defecation, urination, lacrimation, muscular twitching and weakness, and halted respiration. Malathion, along with other phosphorodithioate insecticides (those containing two sulfur atoms bonded to phosphorus) must be oxidized before they have inhibitory potency and toxicity. Oxidation occurs via cytochrome p450 and results in the conversion of the P=S group in malathion to P=O forming its oxon, malaoxon. This alteration of the phosphate group enables the molecule to covalently bind AchE resulting in long lasting inhibition of the enzyme (Matsumura 1985).

Acute Toxicity

Malathion is toxic via the oral route, with reported oral LD50 values of 1000 mg/kg to greater than 10,000 mg/kg in the rat, and 400 mg/kg to greater than 4000 mg/kg in the mouse (Gallo 1991, Kidd and James 1991). It is also slightly toxic via the dermal route, with reported dermal LD50 values of greater than 4000 mg/kg in rats (Gallo 1991, Kidd and James 1991). Effects of malathion are similar to those observed with other organophosphates, except that larger doses are required to produce them (Gallo 1991, US PHS 1995). It has been reported that single doses of malathion may affect immune system response (Gallo 1991). Symptoms of acute exposure to organophosphate or cholinesterase-inhibiting compounds may include the following: numbness, tingling sensations, incoordination, headache, dizziness, tremor, nausea, abdominal cramps, sweating, blurred vision, difficulty breathing or respiratory depression, and slow heartbeat. Very high doses may result in unconscious-

ness, incontinence, and convulsions or fatality. The acute effects of malathion depend on product purity and the route of exposure (NRC 1977). Other factors which may influence the observed toxicity of malathion include the amount of protein in the diet and gender. As protein intake decreased, malathion was increasingly toxic to the rats (Carlson 1987). Malathion has been shown to have different toxicities in male and female rats and humans due to metabolism, storage, and excretion differences between the sexes, with females being much more susceptible than males (Menzer 1987). Numerous malathion poisoning incidents have occurred among pesticide workers and small children through accidental exposure. In one reported case of malathion poisoning, an infant exhibited severe signs of cholinesterase inhibition after exposure to an aerosol bomb containing 0.5% malathion (Gosselin 1984).

Neurotoxicity

In a study of acute neurotoxicity in rats receiving doses of 0, 500, 1000, or 2000 mg/kg bodyweight (bw), an NOAEL was not identified, as clinical signs were present at all doses. In a 13-week study of neurotoxicity, also in rats, at dietary concentrations of 0, 50, 5000, or 20,000 ppm, the NOAEL was 5000 ppm, equal to 350 mg/kg bw per day, on the basis of inhibition of brain acetylcholinesterase at the highest dose (WHO 1997).

Two studies on the neurotoxicity of malathion in hens were reviewed. In neither was there evidence that malathion can cause delayed neuropathy, although some inhibition of neuropathy target esterase was found in the brain at 2000 mg/kg bw (WHO 1997).

Chronic Toxicity

Human volunteers fed very low doses of malathion for 6 weeks showed no significant effects on blood cholinesterase activity. Rats fed dietary doses of 5 mg/kg/day to 25 mg/kg/day over two years showed no symptoms apart from depressed cholinesterase activity. When small amounts of the compound were administered for eight weeks, rats showed no adverse effects on whole-blood cholinesterase activity. Weanling male rats were twice as susceptible to malathion as adults (Gallo 1991).

Carcinogenic Effects

Female rats on dietary doses of approximately 500 mg/kg/day of malathion for 2 years did not develop tumors (Gallo 1991). Adrenal tumors developed in the males at low doses, but not at the high doses (NCI 1979), suggesting that malathion was not the cause. Three of five studies that have investigated the carcinogenicity of malathion have found that the compound does not produce tumors in the test animals.

Reproductive Effects

Several studies have documented developmental and reproductive effects due to high doses of malathion in test animals (Gallo 1991). Rats fed high doses of 240 mg/kg/day during pregnancy showed an increased rate of newborn mortality. However, malathion fed to rats at low dosages caused no reproductive effects (US PHS 1995). It is not likely that malathion will cause reproductive effects in humans under normal circumstances.

Teratogenic and Developmental Effects

Rats fed high doses (240 mg/kg/day) showed no teratogenic effects. Malathion and its metabolites can cross the placenta of the goat and depress cholinesterase activity of the fetus (US PHS 1995). Chickens fed diets at low doses for two years showed no adverse effects on egg hatching (US PHS 1995).

Mutagenic Effects

Malathion produced detectable mutations in three different types of cultured human cells, including white blood cells and lymph cells (Gallo 1991, US PHS 1995). It is not clear what the implications of these results are for humans.

Endocrine

Effects on some endocrine glands and changes in some hormone levels were reported in laboratory animals given repeated oral doses of malathion. The amount of malathion given to animals in these studies, however, exceeds the amount humans are likely to contact from the spraying of malathion (NYSDH 2002).

Skin Sensitization

Acute percutaneous LD_{50} (24 h) for rabbits 4100 mg/kg (Tomlin 2000).

VII. Routes of Human Exposure

Products containing the insecticide, malathion, are available for both occupational and residential uses. Occupational uses include terrestrial food and feed crops, indoor food crops, terrestrial non-food crops, and general wide-area treatments for mosquito vector control. There are outdoor residential uses that include application to vegetable gardens, home orchards, ornamentals and lawns (US EPA 1997).

VIII. Environmental Toxicology and Ecological Effects

Birds

Malathion is toxic to birds. The reported acute oral LD_{50} values are: in mallards, 1485 mg/kg; in pheasants, 167 mg/kg; in blackbirds and starlings, over 100 mg/kg; and in chickens, 525 mg/kg (Gallo 1991, Smith 1993). The reported 5- to 8-day dietary LC_{50} is over 3000 ppm in Japanese quail, mallard, and northern bobwhite, and is 2639 ppm in ring-neck pheasants (Smith 1993). Furthermore, 90% of the dose to birds was metabolized and excreted in 24 hours via urine (Menzer 1987).

Fish

Malathion has a wide range of toxicities in fish: it is toxic in the walleye (96-hour LC_{50} of 0.06 mg/L), brown trout (0.1 mg/L) and the cutthroat trout (0.28 mg/L), fathead minnows (8.6 mg/L), and in goldfish (10.7 mg/L) (Kidd and James 1991, US PHS 1995, Johnson 1980).

Amphibians

Malathion is toxic to the aquatic stages of amphibians (Howard 1991).

Non-Target Aquatic Organisms

Various aquatic invertebrates are extremely sensitive, with EC_{50} values from 1 ug/L to 1 mg/L (Menzie 1980). Because of its very short half-life, malathion is not expected to bioconcentrate in aquatic organisms. However, brown shrimp showed an average concentration of 869 and 959 times the ambient water concentration in two separate samples (Howard 1991).

IX. Environmental Fate

Transport and Degradation Pathways

Malathion is of low persistence in soil with reported field half-lives of 1 to 25 days (Wauchope 1992). Degradation in soil is rapid and related to the degree of soil binding. Breakdown occurs by a combination of biological degradation and nonbiological reaction with water (Howard 1991). If released to the atmosphere, malathion will break down rapidly in sunlight, with a reported half-life in air of about 1.5 days. It is moderately bound to soils, and is soluble in water, so it may pose a risk of groundwater or surface water contamination in situations that may be less conducive to breakdown. The compound was detected in 12 of 3252 different groundwater sources in two different states, and in small concentrations in several wells in California, with a highest concentration of 6.17 ug/L (NRC 1977).

In raw river water, the half-life is less than one week, whereas malathion remained stable in distilled water for 3 weeks. Applied at 1 to 6 lb/acre in log ponds for mosquito control, it was effective for 2.5 to 6 weeks. In sterile seawater, the degradation increases with increased salinity. The breakdown products in water are mono- and dicarboxylic acids (Howard 1991). Residues were found mainly associated with areas of high lipid content in the plant. Increased moisture content increased degradation (NRC 1977).

X. Toxicity Values for Select Aquatic Organisms

Table 86. Malathion Toxicity Values for Select Aquatic Organisms.

	Duration	Effect	Result	Reference
Water Flea	48 hours	EC_{50}	1.0 g/L	USFWS 1986
(Daphnia magna)				
Daphnid	48 hours	LC_{50}	0.7 g/L	USFWS 1986
(Simocephalus serrulatus)				
Glass Shrimp	96 hours	LC_{50}	12 g/L	USFWS 1986
(Palaemonets kadiakensis)				
Pink Shrimp	48 hours	LC_{50}	280 g/L	USEPA 1996
(Penaeus duorarum)				
Scud	96 hours	LC_{50}	0.5 g/L	USFWS 1986
(Gammarus lacustris)				
Eastern oyster	96 hours	EC_{50}	2960 g/L	Wade and Wisk
(Crassostrea virginica)				
Fathead Minnow	96 hours	LC_{50}	8,650 g/L	USFWS 1986
Pinfish (Lagodon rhomboids)	3 days	survival reduced by 60% reduced reduced by 60%	30 g/L	Cook 1976
Bluegill Sunfish	96 hours	LC_{50}	20 g/L	Helfrich et al.
Striped Bass	96 hours	LC_{50}	60 g/L	Wellborn 1971
Rainbow Trout	96 hours	LC_{50}	70 g/L	Helfrich et al.
Flagfish	110 days	LOEC	11 g/L	Hermanutz 1978
(Jordanella floridae)		NOEC	8.6 g/L	

XI. Method Detection Limits

The method detection limit for malathion is reported at 0.01mg/L by EPA. The analytical method used is GC/FPD (Gas Chromatograph/Flame Photometric Detector) (US EPA 2002).

XII. Manufacturer Contact Info

Numerous: including Drexel, Fair, Uniroyal.

XIII. Summary Table

Table 87. Malathion Summary Table.

Primary use	Malathion is a non-systemic, wide-spectrum organophosphate insecticide and acaricide.
Mechanism of Toxicity	Malathion's mode of action is through acetylcholinesterase (AChE) inhibition, which disrupts nervous system function. It is a contact, stomach, and respiratory action insecticide.
Solubility	145 mg/L at 25°C
Fate	In river water, the half-life is less than one week, whereas malathion remained stable in distilled water for three weeks. In sterile seawater, the degradation increases with increased salinity. Because of its very short half-life, malathion is not expected to bioconcentrate in aquatic organisms. However, brown shrimp showed an average concentration of 869 and 959 times the ambient water concentration in two separate samples
Confounding Factors	Decomposed by acids and alkalis.
Data Gaps	Resident Species. Chronic effects on invertebrates (e.g. *Hyallela azteca*).

H. S-Methoprene (Altosid)

According to the World Health Organization and the U.N. Food and Agriculture Organization, "Methoprene is a selective, stable and potent larvicide; an ether and diunsaturated fatty acid ester; a juvenile hormone analogue, its toxicity to insects is manifest through interference with metamorphosis, a process without parallel in mammals. Methoprene is non-persistent and non-toxic to mammals and presents no long-term hazard to other species at recommended application rates" (WHO 2001).

I. Introduction

S-methoprene is an isomer of the compound methoprene, a synthetic organic compound which mimics the action of a naturally occurring insect growth regulation hormone called Juvenile Hormone (JH). S-Methoprene is the form of methoprene used in pesticides specifically labeled for mosquito control. Because the toxicity and environmental profiles of the (S) isomer and the isomer mixture are very similar, they will be discussed as synonyms throughout this section. Where significant differences in biological activity or other properties have been noted, they are explicitly acknowledged.

Methoprene, as individual isomeric forms or as a racemic mixture, is used as an insecticide because it interferes with the normal insect maturation process. While insects normally develop through a series of stages (e.g. egg, four larval stages or "instars", pupa, adult for mosquitoes), methoprene artificially stunts the insects' development, making it impossible for them to mature to the adult stages, and thus preventing them from reproducing. If the adult stage is the pestiferous one, as with mosquitoes, the material not only prevents reproduction, but also prevents outbreaks of the animal pest. Based on its mode of action, methoprene is considered an insect growth regulator (IGR). Methoprene is also considered a larvicide since it is effective in controlling the larval stages of mosquitoes and some other insects.

JH is found during early life stages of the mosquito (and in other insects), but is most prevalent during the early larval instars. As mosquito larva mature, the level of JH steadily declines until the 4th instar molt, when levels are very low. This is considered to be a sensitive period when all the physical features of the adult begin to develop. If methoprene is in the aquatic habitat, even at very low concentrations, it can be absorbed on contact, leading to disruption of the insect's hormone system. When this happens during the sensitive period, the unbalance interferes with 4th instar larval development, allowing transition to pupal form ("pupation") but preventing adult emergence. Since pupae do not eat, they eventually deplete body stores of essential nutrients and then starve to death. To be effective, it is essential that this growth inhibitor be administered at the proper stage of the target pest's life cycle. Methoprene is not toxic to the pupal or adult stages.

Because JH is found in many families of insects, methoprene can potentially affect both a range of insect pests and non-target insects. In addition to its use for mosquito control, methoprene is used to protect a number of foods including meat, milk, eggs, mushrooms, peanuts, rice, and cereals from insect damage. It is also used to control several types of ants, flies, lice, moths, beetles, and fleas. For mosquito control, methoprene can be ap-

plied either in response to observed high populations of mosquito larvae at a site, or as a sustained-release product that can persist for up to about four months, for sites where mosquito production is episodic but repetitive. It is available in suspension, emulsifiable and soluble concentrate formulations, as well as in briquette, aerosol, and bait form. Application can be by hand, ground vehicle, or aircraft.

II. Active Ingredient Identification

S-Methoprene is the (S) isomer of Methoprene. Both the compound in general and its (S) isomer in particular are discussed in the scientific literature, often without a distinction being made. For example, the WHO/FAO Pesticide Data Sheet (WHO 2001) for the product describes it as "Methoprene (ISO, BSI, ANSI)" and does not refer to s-methoprene specifically.

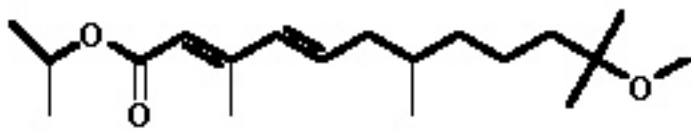
Synonyms

S-Methoprene: S-methoprene; Smethoprene; Isopropyl (2E,4E,7S)-11-methoxy-3,7,11-trimethyl-2,4-dodecadienoate; 2,4-Dodecadienoic acid, 11-methoxy-3,7,11-trimethyl-, 1-methylethyl ester, (S-E)

Methoprene: IUPAC and CAS No. 1: Isopropyl (2E, 4E)-11-methoxy-3,7,11 trimethyl-2-1,4-dodecadienoate (WHO/FAO 2001); Isopropyl(E,E)-(R,S)-11-methoxy-3,7,11-trimethyldodeca-2,4-dienoate

4; Isopropyl (E,E)-11-methoxy-3,7,11-trimethyl-2,4-dodecadienoate ; Isopropyl (2E,4E)-11-methoxy-3,7,11-trimethyl-2,4-dodecadienoate; 1-Methylethyl (E,E)-11-methoxy-3,7,11-trimethyl-2,4-dodecadienoate; 2,4-Dodecadienoic acid, 11-methoxy-3,7,11-trimethyl-, 1-methylethyl ester, (E,E); 2,4-Dodecadienoic acid, 11-methoxy-3,7,11-trimethyl-, ispropyl ester, (E,E)

Structural formula



Active Ingredient Identification Summary Table

Table 88. Methoprene Active Ingredient Identification Summary Table.

Identifier	Methoprene	S-Methoprene	Source(s)
CAS Number	40596-69-8, 40596698	65733-16-6, 65733166	PAN 2003
Molecular Weight	310.48; 310.0	310.48; 310.0	EXTOXNET 1996, WHO 2001
Molecular Formula	$C_{19}H_{34}O_3$	$C_{19}H_{34}O_3$	WHO 2001
USEPA PC Code	105401	105402	PAN 2003
CA DPR Chemical Code	1784, 01784	5026, 05026	PAN 2003
USEPA Chemical Class	Unspecified	Unspecified	PAN 2003
WHO/FAO Chemical Group	Juvenile hormone analogue	Juvenile hormone analogue	WHO/FAO 2001

III. Physical Properties

Appearance

Technical methoprene is an amber or pale yellow liquid with a faint fruity odor (Kidd and James 1991).

Stability

Methoprene is described as a stable compound though non-persistent due to rapid biodegradation mainly to CO_2. The soil half-life is 10 days; in water, less than one day in sunlight and over four weeks in dark and, on plants, 1-2 days (WHO 2001).

Physical Properties Summary Table

Table 89. Methoprene Physical Properties Summary Table.

Characteristic	Value	Source
Specific Gravity	0.261 at 20°C	WHO 2001
Melting Point	Not Available	EXTOXNET 1996
Boiling Point	100°C (0.05 mm Hg)	WHO 2001
Vapor Pressure	3.15 mPa @ 25°C	Kidd and James 1991
Water Solubility	1.4 mg/L @ 25°C; 1.39 mg/l	Kidd and James 1991, WHO 2001
Solubility in Other Solvents	Miscible in organic solvents	Kidd and James 1991, WHO 2001
Partition Coefficient (K_{ow})	LogP >6	Tomlin 2000
Adsorption Coefficient (K_{oc})	Not Available	EXTOXNET 1996
Henry's Constant (K_h)	4.76 X 10^{-1} Pa m^3 mol^{-1}	Tomlin 2000
Half-Life	Soil and water ~10 days, pond water 30-40 hours	EXTOXNET 1996

IV. Active Ingredient Regulatory Status

The safety and specificity of methoprene in general and s-methoprene in particular are confirmed by their regulatory status at all levels of government and by the low concern noted by non-governmental actors.

Table 90. Methoprene Active Ingredient Regulatory Status.

Status	Methoprene	S-Methoprene	Source(s)
UNEP Persistent Organic Pollutant	No	No	PAN 2003
UNEP Prior Informed Consent Chemical	No	No	PAN 2003
WHO/FAO Pesticide Primary Use	Insect Growth Regulator	Insect Growth Regulator	WHO 2001
USEPA Registered Pesticide Active Ingredient	1975 GUP	1975 GUP[6]	US EPA 2001
USEPA Pesticide Use Type	Insect Growth Regulator	Insect Growth Regulator	PAN 2003
USEPA Toxicity Class (Pesticide Products)	IV - Slightly Toxic to Practically Non-toxic	IV - Slightly Toxic to Practically Non-toxic	EXTOXNET 1996
USEPA Signal Word (Pesticide Products)	Caution	Caution	US EPA 2001
USEPA Reregistration	1997	1997	US EPA 2001
USEPA Hazardous Air Pollutant	No	No	PAN 2003
USEPA Minimum Risk Pesticide (25b list)	No	No	PAN 2003
CA Registered Pesticide Active Ingredient	Yes	Yes	DPR 2001
CA Toxic Air Contaminant	No	No	PAN 2003
CA Groundwater Contaminant	N.E.	N.E.	PAN 2003
PAN "Bad Actor"	No	No	PAN 2003
PAN "Dirty Dozen"	No	No	PAN 2003

V. Pesticide Status

While USEPA has issued distinct PC codes for methoprene and S-methoprene, that agency does not generally distinguish the isomeric and racemic forms of the compound in pesticide registration documents. Methoprene was first registered by USEPA in 1975 as a conventional, chemical pesticide for the control of several insect species, including mosquitoes. USEPA issued a Registration Standard for Methoprene in February 1982, and subsequently reclassified the compound as a biopesticide and more specifically as a biochemical pesticide (US EPA 2001) in recognition of its low direct toxicity even to target organisms. US EPA issued a Reregistration Eligibility Document (RED) in 1991, and reregistration of the active ingredient (both racemic and isomeric forms) and all end-use products was completed in 1997 (US EPA 2001). The most recent RED for methoprene was issued in 2001.

Methoprene, including s-methoprene, is officially recognized as a slightly to practically nontoxic compound (EXTOXNET 1996). Therefore, pesticide products containing methoprene as their sole active ingredient are General Use Pesticide's (GUP's) in EPA toxicity

class IV (least toxic), and their container labels must bear the Signal Word CAUTION (lowest level) (EXTOXNET 1996).

Tolerances (40 CFR 180.359) and exemption from tolerances (40 CFR 180.1033 and 185.4150) have been established for Methoprene in or on a number of food commodities (US EPA 2001). Methoprene is also recognized by FDA as a feed additive for use in cattle feeds to control horn flies (40 CFR 186.4150; formerly 21CFR 561.282).

Pests Controlled

Methoprene-based products are registered for use against a range of insects including fleas, flies, moths, pharaoh's ants, boll weevil, lice, mosquitos, leaf hoppers, plant hoppers, cucumber beetles, cigarette beetle, tobacco moth and others (WHO 2001).

Pesticide Trade and Other Names

Mosquito larvicides containing methoprene are all sold under the trade name Altosid, including Altosid Liquid Larvicide (A.L.L.), Altosid Briquets, and Altosid Pellets. A partial list of trade names for other methoprene-based insecticides includes Apex, Diacan (WHO/FAO lists Diacon), Dianex, Kabat, Manta, Minex, Pharorid, Precor, ZR-515, and ENT-70460 (EXTOXNET 1996, PAN 2003).

Formulations and Dosages (summarized, in part, from www.altosid.com)

Methoprene is available in suspension, emulsifiable and soluble concentrate formulations, as well as in briquette, aerosol and bait form (EXTOXNET 1996). Currently, five methoprene formulations are sold under the trade name of Altosid. These include Altosid Liquid Larvicide (A.L.L.) and Altosid Liquid Larvicide Concentrate, Altosid Briquets, Altosid XR Briquets, and Altosid Pellets. In addition, "Altosand" (A.L.L. in a sand carrier) and "Duplex" (A.L.L. mixed with Bti formulations) are commonly prepared by applicators for specific uses.

ALTOSID LIQUID LARVICIDE (A.L.L.) & A.L.L. CONCENTRATE. These two flowable formulations have identical components except for the difference in the concentration of active ingredients. A.L.L. contains 5% (wt./wt.) s-Methoprene while A.L.L. concentrate contains 20% (wt./wt.) s-Methoprene. The balance consists of inert ingredients that encapsulate the s-Methoprene, causing its slow release and retarding its ultraviolet light degradation. Use rates are 3 to 4 ounces of A.L.L. 5% and æ to 1 ounce of A.L.L. Concentrate (both equivalent to 0.01008 to 0.01344 lb. AI) per acre, mixed in water as a carrier and dispensed by spraying with conventional ground and aerial equipment. Because the specific gravity of Altosid Liquid is about that of water, it tends to stay near the target surface. No rate adjustment is necessary for varying water depths when treating species that breath air at the surface.

Liquid formulations are designed to control fresh and saline floodwater mosquitoes with synchronous development patterns. Cold, cloudy weather and cool water slow the release and degradation of the active ingredient as well as the development of the mosquito larvae. Accordingly, formulation activity automatically tracks developing broods.

ALTOSID BRIQUETS. The Altosid Briquet was the first solid methoprene product marketed for mosquito control beginning in 1978. It is made of plaster (calcium sulfate), 3.85% (wt./wt.) r-methoprene, 3.85% s-methoprene (.000458 lb. AI/briquet) and charcoal (to retard ultra violet light degradation). Altosid Briquets release methoprene for about 30 days under normal weather conditions. Application should be made at the beginning of the mosquito season, and under normal weather conditions, repeat treatments should be carried out at 30 day intervals. The recommended application rate is 1 Briquet per 100 sq. ft. in non-flowing or low-flowing water up to 2 feet deep.

Flood water *Aedes* and permanent water *Anopheles*, *Culex*, and *Culiseta* larvae are usual targets. Typical treatment sites include storm drains, catch basins, roadside ditches, ornamental ponds and fountains, cesspools and septic tanks, waste treatment and settlement ponds, flooded crypts, transformer vaults, abandoned swimming pools, construction and other man-made depressions.

ALTOSID XR BRIQUETS. It is made of hard dental plaster (calcium sulfate), 1.8% (wt./wt.) s-methoprene (.00145 lb. AI/briquet) and charcoal (to retard ultraviolet light degradation). Despite containing only three times the AI as the "30-day briquet", the comparatively harder plaster and larger size of the XR Briquet change the erosion rate allowing sustained s-methoprene release up to 150 days in normal weather. XR Briquets should be applied 1 to 2 per 200 sq. ft. in no-flow or low-flow water conditions, depending on the species.

Targets are the same as for the smaller briquets. Appropriate treatment sites for XR Briquets include storm drains, catch basins, roadside ditches, ornamental ponds and fountains, cesspools and septic tanks, waste treatment settlement ponds, flooded crypts, transformer vaults, abandoned swimming pools, construction and other man-made depressions, cattail swamps and marshes, water hyacinth beds, pastures, meadows, rice fields, freshwater swamps and marshes, woodland pools, flood plains and dredge spoil sites.

ALTOSID PELLETS. Altosid Pellets were approved for use in April 1990. They contain 4% (wt./wt.) s-methoprene (0.04 lb. AI/lb.), dental plaster (calcium sulfate), and charcoal. Like the Briquets discussed above, Pellets are designed to slowly release s-methoprene as they erode. Under normal weather conditions, control can be achieved for up to 30 days (Kramer et al. 1993). Label application rates range from 2.5 lbs. to 10.0 lbs. per acre (0.1 to 0.4 lb. AI/acre), depending on the target species and/or habitat.

The species are the same as listed for the briquet formulations. Listed target sites include pastures, meadows, rice fields, freshwater swamps and marshes, salt and tidal marshes, woodland pools, flood plains, tires and other artificial water holding containers, dredge spoil sites, waste treatment ponds, ditches, and other man-made depressions, ornamental pond and fountains, flooded crypts, transformer vaults, abandoned swimming pools, construction and other man-made depressions, tree holes, storm drains, catch basins, and waste water treatment settling ponds.

ALTOSID XR-G Altosid Xr-G was approved for use in 1997. This product contains 1.5% (wt./wt.) s-methoprene. Granules are designed to slowly release s-methoprene as they erode. Under normal weather conditions, control can be achieved for up to 21 days. Label

application rates range from 5 lbs. to 20.0 lbs. per acre, depending on the target species and/or habitat. The species are the same as listed for the briquet formulations. Listed target sites include snow pools, meadows, rice fields, freshwater swamps and marshes, salt and tidal marshes, woodland pools, tires and other artificial water holding containers, dredge spoil sites, waste treatment ponds, ditches, and other natural and man-made depressions.

VI. Toxicity to Humans and Other Mammals

Repeated, comprehensive toxicological evaluations of methoprene and S-methoprene over several decades have demonstrated conclusively that this material does not pose a toxicity risk to humans or other mammals. An extensive safety database has been generated for methoprene since it was first registered in 1975. Toxicological data on file with the USEPA includes an acute toxicity battery, irritation/sensitization studies, subchronic feeding studies, developmental and reproductive toxicity studies, mutagenicity studies, chronic feeding studies and lifetime carcinogenicity studies. In addition, special studies dealing with the metabolism and fate of methoprene in several mammalian species and those dealing with the potential for endocrine effects have also been completed. Studies relating to the effect of methoprene on the immune system were waived by EPA since there was no indication of the immune system being the potential target organ/system in any of the acute, subchronic, chronic, teratology, reproduction or special toxicity studies. Today, some of the submitted data would not even be required under the current guidelines for biochemical pesticides.

Mian and Mulla (1982) provide a review of the literature (field and laboratory), which evaluates the use of insect growth regulators including methoprene, for pest control and the impact on nontarget biota and the environmental dynamics and fate in living and nonliving entities. Wright (1973) reviewed the toxicological properties determined for registration of the IGR and found no significant effects against any of the species tested – swine, sheep, hamsters, rats, dogs, rabbits, guinea pigs and cattle revealed no clinical signs of toxicosis.

Absorption Route

In humans and other mammals, methoprene may be absorbed from the gastrointestinal tract, through the intact skin, and by inhalation of spray mist (WHO 2001).

Fate in Mammals and Excretion Products

Methoprene is not persistent in mammalian bodies. In general, methoprene in mammals is rapidly and completely broken down and excreted, mostly in the urine and feces (EXTOXNET 1996). In addition, methoprene is apparently metabolized rapidly and extensively in mammals into endogenous products such as acetate molecules and these are incorporated into the biosynthesis of naturally occurring constituents of the body such as cholesterol and bile acids (EXTOXNET 1996, US EPA 2001). Finally, ingested methoprene can pass unchanged through the alimentary canal of cattle; it is then excreted in feces in amounts that are sufficient to kill some fly larvae that breed in dung (McEwen and Stephenson 1979).

Methoprene metabolism and excretion have been studied in several vertebrate organisms - cattle, rodents and hens. Methoprene is metabolized primarily by hepatocyte mi-

crosomal esterases, mainly to methoprene acid, which after alpha oxidation is susceptible to beta oxidation to acetate then, via the Krebs' cycle to carbon dioxide or intermediary metabolites. In C_{14}-labelled methoprene studies at low doses, most of the radioactivity was respired from the body as CO_2. The remainder, was found to be associated with complex and simple secondary metabolites in body tissues and fluids and also as primary breakdown products in urine and faeces. A significant amount of radioactivity was also found in the milk of lactating cows and in eggs of laying hens. Less than 1% of this excreted radioactivity was found as methoprene and the rest was associated with natural products; no primary metabolites were found. The finding of large quantities of unmetabolized methropene in faeces but not in urine or blood suggests poor intestinal absorption at higher doses and rapid metabolism of the absorbed material. The primary products of urinary excretion are the hydroxyepter (isopropyl 11-hydroxy-3,7,11-trimethyl - 2,4-dodecadienoate), the hydroxyacid (11-methoxy-3,7,11-trimethyl-2,4-dodecadienoic acid), and several lesser metabolites including 7-methoxycitronellic acid, 7-hydroxycitronellic acid and 7-methoxycitronellal. These are excreted as free compounds and as conjugates (WHO 2001).

Mode of action

Methoprene is an invertebrate metabolic inhibitor that does not seem to cause direct toxic effects in mammals. In in vitro studies of mouse L929 cells, methoprene inhibited macromolecular synthesis including DNA and RNA, at concentrations exceeding its maximum water solubility level. Degeneration of cells and uncoupling of oxidative phosphorylation has also been reported in mouse hepatocyte cultures at very high dose levels (WHO 2001).

Acute toxicity

US EPA has concluded that the "data indicate an extremely low potential for acute toxicity to humans from overexposure to either racemic or (S)-Methoprene via the oral, dermal, ocular or inhalation routes of exposure." (2001). The World Health Organization has likewise determined that methoprene is unlikely to pose an acute toxicity hazard to humans (WHO 2001, PAN 2003). Technical methoprene is practically nontoxic when ingested or inhaled and only slightly toxic by dermal absorption. The FIFRA labels for s-methoprene-based pesticides lists this material as "slightly toxic" as a technical material. S-Methoprene is classified in toxicity categories III and IV (US EPA 2001). The U.S. National Toxics Program does not report any acute toxicity studies for methoprene or its isomers (PAN 2003).

The acute oral toxicity of methoprene in mammals is extremely low (US EPA Category 4 = "practically nontoxic"; WHO List 5 = "Unlikely to present acute hazard in normal use"), which is reflected in the very high doses required to cause mortality in the laboratory. In US EPA reregistration documents (US EPA 2001), the acute oral LD_{50} for racemic and (S)-Methoprene in rats is >10,000 (US EPA 1) and >5000 (US EPA 2) mg/kg, respectively, the highest doses tested (HDT) for both compounds. In another study, the oral LD_{50} for technical methoprene in rats was greater than 34,600 mg/kg (Kidd and James 1991). In dogs, the acute oral LD_{50} value for racemic methoprene is between 5000 to 10,000 mg/kg (US EPA 2001, WHO 2001). Kidd and James report this value as greater than 5000 mg/kg (Kidd and James 1991).

The acute dermal toxicity of methoprene in mammals is also very low. USEPA reregistration data demonstrate an acute dermal LD_{50} for both racemic and (S)-Methoprene in rabbits of >2000 mg/kg (US EPA 2001). Kidd and James (1991) report acute rabbit dermal LD_{50} values of > 2,000-3,000 mg/kg, and the WHO/FAO Pesticide Information Sheet (2001) shows values of 3,000-10,000 mg/kg (rabbit), and >5,000 mg/kg (rat). According to EXTOXNET (1996), methoprene is slightly toxic by skin exposure.

The acute inhalation toxicity to mammals is apparently too low to measure with conventional LC_{50}'s. Acute inhalation LC_{50}'s are reported as greater than 210 mg/L in all available studies, including 4-hr inhalation LC_{50} for racemic methoprene in the rat and guinea pig (US EPA 1982, EXTOXNET 1996, WHO 2001).

Primary eye and skin irritation studies have been conducted in rabbits for both racemic and (S)-Methoprene. Results from these studies indicate that both racemic and (S)-Methoprene are not likely to cause irritation to the skin or eyes of humans when exposed topically. Methoprene is not an eye or skin irritant (Kidd and James 1991). No eye irritation was observed in rabbits up to 72 hours after applications of 0.1 ml of 69.8% solution. No dermal irritation was observed in rabbits exposed to 0.5 ml of a 69.8% solution for 24 hours on either intact or abraded skin under occlusive wraps (WHO 2001). Also, based on data generated for racemic methoprene in guinea pigs, no potential for skin sensitization is expected for (S)-Methoprene (EXTOXNET 1996).

No overt signs of poisoning have been reported in incidents involving accidental human exposure to methoprene (US EPA 1982), and the World Health Organization and U.N. Food and Agriculture Organization observe that there have been no reports of adverse effects on occupationally exposed workers (1994). WHO and FAO do not know of any dangerous doses of methoprene (WHO 2001).

The US EPA is reviewing submitted data regarding the safety of methoprene use on domestic animals. It is used on pets (dogs and cats) and in pet areas (bedding). Incidents of toxicity to cats from the use of products containing methoprene have been reported and the EPA is investigating these incidents and evaluating domestic animal safety data for methoprene to determine if the cause of the reported incidents is due to methoprene or another ingredient in the products. Once the cause of the adverse effect incidents is known the EPA will take appropriate regulatory action.

Neurotoxicity:

Methoprene and its isomers are not cholinesterase inhibitors and have no known neurotoxic effects (PAN 2003). No adverse clinical or pathological findings were noted in the acute, subchronic or chronic studies (WHO 2001).

Chronic Toxicity:

In order to evaluate health effects from short-term exposure, 90-day feeding studies have been conducted with racemic methoprene in rats given doses of 0, 250, 500, 1000 or 5000 ppm in diet and in dogs given doses of 0, 250, 500 or 5000 ppm in diet (EXTOXNET 1996). The NOEL for systemic effects was 500 ppm for both rats and dogs. Increased liver

weights in rats and dogs and renal tubular degeneration effects in some rats were observed at higher dose levels but the significance of these effects are considered negligible since they were not observed in chronic feeding studies. A 30-day dermal toxicity study has been conducted in Japanese rabbits with undiluted methoprene at doses of 0, 100, 300, 900 or 2700 mg/kg/day applied topically to the back of the rabbits (EXTOXNET 1996). The 300-mg/kg dose was concluded to be the NOEL for systemic effects and 100 mg/kg was considered to be the NOEL for local effects. The NOEL for racemic methoprene was 20 mg/L (HDT) in a 21-day inhalation toxicity study in rats (EXTOXNET 1996). These data indicate that oral, dermal or inhalation exposure to Methoprene for an extended duration is not likely to cause adverse health effects in humans.

Published studies indicate that there is no chronic mammalian toxicity associated with methoprene. According to the WHO/FAO Pesticide Report (1994), no signs of toxicity were observed in a 21-day dermal toxicity test in rabbits given 400 mg/kg b.w./day technical methoprene; no toxic effects were observed in a 21-day inhalation test in rats at a 20 mg/l dose level, and there was no evidence of the accumulation of methoprene or its primary metabolites in body tissues and fluid in C_{14}-labelled methoprene tracer studies.

In short-term oral (dietary) studies, there has been no demonstrated toxicity except at extremely high levels. In 90-day studies, dogs and rats showed no toxic effects at the 500-mg/kg diet level and there were no irreversible ill effects at the 5000 mg/kg diet level. No deaths occurred in any of the diet groups. In a 6-month study, male and female rats were fed a 0, 80, 400, 2000 or 10000 mg/kg diet. One female on the 2000 mg/kg diet died. Mild degenerative changes, which would be expected to be reversible, were observed in hepatic parenchyma cells at 10 000 mg/kg, . The maximum no-effect-level for rats was estimated to be 20 mg/kg b.w./ day in a 90-day study.

Similarly low toxicity has been observed in long-term feeding studies. In two-year studies rats were fed diets containing 250, 1000 or 5000 mg/kg of methoprene. The no observed adverse effect level was determined to be 5000 mg/kg (diet), equivalent to 250 (mg/kg b.w.)/day. Mice were fed dietary levels of 250, 1000 or 2500 mg/kg for 18 months. There was no treatment related mortality. Amyloidosis was more prevalent in the high dose group than others and hepatic pigmentation was also observed at this dose level and to a lesser extent at 1000 mg/kg (diet). The NOEL was determined to be 250 mg/kg (diet), equivalent to 37.5 (mg/kg b.w.)/day. No methoprene-related effects were observed in 2-year feeding trials with rats given doses of 250 mg/kg/day, nor in mice given 30 mg/kg/day (Kidd and James 1991). Liver changes were observed in mice fed 50 to 250 mg/kg/day of methoprene during an 18-month study (USEPA 1982). Increased liver weights occurred in rats fed 250 mg/kg/day for 90 days, but not during a 24-month feeding study in which rats were fed 125 mg/kg/day (USEPA 1982). The target organ primarily affected by methoprene after long-term exposure is the liver.

Chronic feeding studies have been conducted in rats and mice (EXTOXNET 1996). Rats exposed to methoprene technical at 0, 250, 1000, or 5000 ppm in the diet daily for two years did not exhibit any adverse health effects even at the highest dose as compared to control animals. No increase in tumor incidence was observed. The NOEL for systemic effects was 5000 ppm, the highest dose tested in the study. No potential for increase in tumors

was observed in another chronic study using CD-1 mice fed diets containing 0, 250, 1000 or 2500 ppm of methoprene daily for 18 months (EXTOXNET 1996). No significant health effects were observed in treated groups. The NOEL for systemic effects in mice was concluded to be 250 mg/kg/day due to the presence of brown pigmentation of the liver in some animals at higher doses. It can therefore be concluded that methoprene is not an oncogenic compound based on the chronic toxicity studies summarized above.

Carcinogenic Effects:

Laboratory studies indicate that methoprene in general and s-methoprene in particular are not carcinogenic. According to the WHO and FAO (1994), no evidence of carcinogenic potential was obtained in the long-term dietary studies with mice and rats nor in the several studies of mutagenicity reported. According to the USEPA, no tumors were seen in an 18-month feeding study with mice, or in a 24-month oncogenicity study with rats (US EPA 1982).

Neither the State of California, the US EPA, the US National Toxics Program, or the IARC, has listed methoprene or S-methoprene as known, probable, or possible carcinogens on any of their lists (PAN 2003). While none of these groups have issued formal "weight of the evidence" evaluations of the potential carcinogenicity of methoprene in general or of s-methoprene in particular (PAN 2003), the lack of formal evaluation by any of these programs is a strong confirmation that there has been no credible evidence presented of cancer risk associated with these materials.

Reproductive Effects

Complete data are available for evaluating the reproductive effects of methoprene in animals. Experimental data indicate that no reproductive hazards are associated with methoprene (US EPA 1982). No methoprene-related effects were observed in three-generation reproduction studies in rats receiving dietary doses of 125 mg/kg/day (Kidd and James 1991). In a three-generation study, rats continuously fed 2500 mg/kg diets showed no toxic or reproductive adverse effects. Mortality, pregnancy and fertility rates, food consumption, duration of gestation, fetal viability, neonatal survival, litter size and sex ratios were normal. No reproductive or embryotoxic effects were seen in quail or ducks at 30 ppm continuous feeding (WHO 2001). California does not list methoprene or S-methoprene as a female or male reproductive toxin in Prop 65 lists (PAN 2003). The three-generation reproduction study conducted in rats also revealed a NOEL of 2500 ppm (HDT) for reproductive effects (EXTOXNET 1996).

Teratogenic & Developmental Effects

Complete data are available for evaluating the developmental effects of methoprene in animals. Methoprene is not a developmental toxicant as evaluated in rabbits (NOEL 2000 mg/kg, the highest dose tested) and mice (NOEL 600 mg/kg/day, the highest dose tested) (EXTOXNET 1996). With such high NOELs for methoprene in these studies at the highest doses tested, no developmental toxicity can be expected in humans from exposure to the residues of methoprene either during pregnancy or during early childhood.

There have been no teratogenic effects observed in animals dosed with methoprene (EXTOXNET 1996). Teratological studies in swine, sheep, hamsters, rats and rabbits resulted in no observable effects in the animals at any level administered (Wright 1975). Teratogenic effects were not seen in rats at doses of about 25 mg/kg/day, or in rabbits at doses of about 15 mg/kg/day (USEPA 1982, USEPA 1991). No evidence of teratogenic activity was observed in sheep (dose unknown), in rabbits at 500 (mg/kg b.w.)/day, in rats at 1000 (mg/kg b.w.)/day or in mice at 600 (mg/kg b.w.)/ day (WHO 2001). California does not list methoprene or S-methoprene as a developmental toxin in Prop 65 lists (PAN 2003).

Mutagenic effects

Methoprene does not appear to be mutagenic. Methoprene was not mutagenically active in a microbial assay with *S. typhimurium* strains sensitive to base pair substitutions and frame shift mutations. It was also not active in a mouse cell culture assay or in a rat dominant lethal mutagenicity study at 2000 mg/kg b.w. (single dose) (WHO 2001). No methoprene-related mutagenic effects were observed in rats following a single dose of 2000 mg/kg (EXTOXNET 1996). Methoprene is not a mutagenic compound based on negative results obtained in the Ames test and several other mutagenicity assays (EXTOXNET 1996).

Endocrine Disruption:

There is no evidence that methoprene or any of its isomers causes endocrine disruption. Methoprene was found to have no estrogenic, androgenic, anabolic or glucocorticoid activity in mice and rats in studies (WHO 2001). Neither methoprene in general nor s-methoprene in particular is on the Illinois EPA ED, Keith, Colborn, or Benbrook lists (PAN 2003). Screening studies relating to endocrine effects indicate that methoprene has no potential for an estrogenic, androgenic, anabolic or a glucocorticoid effect (EXTOXNET 1996). In addition, any potential for these effects would have been revealed in the developmental studies and/or the three-generation reproduction study where animals were exposed to high levels of methoprene technical.

Skin Sensitization

Methoprene is not a skin sensitizer (EXTOXNET 1996). Methoprene showed no sensitization potential in two standard guinea-pig sensitization tests, and following a standard Draize method skin sensitization study on 231 volunteers it was concluded that the test substance, a domestic use formulation of methoprene, was not a human skin sensitizer. (WHO 2001).

VII. Routes of Human Exposure

Through the Diet

Dietary exposure to methoprene is minimal and would only be expected to occur from treatment of mushrooms, stored grains, peanuts and cereals or low-level residues in cattle meat, fat or milk from feed-through applications. Methoprene has been in use for over two decades. The stored grain uses are at a maximum 5 ppm rate. No health hazards have been reported that could be related to the ingestion of methoprene residues. Residues of methoprene are at negligible levels particularly with respect to the NOEL levels in the developmental and reproductive toxicity studies. Due to the high toxicological endpoints and low levels of residues, risk from consumption of treated commodities is considered negligible for the general population and infants and children.

Through Drinking Water

Exposure to methoprene residues is not expected from drinking water. In aqueous solutions, methoprene degrades rapidly under sunlight into at least 50 minor photolysis products (US EPA 2001). Methoprene is rapidly metabolized in soil both under aerobic and anaerobic conditions (half-life 10-14 days) with CO_2 as the major product (US EPA 2001). Degradation in surface water is due to both microbial metabolism and photolysis (US EPA 2001). By the time surface water reaches drinking water treatment plants, residues of methoprene are unlikely to be present and in the unlikely event that residues are present, these would be mitigated by water treatment procedures. In view of these points, drinking water is not considered an additive factor in exposure of the human population to methoprene.

During Application

Non-Dietary Exposure is considered minimal with respect to mixers, loaders and applicators since exposure via dermal and inhalation routes are negligible and methoprene is classified in toxicity category III and IV for dermal and inhalation toxicity, respectively. Furthermore, no evidence exists for neurotoxic, oncogenic, reproductive or developmental adverse effects that can be attributed to methoprene. EPA considers methoprene to pose no risks to people who are occupationally exposed to this biopesticide.

Exposure Guidelines

Table 91. Methoprene Exposure Guidelines.

	Value	**Source(s)**
ADI (Acceptable Daily Intake):	0.1 mg/kg/day	EXTOXNET 1996
MCL (Maximum Contaminant Level)	Not Available	EXTOXNET 1996
RfD (Reference Dose)	Not Available	EXTOXNET 1996
PEL (Permissible Exposure Level)	Not Available	EXTOXNET 1996
HA (Health Advisory)	Not Available	EXTOXNET 1996
TLV (Threshold Limit Value)	Not Available	EXTOXNET 1996

VIII. Environmental Toxicology & Ecological Effects

Methoprene has been shown to be practically non-toxic to terrestrial species including mallard ducks and quail, and methoprene had no effect on mallard or quail reproduction. Ecological effects studies on aquatic species indicate minimal acute and chronic risk to freshwater fish, freshwater invertebrates and estuarine species from exposure to methoprene mosquito products (US EPA 2001).

Extensive research has addressed the effects of methoprene on non-target aquatic and terrestrial organisms. Acute, short-term and subchronic effects studies on non-target immature and adult arthropods (Crustacea, Insecta and Mollusca, including shrimp, damselfly, beetle, tadpole) demonstrate 24- and 48- hour LC_{50} values >900 ppb (US EPA 2001). Confirming these studies, other researchers have demonstrated that sensitive life stages of nontarget organisms, i.e., nymph and larvae, and nontarget aquatic organisms that are highly related to mosquitoes, i.e., dragonfly, are not affected by methoprene up to 1,000 ppb (US EPA 2001).

Preliminary investigations are reported on the effects of methoprene on various life stages of different amphibian species (*B. woodhousei*, *R. catesbeiana* and *R. pipiens*) (US EPA 2001). Acute studies on *R. catesbeiana* and *R. pipiens* larvae indicate LC_{50} values >10,000 ppb and *B. woodhousei* adult LC_{50} values >1,000 ppb (highest dose tested). Chronic studies on *B. woodhousei* indicate a 22 day LC_{50} >1,000 ppb and LC_{50} > 1,000 ppb for *R. catesbeiana* and *R. pipiens*. No other adverse effects were reported.

Rate of release and data generated under laboratory and field conditions with methoprene mosquito product formulations, including slow release briquet formulations, indicate a maximal rate of release of is 4 ppb. Data on nontarget organism support margins of safety of >200 for nearly all organisms tested. Therefore, exposure to methoprene will not reach levels that are toxic to aquatic non-target species either after acute or chronic exposure (US EPA 2001).

Based upon review of data submitted to the EPA between 1993 and 1996, EPA concluded in 1996 that the following label changes should be implemented on all solid methoprene mosquito products:

"Exhaustive recent reviews of published literature on this material attest to its lack of adverse environmental impact (Glare & O'Callaghan, 1999). While Table 4 in Glare & O'Callaghan demonstrates a wide range of organisms potentially affected by methoprene, the authors are careful to emphasize that these effects are seen at dosages/concentrations many times higher than could be achieved during mosquito control activities."

Birds

Methoprene is reported as slightly toxic to birds (Zoecon Corporation 1974, Kidd and James 1991) or as relatively non-toxic to birds (WHO 2001). The reported 5- to 8-day LC_{50} values for Altosid, a methoprene formulation, are greater than 10000 ppm in mallard ducks and bobwhite quail, and the acute oral LD_{50} for Altosid is greater than 4640 ppm in chickens (Zoecon Corporation 1974, Kidd and James 1991, and WHO 2001 report these values as

for technical methoprene). In mallards, an acute oral LD_{50} of greater than 2000 mg/kg was determined

No adverse effects were found in adult birds in reproductive studies of Bobwhite quail and Mallard ducks at a dose level of 30 ppm (continuous feeding of Altosid); no reproductive nor embryotoxic adverse effects were observed in these studies (Zoecon Corporation 1974, WHO 2001). Nonlethal effects that may affect survival of the birds did appear at high acute oral doses of 500 mg/kg. These effects appeared as soon as two hours after treatment and persisted for up to two days and included slowness, reluctance to move, sitting, withdrawal, and poor coordination, potentially decreasing bird survival by making them temporarily more susceptible to predation (Hudson et al. 1984).

Fish

Technical methoprene is reported as practically nontoxic to moderately toxic to fish (US EPA 1991, PAN 2003) or as only slightly toxic to fish (WHO 2001). The reported 96-hour LC_{50} values for the methoprene formulation Altosid were 4.6 mg/L (ppm) in bluegill sunfish, 4.4 mg/L in trout, and greater than 100 mg/L in channel catfish and largemouth bass (Kidd and James 1991, US National Library of Medicine 1995). The WHO/FAO Pesticide Report (1994) has similar values, adding static LC_{50}'s of 32.0 ppm for Coho salmon and 106.0 ppm for trout (unspecified), and noting that 10 weekly treatments of wild populations of mosquito fish (*Gambusia affinis*) in ponds at 56-560 g/ha caused no mortalities or long-lasting ill effects. Methoprene residues may have a slight potential for bioconcentration in bluegill sunfish and crayfish (US EPA 1982).

Amphibians

In addition, it has recently been suggested that methoprene may be associated with deformities in frogs that have been observed in a number of States. The EPA (1996) found no substantial evidence to support this suggestion after conducting exhaustive literature reviews (Glare & O'Callaghan, 1999). First, there is no evidence of a spatial or temporal relationship between Altosid use and amphibian deformities (<frognet.usgs.gov>). Second, in particular, there is no significant evidence of frog deformities anywhere in California where mosquito control occurs. Third, well-documented alternative explanations for frog deformities, including infection with Trematodes, that are more consistent with the epidemiological patterns observed, have been reported (US EPA 1996). Fourth, the observations discussed to support the assertion have not been duplicated by any other researchers (Glare & O'Callaghan, 1999). Fifth, severe deficiencies in methodology and/or interpretation exist in the few reports that make this assertion. Sixth, consultations with Dr. David Jameson, Dr. Mark Jennings, and other eminent herpetologists find no professional agreement with the claims (US EPA 1996).

Non-target Aquatic Organisms

Some non-target aquatic invertebrates are sensitive to methoprene and methoprene-products at moderate to high concentrations. According to the US EPA AQUIRE database, methoprene in aquatic environments can cause toxicity in molluscs, zooplankton, crusta-

ceans, and aquatic insects; s-methoprene is not specifically mentioned in the AQUIRE database (PAN 2003)[7]. However, laboratory and field trials have demonstrated that methoprene and specifically s-methoprene pesticide formulations do not have significant non-target effects when applied at label rates for mosquito control (PAN 2003). Therefore, care must be taken to insure that application rates conform to the FIFRA labels.

Hester et al. (1980) found caged and naturally occurring non-target organisms did not produce any adverse effects when exposed to treatments of sand granule and liquid formulations of methoprene up to a maximum of three and seven weeks, respectively. Acute, short-term toxicity of ZR-515 (methoprene) on various aquatic organisms was studied. In the laboratory, 35 organisms including Protozoa, Platyhelminths, Rotatoria, Annelida, Arthropoda, Mollusca, Chordata and Thallophayta were tested with methoprene (Miura and Takehashi 1973). Dosages used for mosquito larvae control produced no adverse effect on most of the organisms tested. In the field (artificial containers, ponds, and irrigated pastures), a slow-release formulation was used with no visible effect on most of the nontarget organisms. However, larvae of aquatic Diptera (Chironomidae, Ephydridae, Psycodidae) showed some sensitivity. Bircher and Ruber (1988) assessed the toxicity of methoprene to the salt marsh Copepod (*Apocyclops spartinus*). All stages of the life cycle were tested at concentrations ranging from 0.1 to 10.0 ppm. Eggs and the earliest hatched stages, nauplius I-III were most sensitive to methoprene, with little mortality seen in the later stages. Toxic effects were manifested as death, or failure of eggs to hatch, however, no extensions of the life cycle were observed. In general, the Copepods were resistant at concentrations of methoprene used to control mosquitoes. Early nauplii, however, did show some mortality to methoprene concentrations near the lower margins of mosquito susceptibility. This might lead to transient decreases in Copepod population growth rates, but not necessarily to decreases in their standing populations.

Methoprene is very highly toxic to some species of freshwater, estuarine, and marine invertebrates. The acute LC_{50} values are greater than 100 mg/L in freshwater shrimp, and greater than 0.1 mg/L in estuarine mud crabs. Altosid had very little effect, if any, on exposed non-target aquatic organisms including waterfleas, damselflies, snails, tadpoles, and mosquito fish.

Preliminary laboratory and pond assays by Norland and Mulla (1975) determined that Altosid induced mortality in early and late instars of the mayfly, *Callibaetis pacificus* Seeman. During colder winter months, mayflies were eliminated from ponds under repeated treatment but populations in check ponds remained low and contribution to total biomass was slight. Rising water temperatures reduced IGR impact on the mayfly population. The ostracod, *Cyprinotus sp*., was a major prey component and was not affected by treatment. A major predator, the larval dytiscid beetle *Laccophilus sp*., was eliminated from the treated ponds. This loss represented 84% of the predator biomass during one period.

[7]Using the Kamrin narrative descriptions (see Part II above), the Pesticide Action Network database claims that methoprene is slightly toxic to molluscs, moderately to very highly toxic to zooplankton, highly toxic to some crustaceans, and very highly toxic to aquatic insects (PAN 2003). However, as noted in a previous section, these terms are not meaningful in the context of a pesticide applied at very low rates, because the narrative scale does not compare field exposure rates to toxic response. For example, a "highly acutely toxic" material in the Kamrin scale has an aquatic LC50 of 100-1000 ppb, which is 50-500 times the label application rates for methoprene-based pesticide products. Even the "very highly acutely toxic" category starts with LC50's of 100 ppb, over 50 times the altosid label application rates.

Odonata naiads comprised the 2nd major group of predators throughout the study. These naiads preyed heavily on mosquitoes and ostracods and were not affected by the IGR. A study was conducted in a Louisiana coastal marsh to determine the effects of the insectgrowth regulator methoprene on aquatic organism populations (Breaud et al 1977). Six aerial applications of methoprene (28gm AI/ha) during an 18-month period caused statistically significant differences in certain aquatic populations, when treated and untreated populations were compared. Methoprene caused highly significant ($P < 0.01$) reductions in natural populations of the scud, *Hyalella azteca* (Saussure) adults and young; opossum shrimp, *Taphromysis louisianae* (Banner) adults and young; freshwater prawns, *Palaemonetes paladosus* (Gibbs) adults and young; mayflies, *Callibaetis* sp. naiads; dance flies, *Notophila* sp. larvae; midges, *Chironomidae* larvae; fresh water snail, *Physa* sp. adults and young; damselflies and dragonflies, *Enallagma, Anax*, and *Belonia* spp. naiads; burrowing water beetles, *Suphisellus* sp. adults and *Hydrocanthus* sp. adults; and water scavenger beetles, *Berosus infuscatus* Leconte adults and *Berosus* spp. larvae. Populations of the water boatmen, *Trichocorixa louisianae*, Jaczewaski nymphs; moth flies, *Psychoda* sp. larvae; crawfish, *Procambarus clarki* (Girard) and *Cambarellus* sp. adults and young; and predaceous diving beetle, *Liodessus affinis* (Say) adults significantly ($P<0.05$-0.01) increased after the methoprene applications. No statistically significant ($P>0.05$) difference was determined between the population numbers of 28 aquatic organisms when treated and untreated populations were compared.

McKenney and Mathews (1988) reported that larval survival, growth and energy metabolism of an estuarine shrimp *Palaemonetes pugio* were altered by exposure to low ug/l concentrations of an insect growth regulator (the juvenile hormone analogue, methoprene). Larvae were several orders of magnitude more sensitive to methoprene in a flow-through exposure system than in a static-renewal exposure system. The first two larval stages and the final premetamorphic larval stage were more sensitive to methoprene toxicity than the intermediate larval stages. As indicated by reduced net growth efficiency values, elevated metabolic maintenance demands of exposed larvae were related to retarded larval growth rates. A premetamorphic shift in substrate utilization patterns, thought to be a physiological prerequisite for successful metamorphosis in marine crustaceans, was altered by exposure to methoprene concentrations that prevented completion of larval development through metamorphosis. Christiansen et al. (1977) studied the effects of 0.01, 0.1 and 1.0 ppm methoprene on larvae of the mud-crab *Rhithropanopeus harrisii* (Gould) (Brachyura: Xanthidae) from hatching to the first crab stage under optimum and stress conditions of a number of salinities and cyclic temperatures. They found a significant reduction in survival of zoeal larvae with increasing concentrations of methoprene in nearly all combinations of salinity and temperature.

Questions have been raised for a number of years about whether insecticides used against mosquitoes could cause indirect impacts on higher organisms through impacts on food chains, and specifically if larvicides could reduce the populations of *Chironomid* or other midges to a degree significant to waterfowl or wading birds. The EPA (1996) did not find substantial evidence to support this suggestion. Although methoprene, at label rates for mosquito control, can prevent adult emergence of midges, it does not directly kill mosquito or midge larvae and therefore does not remove them from the food chain. In addition,

no bioaccumulation of methoprene has been seen in animals that have eaten mosquito or midge larvae treated with methoprene.

Methoprene is non-toxic to bees. Tests with earthworms showed little if any toxic effects on contact.

IX. Environmental Fate

Transport and Degradation Pathways

All the environmental fate data requirements for Methoprene have been satisfied (US EPA 2001). The available information indicates that Methoprene will not result in unreasonable adverse effects on the environment since Methoprene degrades rapidly in sunlight, in water, and on inert surfaces (US EPA 2001). Methoprene is also metabolized rapidly in soil and does not leach (US EPA 2001). Thus, Methoprene is not expected to persist in soil or contaminate ground water.

Methoprene is of low persistence in the soil environment; reported field half-lives are up to 10 days (US EPA 1982). In sandy loam, its half-life was calculated to be about 10 days (US EPA 1982). When Altosid was applied at an extremely high application rate of 1 pound per acre, its half-life was less than 10 days (US EPA 1982). In soil, microbial degradation is rapid and appears to be the major route of its disappearance from soil (US EPA 1982, 1991). Methoprene also readily undergoes degradation by sunlight (US EPA 1991). Methoprene is rapidly and tightly sorbed to most soils (US EPA 1982). It is slightly soluble in water . These properties, along with its low environmental persistence make it unlikely to be significantly mobile. In field leaching studies, it was observed only in the top few inches of the soil, even after repeated washings with water (US EPA 1982, Zoecon Corporation 1974).

Methoprene degrades rapidly in water . Studies have demonstrated half-lives in pond water of about 30 and 40 hours at initial concentrations of 0.001 mg/L and 0.01 mg/L, respectively . At normal temperatures and levels of sunlight, technical Altosid is rapidly degraded, mainly by aquatic microorganisms and sunlight (Menzie 1980, Zoecon Corporation 1974).

Altosid is biodegradable and nonpersistent, even in plants treated at very high rates. It has a half-life of less than two days in alfalfa when applied at a rate of one pound per acre . In rice, the half-life is less than one day . In wheat, its half-life was estimated to be three to seven weeks, depending on the level of moisture in the plant (US EPA 1982). Plants grown in treated soil are not expected to contain methoprene residues.

X. Toxicity Values for Select Aquatic Species

Table 92. Methoprene Toxicity Values for Selected Aquatic Species.

Common Name	Species	Age Class	End-Point	Time	NOEC	LOEC	LC50	Reference
				(days)	(ppb; ug/L)			
Daphnid	Daphnia pulex	adult, newborn	offspring sex ratio	4		10		Peterson et al. 2001
Daphnid	Daphnia magna	life cycle	first egg deposit time	?*	10			Olmstead and LeBlanc 2001
Daphnid	Daphnia magna	life cycle	growth rate	?*		4		Olmstead and LeBlanc 2001
Daphnid	Daphnia magna	mixed	survival				900	Miura and Takahashi 1973
Cladocera	Moina macrocapa	adult, newborn	survival, fecundity, longevity	2		50	340	Chu et al. 1997
Salt Marsh Copepod	Apocyclops spartinus	egg, nauplii	mortality	2			1000-2000	Bircher and Ruber 1988
Estuarine mysid	Mysidopsis bahia	life cycle	fecundity	~20*		2		McKenney Jr. and Celestral 1996
Estuarine mysid	Mysidopsis bahia	life cycle	survival	~20*		125		McKenney Jr. and Celestral 1996
Amphipod	Hyallela azteca	mixed	survival	1-5			1250	Miura and Takahashi 1973
Fathead minnow	Pimephales promelas	Early Life	length and weight	37	48	84		Ross et al. 1994
Bluegill	Lepomis macrochirus		Death	4			4600	Kidd and James, 1991
Trout			Death	4			4400	Kidd and James, 1991
Channel catfish	Ictalurus puntatus		Death	4			>100,000	Kidd and James, 1991

* Complete life cycle

XI. Method Detection Limits

Table 93. Methoprene Method Detection Limits.

Method Description	MDL	Reference
Liquid-liquid extraction (LLE) using hexane, followed by fused-silica column gas chromatography/mass spectrometry (GC/MS).	0.0059 ppb	Zimmerman et al. 2001
Fused silica column gas chromatography, equipped with a flame ionization detector	0.1 ppb	Ross et al. 1994b

XII. Manufacturer Contact Information

Zoecon Corp.
12005 Ford Rd., Suite 800
Dallas, TX 75234
Phone: Not Available
Emergency: 708-699-1616
www.zoecon.com

XIII. Summary Table

Table 94. Methoprene Summary Table.

Primary use	Selective contact insecticide for control of mosquito outbreaks.
Mechanism of Toxicity	Mimics juvenile hormone, preventing adult emergence, and causing insect pupae to starve to death.
Solubility	1.4 ppm at 25°C
Fate	Photodegrades rapidly in water, with apparent half-life of 30 to 40 hours. No evidence of bioaccumulation in predators of mosquito larva.
Confounding Factors	Not well characterized. Weak evidence of temperature dependence for target organisms.
Data Gaps	Acute or chronic effects on aquatic plants. Chronic effects on fish. Short-term fate in natural waters.

I. Triclopyr

I. Introduction

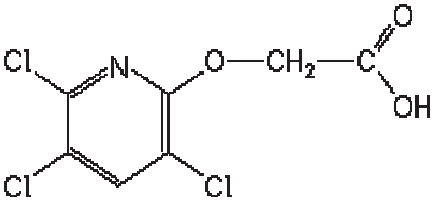
Triclopyr is a selective systematic herbicide that has traditionally been used to control woody and herbaceous broadleaf plants (Hofstra and Clayton 2001). More recently in its triethalymine salt formulation (TEA), it has been used to control aquatic plant species, such as Myriophyllum spicatum L. (Getsinger et al. 1997, Sprecher et al. 1998), Myriophyllum aquaticum (Compliance Services International, 2001), Lythrum salicaria, Eichhornia crassipes and Alternanthera philoxeroides (SePRO 2003). Triclopyr functions as an auxin mimic or synthetic auxin. This type of herbicide kills the target weed by mimicking the plant growth hormone auxin (indole acetic acid) and when applied at effective doses, causes uncontrolled and disorganized plant growth that leads to plant death (Tu et al. 2001). The TEA formulation of triclopyr is sold under the trade name Renovate as an aquatic herbicide.

II. Active Ingredient ID

Synonyms

116001 (US EPA PC Code) , 3,5,6-Trichloro-2-pyridinyloxyacetic acid , 55335-06-3 (CAS Number), Acetic acid, ((3,5,6-trichloro-2-pyridinyl)oxy)- , Dowco 233 , Garlon , trichlopyr , Trichlorpyr , Triclopir , Triclopyr , Triclopyr (ANSI) , Triklopyr, Access, Crossbow, ET, Garlon, Grazon, Pathfinder, Redeem, Remedy, Turflon, Renevate

Structural Formula



Active Ingredient Identification Summary Table

Table 95. Triclopyr Active Ingredient Identification Summary Table.

Characteristic	Value	Source
CAS Number	64700-56-7	PAN 2003
Molecular Weight	256.5	Tomlin 2000
Molecular Formula	$C_7H_4Cl_3NO_3$	Tomlin 2000
USEPA PC Code	116004	PAN 2003
CA DPR Chemical Code	2170	PAN 2004
USEPA Chemical Class	Chloropyridinyl	PAN 2003
WHO/FAO Chemical Group		

III. Physical Properties

Appearance

At room temperature triclopyr is a peachy-amber liquid.

Stability

Renovate, contains 44.4%, triclopyr triethylamine salt (TEA) by weight. This concentration of TEA is equivalent to 31.8% triclopyr acid of the acid equivalent (Compliance Services International, 2001). In water, the TEA formulation of the aquatic triclopyr herbicide converts to triclopyr acid, the compound that causes phytotoxicity (Lewer and Owen 1990). Photolysis is the main degradation pathway in natural water (Woodburn et al. 1993; McCall et al. 1996) and oxamic acid is the main photodegration product with other low molecular-weight organic acids as minor products (Woodburn et al. 1993). In river water, the half-life of triclopyr was determined to be 1.3 days in artificial and natural light (Woodburn et al. 1993). However, triclopyr may have a very long half-life in the field if it is associated with anaerobic sediment (Compliance Services International, 2001).

Physical Properties

Table 96. Physical Properties Summary Table

Characteristic	**Value**	**Source**
Specific Gravity	440mg/L	Kidd & James 1991
Melting Point	148-150°C	Kidd & James 1991
Boiling Point	Decomposes at 208°C	Tomlin 2000
Vapor Pressure	$3.60x10^{-7}$	Kollman & Segawa 1995
Water Solubility	234,000 ppm	Kollman & Segawa 1995
Solubility in Other Solvents	acetone = 581, acetonitrile = 92.1, hexane = 0.09, ethyl acetate = 271	Tomlin 2000
Partition Coefficient (K_{ow})	logP = 0.42(pH 5), -0.45 (pH 7)	Tomlin 2000
Adsorption Coefficient (Koc)	20 (amine salt, estimated)	Wauchope et al. 1992
Henry's Constant (Kh)	$6.00x10-^{10}$	Kollman & Segawa 1995
Half Life	1.3 days in river water	Woodburn et al. 1993
Dissipation Rate		

IV. Active Ingredient Regulatory Status

Table 97. Triclopyr active ingredient Regulatory Status

Agency/ Regulatory Category	Regulatory Status	Source
UNEP Persistent Organic Pollutant	Not Listed	PAN 2003
UNEP Prior Informed Consent Chemical	Not Listed	PAN 2003
WHO/FAO Pesticide Primary Use	Herbicide	PAN 2003
USEPA Registered Pesticide Active Ingredient		
USEPA Pesticide Use Type	Herbicide	PAN 2003
USEPA Toxicity Class (Pesticide Products)		
USEPA Signal Word (Pesticide Products)		
USEPA Reregistration		
USEPA Hazardous Air Pollutant	Not Listed	PAN 2003
USEPA Minimum Risk Pesticide (25b list)	No	PAN 2003
CA Registered Pesticide Active Ingredient		
CA Toxic Air Contaminant	Candidate	PAN 2003
CA Groundwater Contaminant	Not listed	PAN 2003
PAN Bad Actor	Not listed	PAN 2003
PAN Dirty Dozen	Not listed	PAN 2003

V. Pesticide Status

Pests Controlled

Used to control woody and broadleaf plant species in forests, industrial lands, and on grasslands and parklands. In aquatic environments, triclopyr is used in the control of aquatic vegetation in fresh water ponds, lakes, reservoirs, and other still and quiescent waters. It has been proven to control macrophytic aquatic pests such as Myriophyllum spicatum L. (Getsinger et al. 1997, Sprecher et al. 1998), Myriophyllum aquaticum (Compliance Services International, 2001), Lythrum salicaria, Eichhornia crassipes and Alternanthera philoxeroides (SePRO 2003).

Pesticide Trade and Other Names

Garlon 3A, and Renovate 3

Formulations and Dosages

(summarized from SePRO 2003)

Triclopyr is applied in liquid form. Surface application is through use of a spray backpack, spray boom, handgun, or other suitable equipment mounted on a boat of vehicle. Subsurface application of Renovate 3 is also practiced by direct application into the water

through boat mounted distribution systems. Application rates are 1.5 to 6 lb. ae triclopyr (2 to 8 quarts of Renovate 3) per acre. Application can be repeated to control regrowth and plants missed in the previous application, but there should never be more than 6 lbs. (8 quarts of Renovate 3) per acre applied per annual growing season. Use of non-ionic surfactant in the spray mixture is recommended to improve control during application to floating or emergent weeds.

Application Rate Per Acre at Specified Depth

Table 98. Concentration of Triclopyr Acid in Water Post Application (ppm ae)

	Gallons of Renovate 3 Per Surface Acre at Specified Depth (Concentration of Triclopyr Acid in Water (ppm ae))				
Water Depth (ft)	**0.75 ppm**	**1.0 ppm**	**1.5 ppm**	**2.0 ppm**	**2.5 ppm**
1	0.7	0.9	1.4	1.8	2.3
2	1.4	1.8	3.3	3.6	4.6
3	2.1	2.9	4.1	5.4	6.8
4	2.7	3.6	5.4	7.2	9.1
5	3.4	4.5	6.8	9	11.3
6	4.1	5.4	8.1	10.9	13.6
7	4.8	6.3	9.5	12.7	15.8
8	5.5	7.2	10.9	14.5	18.1
9	6.1	8.1	12.2	16.3	20.4
10	6.8	9	13.6	18.1	22.6
15	10.2	13.6	20.4	27.2	33.9
20	13.6	18.1	27.2	36.2	45.3

Note: From SePRO Renovate 3 Product Label

Application to Reservoirs or Ponds Containing a Functional Potable Water Intake For Human Consumption

Table 99. Renovate 3 Functional Potable Water Intake Setback Distances for Floating and Emerged Weeds

	Setback Distance (ft) (Renovate 3 Application Rate (quart/acre))			
Area Treated (acres)	**2 qt/acre**	**4 qt/acre**	**6 qt/acre**	**8 qt/acre**
<4	0	200	400	500
>4-8	0	200	700	900
>8-16	0	200	700	1000
>16	0	200	900	1300

Note: From SePRO Renovate 3 Product Label

Table 100. Renovate 3 Functional Potable Water Intake Setback Distances for Floating and Emerged Weeds

	Setback Distance (ft) From Potable Water Intake (Concentration of Triclopyr Acid in Water (ppm ae))				
Area Treated	**0.75 ppm**	**1.0 ppm**	**1.5 ppm**	**2.0 ppm**	**2.5 ppm**
<4	300	400	600	800	1000
>4-8	420	560	840	1120	1400
>8-16	600	800	1200	1600	2000
>16-32	780	1040	1560	2080	2600
	32 acres, calculate a setback using the formula for the appropriate rate	Setback (ft) =(800*ln (acres) - 160)/ 3.33	Setback (ft) =(800*ln (acres) - 160)/ 2.50	Setback (ft) =(800*ln (acres) - 160)/ 1.67	Setback (ft) =(800*ln (acres) - 160

VI. Toxicity to Humans and Other Mammals

Absorption Route

Triclopyr is low in toxicity via the oral route, however the TEA form (Renovate 3) is corrosive to the eyes.

Fate in Mammals and excretion products

Triclopyr is rapidly eliminated via the urine as the unchanged parent comound (EXTOXNET 1996). At higher oral doses, some triclopyr may be eliminated through the feces as the absorption capacity of the intestine is exceeded (EXTOXNET 1996). Reported half-lives for elimination of triclopyr from mammals are 14 hours (dog) and <24 hours (Monkeys) (EXTOXNET 1996). A human elimination half-life of approximately five hours has been suggested (Carmichael 1989).

Mode of action

Triclopyr kills the target weed by mimicking the plant growth hormone auxin (indole acetic acid) and when applied at effective doses, causes uncontrolled and disorganized plant growth that leads to plant death (Tu et al. 2001).

Acute Toxicity

Oral LD_{50}: 630-729 mg/kg in the rat (Kidd & James 1991); 550 mg/kg in the rabbit; 310 mg/kg in the guinea pig (Kidd & James 1991);

Dermal LD_{50}: 2000 mg/kg in the rabbit (EXTOXNET 1996);

Inhalation LC_0: No effect in rats, but the inhalation of some formulations cause nasal irritation; Similar results occurred in the case of the rabbit (EXTOXNET 1996);

Eyes: Slight irritant to the eyes of rabbits (technical); Some formulations caused significant eye irritation. Garlon 3A™ (Renovate) can cause permanent impairment of vision. Effects on the eye can include severe conjunctival irritation, moderate internal redness, and moderate to severe corneal injury (SSPM 2003).

Neurotoxicity

No information Available

Chronic Toxicity

Triclopyr added to the diets of both male and female rats for 13 weeks at 20 mg/kg was found to result in the degeneration of the proximal tubules within the kidney (EPA 1998). There are no significant changes in the body weight food consumption or blood chemistry of beagle dogs fed up to 2.5 mg/kg/day of triclopyr over 183 days or in dogs fed 5.0 mg/kg/day over one year (EPA 1998). However, beagle dogs fed 20mg/kg/day of triclopyr showed a decrease in body weight, food consumption, blood chemistry; and liver histopathy. There are also significant increases in the male liver and female kidney weights (EPA 1998).

Carcinogenic Effects

In feeding studies involving rats, ingesting triclopyr displayed no evidence of compound-related tumors in male rats. However, there is a significant increase in the presence of mammary gland adenocarcinomas in female mice and rats fed triclopyr at 36 mg/kg/day for two years (EPA 1998)

The Carcinogenicity Peer Review committee (CPRC) at the U.S. EPA classified triclopyr as a group D carcinogen, that is, one that does not induce oncongenic responses (EPA 1998).

Reproductive effects

Triclopyr fed to rabbits on days 6 to 18 of gestation at doses of 25, 50, and 100 mg/kg/day produced no effects on maternal body weight, litter size or fetal body weight (EXTOXNET 1996). A three generation study involving rats at daily doses of 3, 10 and 30 mg/kg for an 8 to 10 week period prior to breeding of each generation showed no impact of triclopyr on fertility rates (EXTOXNET 1996). Triclopyr does not appear to cause reproductive toxicity (EXTOXNET 1996).

Teratogenic and Developmental Effects

In a study in which pregnant rats were administered moderate to high dose of 50,100

and 200 mg/kg/day on days 6 to 15 of gestation had offspring with mild fetotoxicity, but no birth defects. In another study, there was no teratogenic effects in rabbits treated on days 6 to 18 of gestation at dose rates of 10 and 25 mg/kg/day (EXTOXNET 1996). These data suggest that triclopyr is not teratogenic and does not cause pre-natal developmental effects (EXTOXNET 1996).

Mutagenic Effects

Triclopyr is nonmutagenic in bacterial and cytogenetic assay systems. A mutagenicity study using rats was weakly positive, but a negative result was found in mice, the more sensitive species. Based on these data, triclopyr is not likely mutagenic (EXTOXNET 1996).

Endocrine Effects

No evidence at this time (EPA 1998).

Skin Sensitation

Triclopyr is harmful if absorbed through the skin and prolonged or frequently repeated skin contact may cause allergic reactions in some individuals (SePRO 2003). Triclopyr also causes irreversible eye damage (SePRO 2003).

VII. Routes of Human Exposure

Humans are at risk of being exposed predominantly when handling and administering the herbicide. Triclopyr can be absorbed through the eyes and skin and is harmful if ingested orally (SePRO 2003). The general public could be exposed through the drinking water supply if proper distance regulations are not followed when applying the herbicide to reservoirs, lakes and ponds that contain a functioning potable water intake for human consumption.

In a study by Woodburn et al. (1993), moderate levels of bioaccumulation were noted in crayfish and shellfish (BCF</=4 L/kg) with rapid decreases in tissue levels as the aquatic concentrations of triclopyr decreased (Durkin 2003). Therefore, humans consuming these species in proximate time following an application of triclopyr could lead to oral exposure to the herbicide.

VIII. Environmental Toxicological and Ecological Effects

Birds

The U.S. EPA/OPP has classified triclopyr as being slightly toxic to birds (Durkin 2003). The LD_{50} of the parent compound in the mallard duck is 1698 mg/kg, while the formulated compounds are of a lower toxicity (EXTOXNET 1996). In an eight day study, bobwhite and Japanese quail were administered oral doses and their LD_{50}'s were found to be 2935 ppm and 3278 ppm respectively (EXTOXNET 1996).

Fish

EXTOXNET (1996) reports that triclopyr is slightly to practically nontoxic to fish. However, a study performed by Wan et al. (1987) reported LC50 values of many different species of Salmonids in their juvenile stages ranging from 300-1,000 ug/L. This acute toxicity to juveniles has potential to be detrimental to the regeneration of salmonid populations.

Amphibians

The Pesticide Action Network (2003) reports that triclopyr is not acutely toxic to the frog, Rana brevipoda porosa in its tadpole stage (LC50=100,000 ug/L). However aquatic concentrations of triclopyr ranging from 150-1,200 ug/L triggered mortality in the midneurulation (embyo) life stages of the bullfrog, Rana catesbeiana, the green frog, Rana clamitans, and the leopard frog, Rana pipiens (Pesticide Action Network 2003). Mortality is also observed to be more moderately toxic in the tadpole stages of Rana catesbeiana and Rana Clamitans, with lethal dosages of triclopyr ranging from 2,400-4,800 ug/L. Durkin (2003) specifies in his report that triclopyr formulations are not likely to cause reproductive or teratogenic effects in sublethal concentrations.

Insects

The LD50 value for the honeybee, a standard test organism for assessing the potential effects of pesticides on terrestrial invertebrates were over 100 ug/bee. Based on this result, the U.S. EPA has classified triclopyr as practically nontoxic to bees. However, no additional studies on the toxicity of triclopyr to terrestrial invertebrates have been executed (Durkin 2003).

Aquatic Invertebrates

LC50 values for aquatic invertebrates are not as extensive as those pertaining to fish. However, the available data suggests that aquatic invertebrates are as if not more resistant to triclopyr as fish species. In a study performed by Gersich et al. 1984), Daphia magna was exposed to varying concentrations of triclopyr and from this study, the U.S. EPA/OPP (1998) extrapolated an NOEC of 80.7 mg/L and and LOEC of 149 mg/L as data for their risk assessment of triclopyr (Durkin 2003).

IX. Environmental Fate

Transport and Degradation Pathways

In water, hydrolysis of the salt occurs rapidly and results in the formation of triclopyr acid. Half-lives in water are 2.8-14.1 hours depending on season and water depth. In water, photolysis is the main breakdown process for triclopyr (EXTOXNET 1996).

In soil and groundwater environments, the salt formulations quickly convert to triclopyr acid, which in turn is rapidly degraded to a relatively nontoxic salt (EXTOXNET

1996). This salt is effectively degraded further by soil microorganisms and has a relatively moderate persistence in soil environments. The half-life of triclopyr compounds in soil range from 30-90 days depending on soil environment conditions, with an average of 46 days (EXTOXNET 1996). In a study by the U.S. Forest service (1984) the half life of one of the breakdown products (trichloropyridinol) was examined in 15 different soil types. The range of half lives was 8 to 279 days, with 12 of the soil types having half lives of less than 90 days. It is hypothesized that longer half-lives may be a result of colder and/or more arid conditions (EXTOXNET 1996).

Mode of Action

Triclopyr kills the target weed by mimicking the plant growth hormone auxin (indole acetic acid) and when applied at effective doses, causes uncontrolled and disorganized plant growth that leads to plant death (Tu et al. 2001).

X. Toxicity Values for Select Aquatic Species

Table 101. Triclopyr (TEA) LC50 Values for Rainbow Trout

Species	Life Stage	Study Time	Endpoint	LC50 (mg/L)	Source
Oncorhynchus mykiss (Rainbow trout)	53mm; 1.1g	24h	mortality	366	Batchelder 1973
		48h	mortality	265	
		72h	mortality	249	
		96h	mortality	240	
	41mm; 0.7g	24h	mortality	457	Wan et al. 1987
		48h	mortality	435	
		72h	mortality	420	
		96h	mortality	420	

Table 102. Triclopyr (TEA)LC50 Values for Bluegill Sunfish

Species	Life Stage	Study Time	Endpoint	LC50 (mg/L)	Source
Lepomis macrochirus (Bluegill Sunfish)	38mm; 1.003g	24h	mortality	512	Batchelder 1973
		48h	mortality	471	
		72h	mortality	471	
		96h	mortality	471	
	27.7mm; 0.6g	24h	mortality	N/A	McCarty et al. 1978
		48h	mortality	N/A	
		72h	mortality	N/A	
		96h	mortality	891	

Table 103. Triclopyr (TEA) LC50 Values for Fathead Minnow

Species	Life Stage	Study Time	Endpoint	LC50 (mg/L)	Source
Pimephales promelas (Fathead Minnow)	16-31mm; 0.22g	24h	mortality	570	Mayes et al. 1983; Mayes et al. 1984
		48h	mortality	570	
		72h	mortality	570	
		96h	mortality	546	
	31mm; 0.54g	24h	mortality	N/A	McCarty et al. 1978
		48h	mortality	N/A	
		72h	mortality	N/A	
		96h	mortality	947	

Table 104. Triclopyr (TEA) LC50 Values for Coho Salmon

Species	Life Stage	Study Time	Endpoint	LC50 (mg/L)	Source
Oncorhynchus kisutch (Coho Salmon)	NR	96h	mortality	167	Compliance Services International 2001
	NR	31 days	mortality	167	

Table 105. Triclopyr (TEA) LC50 Values for Sockeye Salmon

Species	Life Stage	Study Time	Endpoint	LC50 (mg/L)	Source
Onkorhynchus nerka (Sockeye Salmon)	NR	96h	mortality	112	Compliance Services International 2001
	NR	31 days	mortality	112	

Table 106. Triclopyr (TEA) LC50 Values for Chinook Salmon

Species	Life Stage	Study Time	Endpoint	LC50 (mg/L)	Source
Oncoryhnchus tshawytcha (Chinook Salmon)	NR	96h	mortality	182	Compliance Services International 2001
	NR	31 days	mortality	182	

Table 107. Triclopyr (TEA) LC50 Values for Water Flea

Species	Life Stage	Study Time	Endpoint	LC50 (mg/L)	Source
Daphnia magna (Water Flea)	NR	acute bioassay	mortality	1,496	Durkin 2003
		48h	mortality	133	
		48h	mortality	1,110	
	<24hrs.	24h	mortality	203	McCarty 1977
		48h	mortality	133	

Note on Amphibians

No laboratory work has been conducted on the effects of triclopyr TEA on amphibians.

XI. Method Detection Limits

Table 108. Triclopyr Method Detection Limits

Analytical Method	MDL	Medium	Reference
GC-MS	0.01 ppm	Soil/Sediment	http://www.epa.gov/oppbead1/methods/ecms2z.htm
LC-MS	200 ppm	Sediment	Yee et al. 2004
Immunoassay	190 ppm	Water	http://www.epa.gov/oppbead1/methods/ecms2z.htm
GC-MS	100 ppm	Water	
GC-ECD	0.05 ppm	Water	

XII. Manufacturer Contact Info

SePro Corporation
11550 N. Meridian Street, Suite 600
Carmel, IN 46032, USA
Emergency Phone: 317-580-8282
General Phone: 317-580-8282

XIII. Summary Table

Table 109. Triclopyr Summary Table

Primary Use	For control of emerged, submersed and floating plants in aquatic sites such as ponds, lakes, reservoirs, non-irrigation canals and ditches which have little or no continuous outflow, marshes and wetlands, including broadleaf and woody vegetation on banks and shores within or adjacent to these and other aquatic sites (SePRO, 2003). Applications rates are 1.6 - 6lbs/acre.
Mechanism of Toxicity	Triclopyr kills the target weed by mimicking the plant growth hormone auxin (indole acetic acid) and when applied at effective doses, causes uncontrolled and disorganized plant growth that leads to plant death (Tu et al. 2001).
Solubility	acetone = 581; acetonitrile = 92.1; hexane = 0.09; ethyl acetate = 271 (Tomlin, 2000)
Fate	In water, hydrolysis of the salt occurs rapidly and results in the formation of triclopyr. Half-lives in water are 2.8-14.1 hours depending on season and water depth. In water, photolysis is the main breakdown process for triclopyr (EXTOXNET 1996). In soil and groundwater environments, the salt formulations quickly convert to triclopyr acid, which in turn is rapidly degraded to a relatively nontoxic salt (EXTOXNET 1996). This salt is effectively degraded further by soil microorganisms and has a relatively moderate persistence in soil environments. The half-life of triclopyr compounds in soil range from 30-90 days depending on soil environment conditions, with an average of 46 days (EXTOXNET 1996). There is little evidence of bioconcentration.
Confounding Factors	Much longer half-life of triclopyr in soil than in water. Herbicide break-down is significantly slower in anaerobic environments.
Data Gaps	Amphibian data is not available for the TEA formulation of triclopyr. NOEC and LOEC data is also sparse.

J. 2,4-D

I. Introduction

There are many forms of 2,4-D these include acid, salt (mostly amine) and ester formulations. Ester formulations are toxic to fish and other aquatic life. 2,4-D is a selective herbicide that kills dicots by mimicking the growth hormone auxin causing uncontrolled growth and eventually death in the target species (Tu et al. 2001). It is used in cultivated agriculture, in pasture and rangeland applications, forest management, home, garden, and to control aquatic vegetation (EXTOXNET 1996).

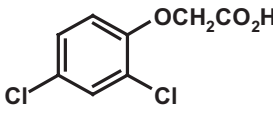
II. Active Ingredient ID

Synonyms

2,4-D is used in many commercial products. Commercial names for products containing 2,4-D include Aqua-Kleen, Barrage, Lawn-Keep, Malerbane, Planotox, Plantgard, Savage, Salvo, Weedone, and Weedtrine-II.

IUPAC name: (2,4-dichlorophenoxy) acetic acid

Structural formula



Active ingredient ID summary table

Table 110. 2,4-D Active Ingredient Summary Table.

Characteristic	Value	Source
CAS Number	94-75-7	Tomlin 2000
Molecular Weight	221.0	Tomlin 2000
Molecular Formula	$C_8H_6C_{l2}O_3$	Tomlin 2000
USEPA PC Code	030001	PAN 2003
CA DPR Chemical Code	636	PAN 2003
USEPA Chemical Class	Chlorophenoxy acid or ester	PAN 2003
WHO/FAO Chemical Group		

III. Physical Properties

Appearance

Colorless powder, with a slight phenolic odor.

Stability

2,4-D is a strong acid, and forms water-soluble salts with alkali metals and amines. Hard water leads to precipitation of the calcium and magnesium salts, but a sequestering agent is included in formulations to prevent this. The half-life of 2,4-D averages 10 days but can be longer if the soil is cold and dry or when the microbial community needed to facilitate degradation is missing (Tu et al. 2001).

Physical Properties Summary Table

Table 111. 2,4-D Physical Properties Summary Table.

Characteristic	**Value**	**Source**
Specific Gravity	0.7-0.8	Tomlin 2000
Melting Point	140.5°C	Tomlin 2000
Boiling Point	> 300°C (decomposition)	Tomlin 2000
Vapor Pressure	$1.86x10^{-2}$ mPa (25°C, OECD 104)	Tomlin 2000
Water Solubility	311 (pH 1), 20031 (pH 5), 23180 (pH 7), 34196 (pH 9) all in mg/L at 25°C	Tomlin 2000
Solubility in Other Solvents	In ethanol 1250, diethyl ether 243, heptane 1.1, toluene 6.7, xylene 5.8 all in g/kg at 20°C; in octanol 120 g/L (25°C). Insoluble in petroleum oils.	Tomlin 2000
Partition Coefficient (K_{ow})	LogP=2.58-2.83 (pH1), 0.04-0.33 (pH 5)	EXTOXNET 1996
Adsorption Coefficient (K_{oc})	45.0 K_{OC}	PAN 2003
Henryís Constant (K_h)	1.32 X 10^{-5} Pa m^3 mol^{-1} (calc)	EXTOXNET 1996
Half-Life	Soil >7 days, water 1-7 weeks	EXTOXNET 1996

IV. Active Ingredient Registration Status

2,4-D is a General Use Pesticide in the U.S. The diethylamine salt is classified as toxicity class III- slightly toxic orally, but toxicity class I- highly toxic by eye exposure. It bears the Signal Word DANGER - POISON because 2,4-D has produced serious eye and skin irritation among agricultural workers (EXTOXNET 1996). All salt formulations of 2,4-D are registered for use against aquatic weeds. Ester formulations of 2,4-D are toxic to fish and aquatic invertebrates (Tu et al. 2001).

Table 112. 2,4-D Regulatory Status.

Agency/Regulatory Category	Regulatory Status	Source
UNEP Persistent Organic Pollutant	Not Listed	PAN 2003
UNEP Prior Informed Consent Chemical	Not Listed	PAN 2003
USEPA Registered Pesticide Active Ingredient	Yes	PAN 2003
USEPA Pesticide Use Type	Herbicide, Plant Growth Regulator	PAN 2003
USEPA Toxicity Class (Pesticide Products)	III orally I eye exposure	EXTOXNET 1996
USEPA Signal Word (Pesticide Products)	DANGER - POISON	EXTOXNET 1996
USEPA Registration	Yes	PAN 2003
Agency/Regulatory Category	Regulatory Status	Source
USEPA Hazardous Air Pollutant	Yes	PAN 2003
USEPA Minimum Risk Pesticide (25b list)	No	PAN 2003
CA Registered Pesticide Active Ingredient	Yes	PAN 2003
CA Toxic Air Contaminant	Potential	PAN 2003
CA Groundwater Contaminant	HAPTAC	PAN 2003
PAN ìBad Actorî	Not Listed	PAN 2003
PAN ìDirty Dozenî	Not Listed	PAN 2003

V. Pesticide Status

Pest Controlled

Post-emergence control of annual and perennial broad-leaved weeds in cereals, maize, sorghum, grassland, established turf, grass seed crops, orchards (pome fruit and stone fruit), cranberries, asparagus, sugar cane, rice, forestry, and on non-crop land (including areas adjacent to water). Control of broad-leaved aquatic weeds. The isopropyl ester can also be used as a plant growth regulator to prevent premature fruit fall in citrus fruit.

Pesticide Trade and Other Names

2,4-D is used in many commercial products. Commercial names for products containing 2,4-D include Aqua-Kleen, Barrage, Lawn-Keep, Malerbane, Planotox, Plantgard, Savage, Salvo, Weedone, and Weedtrine-II.

Formulation and Dosages

2,4-D is available as a liquid, water-soluble powders, dust granules, or pellet. Pellets may have a mixture of other herbicides such as picloram or clopyralid (Tu et al. 2001). Recommended dosages of the product Aqua-Kleen are as follows: For susceptible weeds such as Water milfoil (*Myriophyllum spp.*) and Water stargrass (*Luziola spp.*) use 100-200 pounds per acre or 5 lbs per 2000 sq. ft. For slightly to moderately resistant weeds such as bladderwort (*Utricularia spp.*) and white water lily (*Nymphaea odorata*) use 150-200 pounds per acre or 7 1/2 –10 lbs per 2000 sq. ft. The recommended application method is the use of a portable spreader that can uniformly apply the product. Hard water leads to precipitation of the calcium and magnesium salts, but a sequestering agent is included in the formulations to prevent that. Active Ingredient: 27.6% Butoxyethyl Ester of 2,4-Dichlorophenoxyacetic Acid, 72.4% Other Ingredients (Cerexagri, Inc. Product Label).

VI. Toxicity to Humans and Mammals

Absorption Route

The absorption of 2,4-D is almost complete in mammals after ingestion and nearly all of the dose is excreted in the urine. The compound is readily absorbed through the skin and lungs.

Fate in Mammals and Excretion Products

Men given 5 mg/kg excreted about 82% of the dose as unchanged 2,4-D. The half-life is between 10 and 20 hours in living organisms. There is no evidence that 2,4-D accumulates to significant level in mammals or in other organisms (Howard 1991). Between 6 and 8 hours after doses of 1 mg/kg, peak concentrations of 2,4-D were found in the blood, liver, kidney, lungs, and spleen of rats. There were lower levels in muscle and brain. After 24 hours, there were no detectable tissue residues. Only traces of the compound have been found in the milk of lactating animals for six days following exposure. 2,4-D passes through the placenta in pigs and rats.

Mode of Action

2,4-D is a selective systemic herbicide that acts as a growth inhibitor (Tomlin 2000).

Acute Toxicity

The acid form of 2,4-D has shown toxicity in experiments. The oral LD_{50} of 2,4-D ranges from 375 to 666 mg/kg in the rat, 370 mg/kg in mice, and from less than 320 to 1000 mg/kg in guinea pigs. The dermal LD_{50} values are 1500 mg/kg in rats and 1400 mg/kg in rabbits, respectively (Stevens and Sumner 1991, WSSA 1994, U.S. National Library of Medicine 1995). In humans, prolonged breathing of 2,4-D causes coughing, burning, dizziness, and temporary loss of muscle coordination (Stevens and Sumner 1991). Other symptoms of poisoning can be fatigue and weakness with possible nausea.

Neurotoxicity

On rare occasions following high levels of exposure, there can be inflammation of the nerve endings with muscular effects (Gosselin 1984).

Chronic Toxicity

Rats given high amounts, 50 mg/kg/day, of 2,4-D in the diet for two years showed no adverse effects. Dogs fed lower amounts in their food for two years died, probably because dogs do not excrete organic acids efficiently. A human given a total of 16.3 g in 32 days therapeutically, lapsed into a stupor and showed signs of incoordination, weak reflexes, and loss of bladder control respectively (Stevens and Sumner 1991, WSSA 1994, U.S. National Library of Medicine 1995).

Carcinogenic Effects

2,4-D fed to rats for two years caused an increase in malignant tumors (U.S. National Library of Medicine 1995). Female mice given a single injection of 2,4-D developed cancer (reticulum-cell sarcomas) (U.S. National Library of Medicine 1995). Another study in rodents shows a low incidence of brain tumors at moderate exposure levels (45 mg/kg/day) over a lifetime (Stevens and Sumner 1991, U.S. National Library of Medicine 1995). However, a number of questions have been raised about the validity of this evidence and thus about the carcinogenic potential of 2,4-D. In humans, a variety of studies give conflicting results. Several studies suggest an association of 2,4-D exposure with cancer. An increased occurrence of non-Hodgkin's lymphoma was found among a Kansas and Nebraska farm population associated with the spraying of 2,4-D (Gosselin 1984). Other studies done in New Zealand, Washington, New York, Australia, and on Vietnam veterans from the U.S. were all negative. There remains considerable controversy about the methods used in the various studies and their results (US EPA 1992). Thus, the carcinogenic status of 2,4-D is not clear.

Reproductive Effects

High levels of 2,4-D (about 50 mg/kg/day) administered orally to pregnant rats did not cause any adverse effects on birth weights or litter size. Higher doses (188 mg/kg/day) resulted in fetuses with abdominal cavity bleeding and increased mortality respectively (Stevens and Sumner 1991, WSSA 1994, U.S. National Library of Medicine 1995). DNA synthesis in the testes was significantly inhibited when mice were fed large amounts (200 mg/kg/day) of 2,4-D (U.S. National Library of Medicine 1995). The evidence suggests that if 2,4-D causes reproductive effects in animals, this only occurs at very high doses. Thus reproductive problems associated with 2,4-D are unlikely in humans under normal circumstances.

Teratogenic and Developmental Effects

2,4-D may cause birth defects at high doses. Rats fed 150 mg/kg/day on days 6 to 15 of pregnancy had offspring with increased skeletal abnormalities, such as delayed bone devel-

opment and wavy ribs (U.S. National Library of Medicine 1995). This suggests that 2,4-D exposure is unlikely to be teratogenic in humans at expected exposure levels.

Mutagenic Effects

2,4-D has been very extensively tested and was found to be nonmutagenic in most systems. 2,4-D did not damage DNA in human lung cells. However, in one study, significant effects occurred in chromosomes in cultured human cells at low exposure levels (U.S. National Library of Medicine 1995). The data suggest that 2,4-D is not mutagenic or has low mutagenic potential.

Endocrine

EPA (1997) classified 2,4-D as "a chemical known to have no endocrine effects".

Skin Sensitization

The acute percutaneous LD_{50} for rats is >1600 and for rabbits is >2400 mg/kg. 2,4-D is a skin and eye irritant in rabbits, but not a skin sensitizer in guinea pigs (Tomlin 2000).

VII. Routes of Human Exposure

For the widely used herbicide 2,4-D, there should be widespread dietary exposures to trace levels of the chemical in crops, although it has a relatively short environmental half-life and does not bioaccumulate in soil, plants or animals. Pesticide tolerances for 2,4-D are generally less than 1 ppm in edible portions of food, and actual detected residues average much lower (EXTOXNET 1996).

Exposures to 2,4-D in air should be low-level and infrequent for the general population, caused mostly from overspray during application of the product to lawns for weed control. The RSC from drinking water will therefore be set at 20%, based on exposure to trace levels of 2,4-D in both air and food (EPA 1997).

VIII. Environmental Toxicology and Ecological Effects

According to the label for Aqua-Kleen Aquatic Herbicide the formulation 2-butoxyethyl 2,4-dichlorophenoxy acetate, is moderately toxic to bleak (96-hr LC_{50} 3.2-3.7 mg/l), daphnia magna (48-hr EC_{50} 7.2 mg/l), and coho salmon (96-hr LC_{50} 1.5 mg/l). It is highly toxic to bluegill (96 hr LC_{50} 0.61 mg/l), chinook salmon (96-hr LC_{50} 0.518-2.0mg/l), and pink salmon (96-hr LC_{50} 0.8 mg/l). It is moderately to highly toxic to rainbow trout (96-hr LC_{50} 0.518-2.0 mg/l) and fathead minnow (96-hr LC_{50} 0.95-2.5 mg/l).

Birds

2,4-D is toxic to wildfowl and toxic to birds. The LD_{50} is 1000 mg/kg in mallards, 272 mg/kg in pheasants, and 668 mg/kg in quail and pigeons (WSSA 1994, U.S. National Library of Medicine 1995).

Fish

Some formulations of 2,4-D are toxic to fish while others are less so. For example, the LC_{50} ranges between 1.0 and 100 mg/L in cutthroat trout, depending on the formulation used. Channel catfish had less than 10% mortality when exposed to 10 mg/L for 48 hours (Stevens and Sumner 1991, US EPA 1988). Green sunfish, when exposed to 110 mg/L for 41 hours, showed no effect on swimming response. Limited studies indicate a half-life of less than two days in fish and oysters (NRC 1977).

Amphibians

A potential acute risk to amphibians from overspray contamination during aerial application was identified. Frog and toad tadpole 96-hour LC_{50} values ranged from 8 mg/l for the free acid to 477 mg/l for the DMA salt (WHO 1997).

Non-Target Aquatic Organisms

Concentrations of 10 mg/L for 85 days did not adversely affect the survival of adult dungeness crabs. For immature crabs, the 96-hour LC_{50} is greater than 10 mg/L. Brown shrimp showed a small increase in mortality at exposures of 2 mg/L for 48 hours (U.S. National Library of Medicine 1995).

IX. Environmental Fate

Transport and Degradation Pathways

2,4-D has low soil persistence. The half-life in soil is less than seven days (Wauchope 1992). Soil microbes are primarily responsible for its disappearance (Howard 1991). Despite its short half-life in soil and in aquatic environments, the compound has been detected in groundwater supplies in at least five states and in Canada (Howard 1991). Very low concentrations have also been detected in surface waters throughout the U.S. (US EPA 1992).

In aquatic environments, microorganisms readily degrade 2,4-D. Rates of breakdown increase with increased nutrients, sediment load, and dissolved organic carbon. Under oxygenated conditions the half-life is one to several weeks (Howard 1991).

2,4-D interferes with normal plant growth processes. Uptake of the compound is through leaves, stems, and roots. Breakdown in plants is by a variety of biological and chemical pathways (US EPA 1987). 2,4-D is toxic to most broad leaf crops, especially cotton, tomatoes, beets, and fruit trees (U.S. National Library of Medicine 1995).

Mode of Action

2,4-D is a post emergent systemic herbicide used for hyacinth and water milfoil. 2,4-D acts on the hormone that stimulates stem elongation & nucleic acid/protein synthesis, stimulating uncontrolled growth until death. It also affects enzyme activity, respiration, and cell division (Tomlin 2000).

X. Toxicity Values for Select Aquatic Species

NOEC Values for Select Aquatic Species

Table 113. 2,4-D NOEC Values for Select Aquatic Species.

Species	Result	Reference
Water flea	27.5ppm	WSDE 2001 (predicted)
Grass shrimp	8.3ppb	WSDE 2001 (predicted)
Fathead minnow	100mg/L	CDFG 2002
Delta smelt	128mg/L	CDFG 2002
Rainbow Trout	5.6ppm	WSDE 2001 (predicted)

LOEC Values for Select Aquatic Species

Table 114. 2,4-D LOEC Values for Select Aquatic Species.

Species	Result	Reference
Fathead minnow	200mg/L	CDFG 2002
Delta smelt	230mg/L	CDFG 2002

LC_{50} Values for Select Aquatic Species

Table 115. 2,4-D LC_{50} Values for Select Aquatic Species.

Species	Duration	Result	Reference
Water flea	48hr	7.2 mg/l	Cerexagri MSDS 2002
Delta smelt		149.4mg/L	CDFG 2002
Fathead minnow		250mg/L	CDFG 2002
Fathead minnow	96hr	0.95-2.5mg/l	Cerexagri MSDS 2002
Bluegill Sunfish		263mg/L	Tu et al. 2001
Bluegill sunfish	96hr	0.61mg/l	Cerexagri MSDS 2002
Rainbow Trout		377mg/L	Tu et al. 2001
Rainbow trout	96hr	0.518-2.0 mg/l	Cerexagri MSDS 2002
Bleak	96hr	3.2-3.7mg/l	Cerexagri MSDS 2002
Coho salmon	96hr	1.5mg/l	Cerexagri MSDS 2002
Chinook salmon	96hr	0.315mg/l	Cerexagri MSDS 2002
Pink salmon	96hr	0.8mg/l	Cerexagri MSDS 2002

Table 116. 2,4-D Toxicity Data from Washington State SEIS

Test Substance	%A.I. or Form	Species	Test Type	Water Type	Size Class/ Age	Time (hours)	LC50 (mg a.i./L)	NOEC (mg a.i./L)	Status	Reference	MRID Number
2,4-D Acid	NN	*Oncorhynchus mykiss* (Rainbow trout)	Static	FW	NS	96	358.0	NS	NS	Bentley, 1974[J97]	
2,4-D Acid	NN	*Oncorhynchus mykiss* (Rainbow trout)	Static	pH 4.54	Finger-lings	96	<100	NS	NS	Doe et al., 1988[J97]	
2,4-D Acid	NN	*Oncorhynchus mykiss* (Rainbow trout)	Static	pH 5.6	Finger-lings	96	<400	NS	NS	Doe et al., 1988[J97]	
2,4-D Acid	NN	*Oncorhynchus mykiss* (Rainbow trout)	Static	pH 6.8	Finger-lings	96	<1000	NS	NS	Doe et al., 1988[J97]	
2,4-D Acid	NN	*Oncorhynchus mykiss* (Rainbow trout)	Static	pH 8.48	Finger-lings	96	>1000	NS	NS	Doe et al., 1988[J97]	
2,4-D Acid	98.7	*Oncorhynchus mykiss* (Rainbow trout)	Static	FW	0.34g	96	358	320	C	DOW, 1983[B99]	41158301
2,4-D Acid	98.7	*Oncorhynchus mykiss* (Rainbow trout)	Static	FW	0.3g	96	110	NS	C	FWS, 1986[B99]	40098001
2,4-D Acid	100	*Salvelinus namaycush* (Lake trout)	Static	FW	0.3g	96	45	NS	C	Johnson & Finley, 1980	40098001
2,4-D Acid	~100	*Oncorhynchus clarkii* (Cutthroat trout)	Static	FW	Finger-lings	96	64	NS	Y	Johnson & Finley, 1980	

Table 117. 2,4-D Toxicity Data from Washington State SEIS (cont'd).

Test Formulation	1.3 Species	Test Type	Water Type	Size Class/ Age	Time (hrs)	EC50 (mg a.i./L)	NOEC (mg a.i./L)	Reference
2,4-D, Sodium Salt	*Macrobranchium dayanum* (Freshwater prawn)	Static	FW	NS	96	2275	NS	Omar & Shukla, 1984[J97]
2,4-D, Free Acid	*Tubifex tubifex* (Tubifex worm)	Flow	FW	NS	96	122	87	Bailey & Liu, 1981[J97]
2,4-D, Acid		Static	FW	20mm	96	161	NS	Fargasova, 1994
2,4-D, Acid	*Daphnia magna* (Daphnid)	Static/NS	FW	<24 hrs	48	25-418 (209)	<12	Alexander et al., 1983b[J97]; DOW, 1983[B99]; McCarty & Batchelder, 1977[J97]; Fargasova, 1994; Presing, 1981[J97]; Bunting & Robertson, 1975[W89,E93];FWS, 1970[B99]
2,4-D Acid	*Ceriodaphnia dubia* (Daphnid)	Flow	FW	<24 hrs	24	236	NS	Orius et al., 1991[J97]
2,4-D Acid	*Cyclops vernalis* (Cyclops)	NS	FW	NS	NS	37	NS	Bunting & Robertson, 1985[E93]
2,4-D, Acid	*Gammarus fasciatus* (Lined scud)	NS	FW	NS	NS	3.2	NS	Sanders, 1970[E93]
2,4-D, Free Acid	*Mytilus edulis* (Bay mussel)	NS	SW	NS	96 Mortality	259	NS	Liu & Lee, 1975[J97]
2,4-D, Free Acid	*Mytilus edulis* (Bay mussel)	NS	SW	NS	96 Attachment	262	NS	Liu & Lee, 1975[J97]
2,4-D, Free Acid	*Mytilus edulis* (Bay mussel)	NS	SW	Tocophore	48 Norm. Develop.	212	NS	Liu & Lee, 1975[J97]
2,4-D, Acid	*Crassostrea virginica* (Eastern oyster)	Flow	SW	Juvenile	96	57-467 (123)	30-<135 (<63)	Wade & Overman, 1991[B99]; Ward et al., 1993[J97,B99]; ESE, 1991[B99]
2,4-D, Acid	*Crassostrea virginica* (Eastern oyster)	Flow	SW	Larvae	96 Sell Deposition	57	30	Ward et al., 1993[J97,B99]

[1] FW – Freshwater
[2] NS – Parameter not specified.
[3] Number in parenthesis is the geometric mean of all accepted values.
[4] SW – Saltwater
[5] LC50s that appear to be outliers are 0.019, 0.054 and 0.5 mg a.i./L by EPA, 1975[B99]; ARC, 1976[B99]; UNI, [1977b99]. Tests were conducted prior to institutio EPA Pesticide Assessment Guidelines and have been discounted.
[6] LC50s conducted by EPA, 1988 ranged from 4.0 to 100 mg.a.i./L. This data was discounted due to its wide range.
[7] LC50 that appears to be an outliers (>100 mg a.i./L) by REF, 1970[B99]. Test was conducted prior to institution of EPA Pesticide Assessment Guidelines have been discounted.
[J97] JMPR, 1997
[B99] Brian Database, 1999
[W89] Ecology, 1989
[W80] Ecology, 1980
[E93] Ebasco, 1993 Many of the items that can be found in Ebasco can also be found in other reference. Usually only one compendium reference is cited

Table 118. 2,4-D Toxicity Data from Washington State SEIS (cont'd).

2,4-D Formulation	Test Type	Exposure Medium	Species	EEC[1] (mg a.i./L)	Acute LC50[2] (mg a.i./L)	Estimated or Measured Chronic NOEC[3] (mg a.i./L)	Risk Quotient (RQ)[4] (unitless)	Level of Concern (LOQ)[5] (unitless)	RQ exceeds LOQ
2,4-D acid	Acute	Water	*Cyprinus carpio* (Common carp)	0.100[11]	20	NA	0.05	0.1[A,C]	No
2,4-D acid	Acute	Water	*Gammarus fasciatus* (Lined scud)	3.25[9]	3.2	NA	1.02	0.1[A,C]	Yes
2,4-D acid	Acute	Water	*Gammarus fasciatus* (Lined scud)	0.19[10]	3.2	NA	0.059	0.1[A,C]	No
2,4-D acid	Acute	Water	*Gammarus fasciatus* (Lined scud)	0.100[11]	3.2	NA	0.0313	0.1[A,C]	No
2,4-D acid	Acute	Sediment	*Gammarus fasciatus* (Lined scud)	0.05 – 0.46 (0.15)[6]	3.2	NA	0.015-0.144 (0.047)[6]	0.1[A,C]	Probably No
2,4-D acid	Acute	Water	*Cyclops vernalis* (Cyclops)	0.19[10]	37	NA	0.0051	0.1[A,C]	No
2,4-D acid	Acute	Water	*Cyclops vernalis* (Cyclops)	0.100[11]	37	NA	0.0027	0.1[A,C]	No

[1] EEC – Expected environmental concentration.
[2] Acute LC50 – Concentration of 2,4-D that kills or immobilized 50% of the test animals in 96 hours.
[3] Estimated Chronic NOEC – (acute LC50/(acute/chronic toxicity ratio).
[4] RQ – Risk Quotient

LOC – Level of Concern – Value (EEC/toxicity) which should not be exceeded as an indicator of the safety of a particular pesticide application to the biota.
Values in parenthesis are geometric means of range presented.
1.36 mg a.i. /L is the typical United States use rate for 2,4-D DMA.
4.8 mg a.i./L. is the maximum labeled use rate in the United States for 2,4-D DMA products
3.25 mg/L is the concentration of 2,4-D found in bottom-waters of Northwest (Canadian) open water lakes after application of 2,4-D BEE.
0.19 mg/L is the concentration of 2,4-D found in surface of Northwest (Canadian) open water lakes after application of 2,4-D BEE.
0.100 mg./ is the concentration of 2,4-D found 2 to 6 days after application of 2,4-D BEE to Northwest (Canadian) open water lakes.
0.010 mg/L is the geometric mean of the concentration of 2,4-D found 2 to 6 days after application (0.100 mg/L) and 5 to 22 days after application (0.001 mg/l
of 2,4-D BEE to Northwestern (Canadian) lakes.
A – Acute RQ – (Short term EEC)/(acute LC50)
B – Chronic RQ – (Long term EEC)/(estimated chronic EEC)
C – Acute LOC – 0.1 –(short term (EEC)/ (96 hour LC50)
D – Chronic LOC – 1.0 – (long term EEC)/(≥28 day NOEC

Table 119. 2,4-D Toxicity Data from Washington State SEIS (cont'd).

Species	Length of Chronic Test	2,4-D Formulation	Acute Toxicity (LC50 mg/L)	Chronic Toxicity NOEC[1] (mg/L)	Ratio[2]
Chinook salmon	86 days	2,4-D BEE	0.32-0.38 (0.35)[2]	0.040	8.75
Fathead minnow	32 days	2,4-D BEE	2.5-3.25 (2.85)	0.0805	35.4
Fathead minnow	Life Cycle 10 months	2,4-D BEE	2.5-3.25 (2.85)	0.3	9.5
Fathead minnow	32 days Early Life-Stage	2,4-D 2-EHE	>5	0.12	>41.7[3]
Fathead minnow	32 days Early Life-Stage	2,4-D DMA	266-355 (307)	17.1	18.0
Rainbow trout	23-27 days Early Life-Stage	2,4-D K Salt	358	LC50 = 4.2-11[4] (6.79)[5]	52.7
Goldfish	8 days	1,4-D K Salt	>187 to >201 (>194) or >164[6,7,8]	LC1 = 8.9-18.2[4] (12.7 a.i. 10.8 a.e.)	>15.2
Largemouth bass	7.5 days	2,4-D K Salt	161-165 (163)	LC1 = 3.2-13.1 (6.5)	25.1
Fathead minnow	32 days	2,4-D Acid	133-320 (206)	63.4	3.2
Medaka	28 days	2,4-D acid	2780	27.2-30 (28.6)	97.2
Daphnid	21-day Life-Cycle Flow	2,4-D BEE	7.2[9]	0.29[9]	24.8
Daphnid	21-day Life-Cycle	2,4-D 2-EHE	5.2[9]	0.015[9]	346.7[3]
Daphnid	21-day Life-Cycle	2,4-D DMA	184[9]	27.5[9]	6.69
Daphnid	21-day Life-Cycle	2,4-D Acid	25->100[10] (>45)	79[9]	0.57[11]

1 Chronic Values are NOEC unless otherwise noted
2 Geometric mean excluding 2,4-D 2-EHE product and extreme outlier and "greater thans" = 18.0 (limits 6.4 to 50.5 ± one standard deviation)
3 2,4-D 2-EHE is not usually used for the control of fully aquatic weeds
4 2,4-D K Salt
5 Values in parenthesis are geometric means of all valid individual values
6 2,4-D Acid
7 Neskovick, 1994
8 *Cyprinus carpio* (related species that may not be a separate species)
9 All work conducted under current Pesticide Assessment Guidelines according to current GLP Guidelines
10 Data exhibits extreme variability between laboratories
11 Extreme outlier

Table 120. 2,4-D Toxicity Data from Washington State SEIS (cont'd).

Test Substance	%A.I. or Formulation	Species	Test Type	Water Type	Growth Stage/ Age	Time (Hours)	LC50 mg a.i./L	NOEC mg a.i./L	Status	Reference	MRID Number
2,4-D, DMA	66.7	*Skeletonema costatum* (Marine diatom)	Static	MANM	Log	120	36.60	96.25	C	Hughes, 1990f	41505901
2,4-D, DMA	EC Form	*Phaeodactylum tricornutum*	Static	20 mg/mL SW	Log	20 days	362.00	NS	NS	Okay & Gaines, 1995	NS
2,4-D, DMA	66.7	*Naviculla Pelliculosa* (diatom)	Static	SiAAP	Log	120	5.28	1.70	C	Hughes, 1990d	51505903
2,4-D, DMA	66.7	*Lemna gibba* (Duckweed)	Static	Hoagland's	Log	336	0.58	0.27	C	Hughes, 1990l	41505904
2,4-D, Acid	96.1	*Selenastrum capricornutum* (Green algae)	Static	AAP	Log	120	51.20	19.20	C	MPI, 1990[899] Brian, 1999	41420002
2,4-D, Acid	96.1	*Selenastrum capricornutum* (Green algae)	Static	AAP	Log	120	33.20	26.20	S	Hughes, 1990n[397]	41420001
2,4-D, Acid	96.1	*Selenastrum capricornutum* (Green algae)	Static	AAP	Log	96	25.90	24.20	C	St. Laurent, 1992 JMPR, 1997	NS
2,4-D, Acid	NS	*Scenedesmus quadricauda* (Green algae)	Static	AAP	Log	20 days	98.00	NS	NS	Fargasova, 1994	NS
2,4-D, Acid	87	*Chlorococcum sp.* (Green algae)	Static	AAP	Log	240	50.00	NS	S	EPA, 1986	40228401
2,4-D, Acid	Tech	*Chlorella fusca* (Green algae)	Static	AAP	Log	120	88.90	NS	C	Faust et al., 1994[397]	

Table 121. 2,4-D Toxicity Data from Washington State SEIS (cont'd).

Test Formulation	Species	Test Type	Water Type	Size Class/ Age	Time (hrs)	EC50 (mg a.i./L)	NOEC (mg a.i./L)	Reference
2,4-D, BEE	*Daphnia magna* (Daphnid)	Flow	FW[1]	<24 hrs	48	7.2	<3.4	Alexander et al., 1983e[B99]
2,4-D,BEE	*Daphnia magna* (Daphnid)	Static/NS[2]	FW	1st Instar/NS[2]	NS[2]	1.7-5.6 (4.0)[3]	NS[2]	Sanders, 1970[E93]; FWS, 1986[B99]; Johnson & Finley, 1980; FWS, 1986[B99]
2,4-D, Acid	*Daphnia magna* (Daphnid)	Static/NS	FW	<24 hrs	48	25-418 (209)	<12	Alexander et al., 1983b[J97]; DOW, 1983[B99]; McCarty & Batchelder, 1977[J97]; Fargasova, 1994; Presing, 1981[J97]; Bunting & Robertson, 1975[W89,E93];FWS, 1970[B99]

XI. Method Detection Limits

Table 122. 2,4-D Method Detection Limits.

Analytical Method	MDL	Reference
HPLC	0.5mg/L	Oris et al. 1990
HPLC	0.15mg/L	USGS 1999
GC/MSD	0.1ppb	Jones et al. 2000

XII. Manufacturer Contact Information

Cerexagri, Inc.; Aqua-Kleen 1-800-438-6071; Amvac; Ancom; Atanor; Atul; CAC; Crystal; Defensa; Dow AgroSciences; Krishi Rasayan, Marks; Nissan; Nitrokemia; Nufarm GmbH; Nufarm Ltd.; Sanachem; Uniroyal; United Phosphorus.

XIII. Summary Table

2,4 D DMA (dimethylamine salt) formulation

Table 123. 2,4-D Summary Table.

Primary use	Post emergent systemic herbicide –used for hyacinth, milfoil (liquid). Often used with polymeric thickener.
Mechanism of Toxicity	Hormone that stimulates stem elongation & nucleic acid/protein synthesis, stimulating uncontrolled growth until death. Affects enzyme activity/respiration/cell division.
Solubility	Relatively soluble. Precipitates in hard water as Ca/Mg salts
Fate	Rapid hydrolysis to 2,4 D acid then bound to sediments. 2,4 D DMA < 2,4 D BEE in sediments. Bioaccumulation not expected.
Confounding Factors	Persistent at temps. < 7^{ø} C
Data Gaps	Resident species, aquatic insects.

[6]Not distinguished from methoprene by USEPA.

References

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