Supplemental Environmental Impact Statement
Assessments of Aquatic Herbicides

Appendix E
1992 SEIS Appendices: Grass Carp Supplement, Copper Compounds, Fluridone Human Health Risk Assessment, Fluridone Aquatic Risk Assessment, Glyphosate Risk Assessment
1992 SEIS Responsiveness Summary

WASHINGTON STATE
DEPARTMENT OF
ECOLOGY

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Appendix E

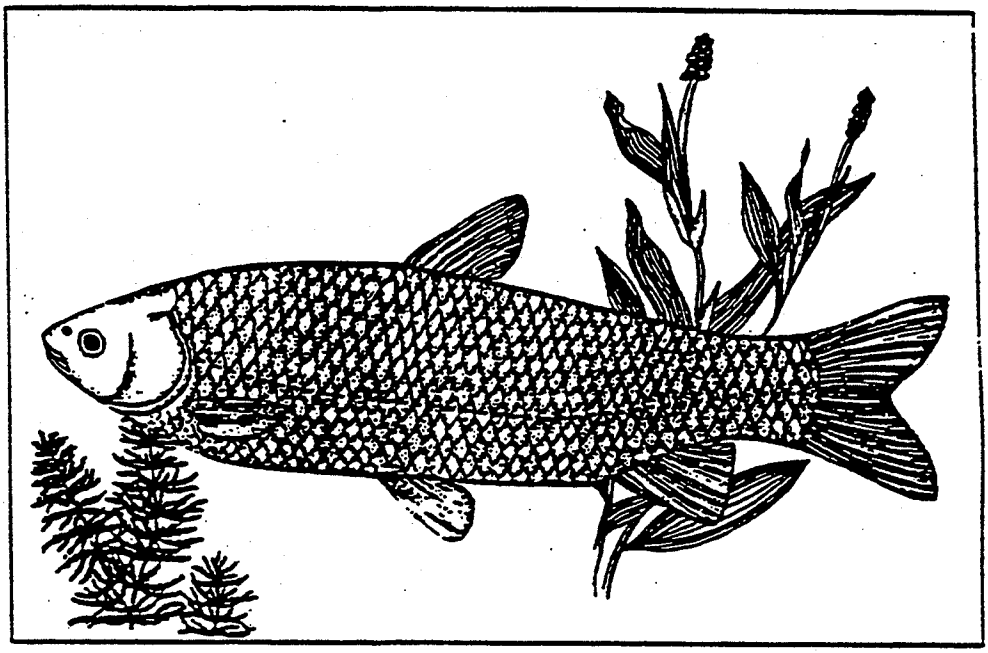
1992 SEIS Appendices:

Grass Carp Supplement

Washington Department of Wildlife
Fisheries Management Division
F.M. No. 90-4

GRASS CARP USE IN WASHINGTON

Prepared by WDW Fisheries Managment Division



March 1990

INTRODUCTION

Aquatic plants are a common and beneficial component of freshwater ecosystems. Plants provide important fish and wildlife habitat and, when not overly abundant, can have a positive impact on water quality. However, in certain situations, plant growth can become excessive and severely restrict the recreational use of a body of water. In extreme cases, excessive plant growth can also be detrimental to the water quality and fish populations of a lake or river. Aquatic plant problems typically occur in response to nutrient enrichment of a system and, as a result, are most common in agricultural or urban areas. Introduction of exotic plant species such as Eurasian water milfoil can also lead to severe problems.

Each year a substantial amount of money and effort is expended in attempts to control excessive plant growth in Washington waters. At the present time there are only a few categories of acceptable aquatic weed control practices in the United States. These are chemical treatment, mechanical harvesting, water level reduction, dredging, bottom screening and biological control. No utopian solution exists with any of these methods. However biological control is attractive because it is usually inexpensive and produces long-term control when compared to other methods, and it produces no toxic residue. An ideal biological control agent would have the following attributes.

1. It must attack only those target plants deemed undesirable in a given locale.
2. It must be able to survive the new environment to which it is introduced.
3. It must be capable of reducing problem plants to acceptable levels.
4. It must not proliferate and become a nuisance.
5. It must not disturb those things in the ecosystem considered desirable.

This is obviously a tall order. No biological control at present has all these attributes. However, under certain conditions the grass carp (Ctenophyaryngodon idella) does have the ability to reduce some types of nuisance aquatic plants without undue environmental side affects.

AQUATIC PLANT CONTROL WITH GRASS CARP

Grass carp have been used successfully to control certain species of aquatic plants in various situations around the world. Irrigation reservoirs, canals, aquaculture ponds, cooling reservoirs and drinking water reservoirs have all had nuisance levels of plants controlled with grass carp. Grass carp do prefer some species of plants and will not consume others. However, given a plant community that grass carp will consume, it is conservatively estimated that the cost of weed control with grass carp in Washington will be approximately 25 percent of mechanical methods and 50 percent of chemical methods.

The potential of the fish in the United States was first recognized by the state of Arkansas, which imported them in 1963. Since 1963 many other states have imported the fish. As of March 1989, 30 states allow regulated use of triploid grass carp (See Figure 1). Eleven of those states allow use of fertile fish (See Figure 2). Several states, like Oregon and Washington, only allow importation of the fish for scientific research.

LIFE HISTORY AND DISTRIBUTION OF GRASS CARP

The grass carp, also known as the white amur, is a member of the minnow family. Its closest relative in that family is the shiner. However, unlike the relatively small shiner, grass carp can grow to 100 pounds in its native home range (40 in the United States) and live 15 years.

The fish's natural habitat is the large, swift, cool rivers of China. Its homeland includes rivers that drain into the Pacific Ocean between the Amur River at approximately latitude 50 North and the West River at approximately latitude 23 North. The grass carp has been introduced into 50 countries including the United States and is established outside its native range in Japan, the Soviet Union and Mexico. Reproduction has also been documented in the Philippines, Taiwan, Yugoslavia and the United States.

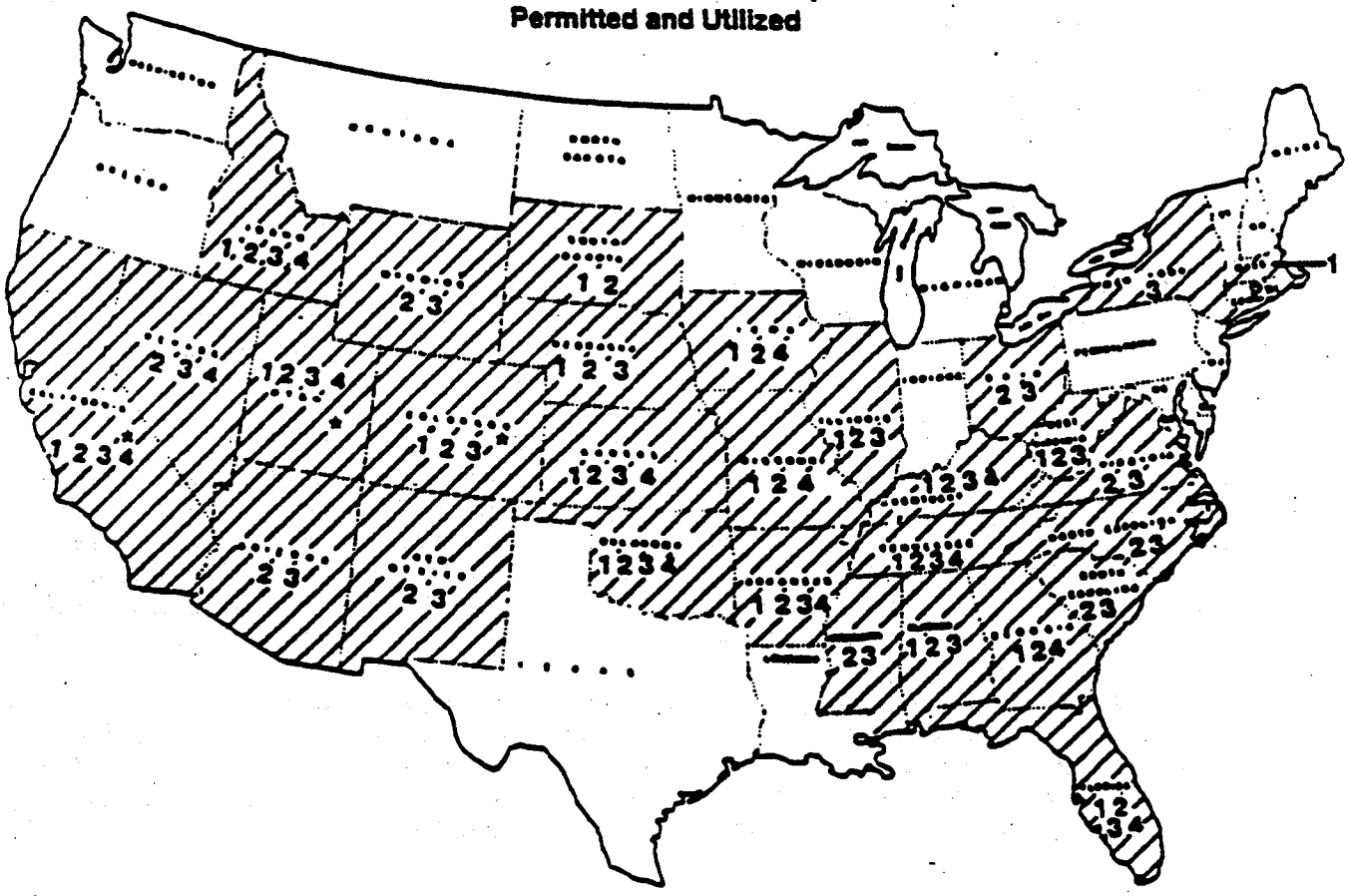
Female grass carp usually reach sexual maturity a year ahead of males. The age at which females reach maturity depends on climate and nutrition and ranges from two years in the tropics, four or five years in temperate climates and eight to ten years in cold climates. Female size at maturity is usually five to ten pounds. The average ten to 15 pound female will produce 500,000 eggs each year.

Grass carp spawn from April to August or September. Water temperatures in the 59 F to 63 F range trigger upstream migration to spawning grounds. Spawning requirements are very specific. The conditions most frequently associated with reproduction are a rise in water level, temperatures above 63 F (as high as 86 F) current velocity greater than two feet per second (as high as five feet per second) and a flowing section of river from ten to 100 miles long depending on temperature and flow. Spawning grounds usually occur immediately downstream from an island or other feature which causes strong vertical mixing. The substrate is usually rock and gravel. Other factors associated with spawnings are pH of 7.2 to 7.7 and dissolved oxygen of at least four parts per million (ppm). Depending on temperature, eggs hatch in 16 to 60 hours. The eggs are free floating and drift with the current.

The newly hatched larvae absorb their yolk sacs at about one-third inch long and begin feeding on plankton (rotifers, crustaceans, midge larvae and algae). Fry must have access to rich back water areas to survive. At one inch the grass carp fry start feeding on aquatic vegetation and the reliance on

Triploid Grass Carp

Permitted and Utilized



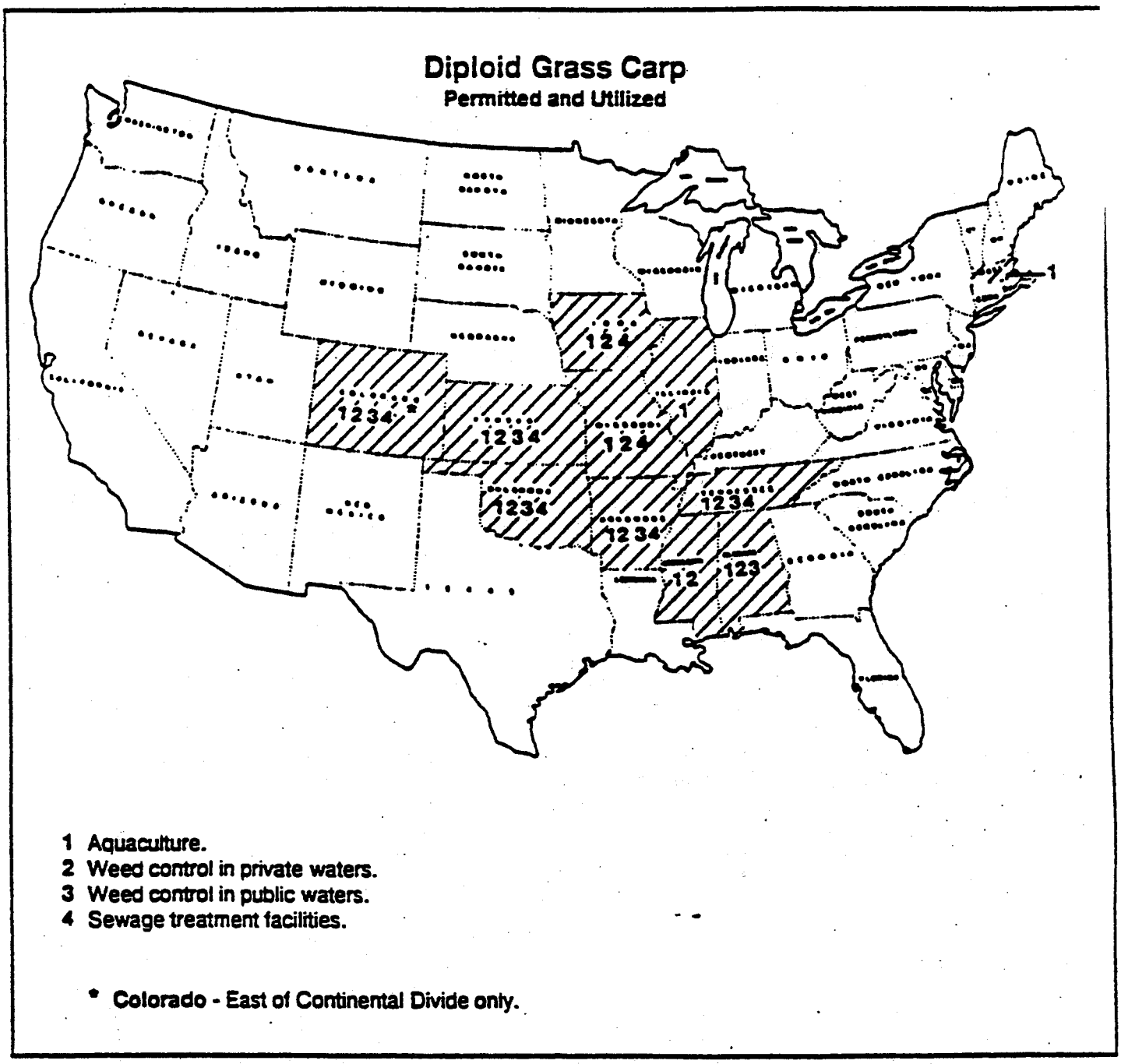
1 Aquaculture.
2 Weed control in private waters.
3 Weed control in public waters.
4 Sewage treatment facilities.

* California - only in Imperial and Coachella Valleys.

* Colorado - East of Continental Divide only.

* Utah - approved, but not yet implemented.

Figure 1


Diploid Grass Carp
Permitted and Utilized
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1 2 3
1 Aquaculture.
2 Weed control in private waters.
3 Weed control in public waters.
4 Sewage treatment facilities.
* Colorado - East of Continental Divide only.

Figure 2

plankton decreases. Fish above one inch long eat aquatic vegetation and some small invertebrates, but are primarily plant consumers. Small fish have consumed animal matter in lab studies, but in pond studies the occurrence of animal matter is believed to be the result of inadvertent consumption with aquatic plants. Small grass carp prefer tender, succulent plants. As the fish grow their preference range for aquatic plants broaden. Increasing temperature also broadens the preference range of plants that are eaten.

Intensive feeding begins at water temperatures above 68 F. At 53 F and below, feeding diminishes. Dissolved oxygen levels less than four ppm also reduce food intake by as much as 40 percent. Grass carp can consume up to 150 percent of their body weight per day when temperatures are above 77 F, but consumption decreases at temperatures above 90 F. Grass carp have specially developed pharyngeal teeth in their throats and a horny pad that enables them to cut, rasp and grind vegetable matter. This ruptures the plant cell membranes and allows digestion of the plant material. Grass carp do not pull plants up by the roots like the common carp, they eat from the top down without disturbing roots or sediment.

Grass carp can survive a wide range of temperatures from water bodies that freeze over to temperatures of up to 95 F. Although they cannot survive in the marine environment they can migrate through brackish water.

WASHINGTON BACKGROUND

Although grass carp were first brought to this country (Arkansas) in 1963, it wasn't until almost ten years later that the fish became an issue in Washington state. The Washington State Department of Fisheries proposed planting grass carp into Capitol Lake. The Washington Department of Wildlife (formerly Game) opposed the introduction because of unknown potential impacts to game fish. The fish's spawning requirements, although specific, were thought to exist in several of the state's larger rivers. In order to prevent importation of the potentially dangerous carp into Washington, the Department of Wildlife declared them deleterious exotic wildlife in 1973.

By the early 1980's triploid grass carp were being produced in the United States. Triploids develop when eggs of a normal (diploid) pair of grass carp are shocked either chemically, with excessive pressure, or with heat. This results in eggs with an extra chromosome that develop into triploid fish. The triploid progeny (as opposed to normal diploid fish) are sterile. This alleviated one of the major concerns about grass carp, reproduction in the wild. Faced with a growing demand for alternative methods of aquatic plant control, the Washington Department of Wildlife supported research on the triploid grass carp.

WASHINGTON STUDY

In 1983 the Washington Departments of Wildlife and Ecology initiated a long-term agreement through the Washington Cooperative Fish and Wildlife Research Unit at the University of Washington to study the potential use of the triploid grass carp in Washington State. Subsequent to this cooperative effort the Seattle District of the Army Corps of Engineers, the U.S. Fish and Wildlife Service and the U.S. Environmental Protection agency all agreed to participate. The ultimate goal of this study was to determine if triploid grass carp could be used safely and effectively to control nuisance levels of aquatic plants in Washington State. A key factor of the investigation was to determine if the fish could control aquatic plants without eliminating them. The study objectives were as follows.

1. Evaluate current methods for determining if a fish is triploid (sterile).
2. Verify the sterility of triploid fish.
3. Evaluate the efficiency of plant control by triploid grass carp (plant preference, consumption rates, etc.)
4. Determine the effect of triploid grass carp on Washington ecosystems.
5. Develop a stocking rate model for Washington waters.

All objectives were to be met by June 1990, but additional follow-up work is scheduled through June 1992.

Triploid Determination

Each individual grass carp has blood drawn and is tested for triploidy by the commercial facilities raising the fish. The method utilized (Coulter Counter with a channelizer) was determined to be 100 percent accurate by University of Washington researchers. Additionally, before triploid fish are shipped out of commercial grass carp facilities, the U.S. Fish and Wildlife Service retests a sample and certifies the fish as triploids before delivery. The chances of a fertile fish being exported are quite small.

Sterility Verification

Scientific research has shown that female triploid grass carp are functionally sterile. The odds of a triploid male's sperm being viable and actually finding a fertile diploid female to spawn with have been estimated to be more than 20 billion to one. Based on these conclusions, the U.S. Fish and Wildlife service recently issued a letter stating, "There seems to be no compelling reason to prohibit the use of certified triploid grass carp in open systems because there is every reason to assume that they will not reproduce themselves. Any adverse impact on desirable aquatic plants will be short lived and reversible." The letter concluded, "The stocking of triploid grass carp in either closed or open water situations will result in no adverse impact to the environment."

Efficiency of Plant Control

Five plant infested lakes, two west of the Cascade Mountains and three east of the Mountains, were stocked with triploid grass carp. Plant communities in the western sites were dominated by floating-leaved species, while those in eastern Washington were dominated by submergents. Planting rates varied and were based on studies done elsewhere in the world. On both sides of the state, some species of plants preferred by grass carp were reduced while other less palatable plants increased. However, the overall net effect was more open water. Similar results were found in recent studies at Devil's Lake, Oregon.

Washington post introduction results are based on two years (three to five planned) of data collection and analysis. Grass carp usually take three to five years for full impacts of an introduction to be realized. However, the results, to date, suggest that high stocking rates, similar to those used in Northern and Central Europe, will be required for plant control in the Northwest. It appears that triploid grass carp have the ability to control aquatic plants in the Northwest as they have in numerous other localities around the world.

Effect on Ecosystem

This portion of the grass carp study was divided into four areas:

1. impacts on water quality,
2. impacts on fish populations,
3. impacts on waterfowl, and
4. impacts on invertebrates.

Water quality in Washington study lakes generally improved after introduction of grass carp. With the elimination of large mats of vegetation, bottom dissolved oxygen generally increased from levels lethal to fish. Calcium and conductivity levels also increased while pH readings dropped from levels lethal to fish because of decreases in photosynthesis. Studies by other researchers elsewhere in the United States produced similar results. Although not documented in Washington, nuisance algae blooms have been recorded after introductions of grass carp. These have only occurred when all vegetation was removed.

While it is possible that the triploid grass carp may have a direct impact on fish populations, most evidence suggests harmful effects only occur if all vegetation is removed. Harmful effects have not been observed in the Northwest. However, the indirect effects of excessive plant growth, such as low dissolved oxygen and high pH, are likely more harmful than the effects of complete eradication of plants. It has been documented in ponds that 30-40 percent of viable plant cover maximizes largemouth bass production and can alleviate some of the deleterious water quality effects of dense covers of plants. Excessive cover provides many hiding places for prey species of fish resulting in "out-of-balance" fish populations (numerous small fish). Other studies have shown that fishing activity increases after introduction of grass

carp because the reduction in plants makes fishing possible. Although complete plant removal has proven detrimental to largemouth bass populations, it may be beneficial to salmonids if water quality remains good after plant eradication.

Although no negative impacts to fish have been documented in Washington studies, questions related to predation and competition will still be asked. According to the scientific literature, young grass carp do eat small invertebrates and can compete with other species of fish for food. However, most triploid grass carp are not introduced into a water until they are approximately ten inches and have switched to vegetation. The fish are planted at a larger size because of extreme susceptibility to predation by other species such as largemouth bass. Once grass carp have switched to plant material, direct food competition with other fish will be nonexistent. Even when all vegetation in a lake has been removed because too many grass carp are planted, feeding on other fish species has not been documented.

Large numbers of Pacific Flyway waterfowl spend all or part of the year in Washington. Since food availability is a major determinant of their presence, it is logical to assume that the introduction of grass carp may change the quality and quantity of aquatic plant food available to waterfowl. Declines in waterfowl abundance have been observed outside Washington after grass carp grazing reduced aquatic plants. Grass carp and some waterfowl prefer similar plants. Unfortunately, funding for this portion of the study was withdrawn by the U.S. Fish and Wildlife Service before any grass carp were planted. However, one could conclude that, where plant control is desirable, grass carp may have less impact than other methods. With grass carp, aquatic plants can be reduced to a desirable level. Other methods often result in complete eradication of aquatic plants. A more appropriate issue would be to determine the compatibility of aquatic vegetation control, in general, with waterfowl. Grass carp are just one of the tools used to manipulate aquatic vegetation. Other tools currently used in Washington include herbicides, mechanical harvesting, and dredging.

It is recognized that drastic changes in the plant community will affect the invertebrate populations that depend on it. Baseline invertebrate data has been collected in Washington. However, that data will only be considered at a later time as it relates to food items found in fish stomachs. Much of the same conclusions drawn about waterfowl/grass carp interactions can be drawn about invertebrates. If invertebrate populations are altered by introduction of grass carp, those same impacts, and likely greater ones, would occur with other methods of plant removal.

Post introduction impacts to the aquatic community have been measured for two years following grass carp introductions in Washington. As stated earlier, it takes three to five years for a grass carp introduction to achieve full effect. Additional data will be forthcoming. We do know from Washington studies that water quality has improved. To date, negative impacts to water quality and fish populations have only been documented outside of Washington

where grass carp have been planted at rates that cause complete removal of plants. However, any negative effects can be reversed by removal of the grass carp population.

Stocking Model

A worldwide survey of 38 grass carp experts was conducted to develop a predictive stocking rate model for Washington. Stocking criteria are critical because, as stated earlier, complete eradication of aquatic plants can be detrimental to the aquatic ecosystem. Therefore, determining appropriate stocking rates for the Northwest is vital. Response to the survey clearly showed that grass carp were effective in controlling some plant species and not others. Respondents were asked if they had reservations about using grass carp to control any of the six listed plant types. All respondents recommended stocking fish for the control of submergent plants that grass carp prefer to eat, 97 percent believed grass carp would control the less preferred submergents, 69 percent believed control of small floating leaved plants could be achieved and 88 percent felt grass carp could control filamentous algae. In contrast, only 41 percent believed emergent plants could be controlled with grass carp and only 29 percent felt control of large floating leaved species was possible. However, recent information suggests that larger fish (eight to nine years old) may be successful in controlling large-leaved plants. The results of the survey and feeding preference studies completed by the University of Washington produced similar results.

Basically two types of aquatic plant control with grass carp are desirable in Washington:

1. total and rapid eradication of plants where water flow and navigation are important and,

2. slow reduction of plants to intermediate levels to enhance fish production and water dependant recreation (obviously some overlap will be desirable in many instances).

Two preliminary planting models have been developed for various types of plants and desired levels of control for Washington. The main predictive factor in the first is accumulated air temperature units for an area and the main predictive factor for the second is estimated weight of plants. The preliminary models will be refined annually with additional field data from 1989-1991. However, the models do show that Washington's cool temperature climate is extreme for grass carp and that planting rates will need to be higher in the Northwest than much of the rest of the United States. The west side of the state will generally require higher rates than the east side.

Generally, stocking rates for complete eradication will need to range from 80 to 100 fish per vegetated acre. Planting rates for plant control, as opposed to eradication, will need to range from 25 to 80 fish per vegetated acre. Approximately 40 to 60 fish per acre will be needed to control filamentous algae. More precise information on planting rates will be available in May 1990.

OTHER GRASS CARP ISSUES

Movement

Grass carp have a desire to be in flowing water. Their instinct to move from one place to another is stimulated not only by the need to spawn, but also by any rising water scenario. Grass carp, including triploids, may move out of a lake environment whenever rains cause an increase in the lake level or flows. The removal of vegetation in a nontarget area and lack of removal in the target area are the worst that could be expected if sterile fish move out of a target water. Also, grass carp are expensive to replace and it would be unwise to introduce even triploids into unscreened waters.

Diseases

Grass carp have been diagnosed with over 100 diseases and parasites. However, only 29 pathogens have been documented in the United States. The first 11 listed below are considered common in the U.S.

1. Capillaria catostomi
2. Spiroxys
3. Metacercarial cysts
4. Dactylogyrus
5. Trichodonella
6. Bothriocephalus opsarichthydis
7. Cryptobia branchialis
8. Trichodina
9. Camallanus
10. Chilodonella
11. Aeromonas hydrophila
12. Hexamita
13. Apiosoma
14. External fungus
15. Spheres
16. Lernaea elegans
17. Ich
18. Clinostomum complanatum
19. Gyrodactylus
20. Golden shiner virus
21. Ambiphrya
22. Proteocephalus
23. Flexibacter columnaris
24. Trichophrya
25. Ichtyobodo
26. Chloromyxum
27. Dilepid tapeworm
28. Cryptobia agitans 1)
29. IPN-like virus

These pathogens are either already present in Washington or are not considered dangerous to important fish species located within the state. Number 6, the Asian tapeworm, may be an exception. However, importation of the tapeworm can be eliminated by shipping grass carp that are over eight inches in length. Generally grass carp do not pose a significant disease threat to existing Washington fish species.

Illegal Introductions

In 1987 the Department of Wildlife was informed by the U.S. Fish and Wildlife Service that approximately ten illegal shipments of diploid (fertile) grass carp were delivered to Washington. The United States Government prosecuted the shipper, but it was left up to the State of Washington to deal with the

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1) Not pathogenic to salmonids.

illegal introductions. The Department of Wildlife did not prosecute the individuals who introduced the fish into their private ponds. However, all ponds were treated with rotenone to eradicate the fish. In one instance, fertile grass carp were planted into a pond adjacent to the Columbia River. This pond's outflow entered the river. Therefore, fertile grass carp may be present in the Columbia River where both spawning and rearing requirements exist. The ten documented illegal introductions into Washington State suggest that the extent of unreported introductions may be substantial.

SUMMARY/CONCLUSIONS

1. Substantial effort is expended each year in attempts to control aquatic plants in Washington. Many techniques used are expensive, have short term results, and are potentially harmful to fish and wildlife.

2. The grass carp, a vegetarian native to China, has been used as an environmentally safe and effective biological control of some aquatic plants around the world. The grass carp was first introduced into the United States in 1963 by the state of Arkansas.

3. The large rivers of the Northwest may provide fertile grass carp with suitable spawning and rearing habitat. Reproduction in lakes is unlikely.

4. Grass carp are now legal in at least 30 states. The fish are only allowed in Washington for purposes of scientific research.

5. With the development of sterile fish (triploids) in the early 80's, Washington State embarked on research directed at potential use in the Northwest.

6. Research has shown that methods of determining if grass carp are triploids are 100 percent accurate. The possibility of a triploid fish being fertile and finding another fertile fish to reproduce with is 20 billion to one.

7. Preliminary research results from Washington State and research from elsewhere, indicate that introduced grass carp populations produce little negative impact to aquatic ecosystems. The negative impacts that have been documented occur when too many fish are planted and all vegetation is removed. Using sterile, triploid grass carp prevents uncontrolled population expansion of the fish, and helps ensure plant populations are controlled, not eradicated. Sterility ensures that the exotic fish will not become a nuisance itself, because its impact is limited to one lifespan and, therefore, is reversible.

8. Waterfowl can be negatively affected by grass carp.

9. Preliminary research results from Washington indicate grass carp planting rates for the Northwest will need to be high because of cool temperature conditions. Planting rates may range from 25 to 100 fish/per vegetated acre.

10. Grass carp have a tendency to move out of lakes when water levels rise.

11. Grass carp importation into Washington State will not pose a disease threat to existing important species of fish.

12. Fertile grass carp have been illegally planted in Washington in waters connected to the Columbia River.

RECOMMENDATIONS

The scientific literature and research conducted in the Northwest suggest that the grass carp could be a safe and effective tool for control of nuisance aquatic plants in Washington state. Regulated use of grass carp should be allowed in Washington.

Diploid (fertile) grass carp spawning and rearing habitat exists in many large rivers of the Northwest. Although aquatic vegetation is limited in most of these waters (the Columbia, Pend Oreille, and Okanogan Rivers are exceptions) it is still quite feasible that small wild populations of grass carp could become established. It is unlikely that these populations would pose a significant threat to fish or wildlife. However, competition for food with waterfowl could be important in the lower Columbia River. The risk of negative impacts of developing wild grass carp populations is small, but it is not a risk that we must take. Grass carp introductions in Washington should be limited to the sterile triploid grass carp, thus eliminating any chance of reproduction in the wild.

The scientific literature and experiences in the Northwest indicate that grass carp are a safe and effective tool for controlling some nuisance aquatic plants. However, the same scientific literature also concludes that negative impacts have occurred as a result of planting too many grass carp. With the use of triploid fish, any negative impact would be reversed as the fish die. However, fish can live for 15 years. Without an active removal program in an overplanted water, negative impacts could last for many years. Therefore it is important to plant the correct number of fish, especially for larger public waters where the effects of an introduction will be very visible. This is even more important in the Northwest because the data produced, to date, indicate planting rates need to be much higher than most other areas. Severe climate areas, like Washington, have the least information on planting rates.

Grass carp stocking models for the Northwest are being developed by the University of Washington. The models are preliminary and will be more accurate by the summer of 1990. However, planting rate "fine tuning" will be an ongoing process as more and more is learned. There is currently sufficient information to recommend conservative planting rates for various situations in Washington. We should be most concerned with waters of the state that are five or more acres in area. These waters make up the bulk of aquatic fish and wildlife habitat in the state. The Washington Department of Wildlife should be responsible for planting rate decisions for important state waters.

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PROPOSED RULE CHANGES

Only triploid grass carp will be allowed into Washington State, therefore only the triploid form should be removed from the deleterious category. This is accomplished by adding the word diploid before grass carp.

WAC 232-12-017 Deleterious exotic wildlife. Deleterious exotic wildlife includes:

(1) Walking catfish, Clarias batrachus
(2) Mongoose, all forms of the genus Herpester
(3) Diploid Grass carp, Ctenopharyngodon idella
(4) African clawed frog, Xenopus laevis
(5) Wild boar, Sus scrofa and hybrids involving the species Sus scrofa
(6) Collared peccary (javelina), Dicotyles tajacu

It is unlawful to import or possess live specimens of deleterious exotic wildlife except for purposes of scientific research as authorized by the director. [Statutory Authority: RCW 77.12.040.85-09-014 (Order 247), 232-12-017, filed 4/9/85; 81-22-002 (Order 174), 232-12-017, filed 10/22/81; 81-12-029 (Order 165), 232-12-017, filed 6/1/81.]

Triploid grass carp are expensive ($4.00-$5.00 each), can be caught on rod and reel, and are very palatable. Planting grass carp into a body of water for aquatic vegetation control, and removing them by angling will not be compatible. If we are to remove triploid grass carp from the deleterious exotic wildlife category (WAC 232-12-017), they will need protection.

Grass carp are not considered wildlife because they do not reproduce in the wild (RCW 77.08.010 Definitions #16). Therefore, there is no mechanism to regulate their harvest unless they can be classified as game fish.

WAC 232-12-019 Classification of Game Fish.

As provided in RCW 77.12.020 and in addition to those species identified in RCW 77.08.020 the following species of the class Osteichthyes are classified as game fish:

Scientific Name	Common Name
Salvelinus confluentus	Bull Trout
Esox lucius	Northern Pike
and hybrid involving genus Esox	Tiger Muskellunge
Ctenopharyngodon idella	Grass Carp

[Statutory Authority: RCW 77.12.040. 88-23-046 (Order 320), 232-12-019, filed 11/10/88. Statutory Authority: RCW 77.12.020 and 77.12.040. 83-21-003 (Order 218), 232-12-019, filed 10/6/83. Statutory Authority: RCW 77.12.040. 81-12-029 (Order 165), 232-12-019, filed 6/1/81. Formerly WAC 232-12-015.]

As stated earlier, it will not be appropriate to harvest these expensive fish. Therefore angling for grass carp should be prohibited.

WAC 232-28-618 1990-1991 Washington Game Fish Seasons and Catch Limits

Add the following in all grey boxes below "whitefish".

Grass Carp	Closed Season

PROPOSED POLICY

This policy applies whenever a grass carp introduction is proposed for any water in the State of Washington.

I. Definitions for the purpose of this policy only.

A. Public Access - Public access is considered any point of entry to a body of water provided by federal, state or municipal governments for recreation. Access may be owned or leased by the government agency. Municipally owned golf course, sewage treatment or settling ponds are exceptions to this definition.

B. Triploid grass carp - A sterile grass carp (Ctenopharyngodon idella) with an extra chromosome.

II. Only triploid grass carp over eight inches in length may be planted into Washington waters.

III. Triploid grass carp may only be planted into naturally closed water systems, into waters that are screened or into waters managed in such a way as to prevent substantial escapement into nontarget waters.

IV. Lakes, ponds or reservoirs less than five acres and without public access may be planted with triploid grass carp at the expense of the property owner(s). A list of all property owners, with land adjacent to the water, and their opinion of the proposed introduction, must be provided to Department of Wildlife.

A. The planting rate will be determined by the property owner(s) based on information provided by Department of Wildlife.

V. Manmade irrigation and power canals may be planted at the expense of the property owner(s) with triploid grass carp by the owner(s) or their representative(s).

A. The planting rate will be determined by the owner(s) or representative(s) based on information provided by Department of Wildlife.

VI. Lakes, ponds or reservoirs greater than five acres and without public access may be planted at the expense of the property owner(s) with triploid grass carp. A list of property owners, with land adjacent to the water, and their opinion of the proposed introduction, must be provided to Department of Wildlife.

A. The Department of Wildlife will determine the planting rate based on the needs of the property owner(s) and the fish and wildlife using the area.

VII. Lakes, ponds or reservoirs with public access may be planted with triploid grass carp if a professional lake restoration feasibility assessment has been completed that addresses all of the following:

A. Cultural Assessment

1. Collection of historical and background data including lake description, watershed description, public access benefits, recreational use and pollutant sources.

B. Water Quality Assessment

1. Aquatic plant survey (biomass or volume estimates, species composition, water temperature cycle)
2. Nutrient budget
3. Hydraulic budget
4. Nutrient limitation
5. Biological relationships
6. Lake response (cause and effect relationships between nutrients and the plant and animal communities).

C. Restoration Feasibility

1. Evaluate potential lake restoration techniques
2. Develop matrix for alternatives
3. Identify restoration plan

D. Public Involvement

1. Public meetings on restoration plan.

E. If the restoration plan identifies grass carp as a solution to the water's problems, and there are plans to monitor the effectiveness of the introduction, the Department of Wildlife will consider approval of a grass carp introduction.

1. The Department of Wildlife will determine the planting rate based on the needs of the public and the fish and wildlife using the area.

2. Funding for purchase of grass carp under this category will be determined by the proponants of the project. Generally the Department of Wildlife will provide no funding for purchase of fish.

VIII. Lakes, ponds, or reservoirs with public access may be planted with triploid grass carp for the purpose of scientific research as authorized by the Director of Wildlife.

IX. Before planting grass carp an applicant must have:

A. followed the Washington Department of Wildlife Exotic Species Policy (POL-4001, includes SEPA),
B. obtained, in writing from the U.S. Fish and Wildlife Service, documentation that the fish to be planted are triploid grass carp,
C. obtained, in writing, that the fish to be planted are certified disease free by the commercial facility shipping them, and
D. obtained a Game Fish Planting Permit from the Washington Department of Wildlife.

X. The Washington Department of Wildlife may plant triploid grass carp into any water for the purpose of fish or wildlife enhancement.

XI. The Washington Department of Wildlife may remove grass carp from any water if fish or wildlife resources are being threatened by the presence of the fish.

BAE/M00589

Appendix E

1992 SEIS Appendices:

Copper Compounds

Copper Compounds

The information found in this appendix was consolidated from the copper compound information found in the 1992 SEIS and a Copper Compound Chemical Fact Sheet produced by Ecology, dated January 1994.

Registration Status Copper was reviewed in the 1980 Draft and Final Environmental Impact Statements on Aquatic Plant Management in Washington State. An updated and more thorough review was undertaken in the 1992 Supplemental Environmental Impact Statement in response to uncertainties regarding copper's impact on aquatic systems. It will be assessed again in 2001.

Copper compounds for aquatic use are manufactured either as copper sulfate (pentahydrate) or as a copper chelate product. Both forms contain metallic copper as the active ingredient, but in the chalate forms the copper combined with other compounds to help prevent the loss of active copper from the water. As of 1994, the following copper products are registered for use in WSDA, Registration and Records, for aquatic use in Washington State:

Product Name	% Copper	Fromulation
Copper Sulfate Products:		
Copper Sulfate Medium Crystals	25.2	crystals
Triangle Brand Copper Sulfate	25.2	crystals
Copper Sulfate Instant Bluestone	25.2	powder
Copper Sulfate Superfine Crystals	25.2	crystals
Kocide copper Sulfate Crystals	25.2	crystals
Copper Chalate Products:		
Algimycin PH-C	5.0	liquid
Aquatrine Algaecide	9.0	liquid
AV-70 and AV-70 Plus	8.0 9.0	liquid
Cutrine – Plus Algaecide/Herbicide	9.0	liquid
Slow Release Algimycin	5.0	pellets
Cutrine – Plus Algaecide/Herbicide	3.7	granular
Stocktrine II	1.25	liquid
K-Tea Algaecide	8.0	liquid

Description Copper is an element with atomic number 29 and an atomic weight of 63.546. It consists of two natural isotopes: copper-63 (69.09% of total copper) and copper-65 (30.91% of total copper). It occurs in nature as the metal and in the +1 and +2 oxidation states. The +3 oxidation state is known in solids such as Cu_2O_3, but such compounds are powerful oxidizing agents in water and are not stable. In aquatic systems, most cuprous (Cu^{+1}) compounds are oxidized readily to Cu^{+2} but further oxidation to Cu^{+3} is uncommon. Copper belongs to the main group of transition elements that have the ability to form complexes, or coordination compounds, with a number of neutral molecules or ligands. Thus, copper binds strongly to the $-NH_2$ and -SH groups of organic ligands and to a lesser degree to -OH groups.

The distribution and fate of copper and its availability to biota depend on how the copper is partitioned in the ecosystem (Harrison 1986). Released copper may be present in both soluble and particulate forms. Copper in its soluble forms may be retained as such and be diluted in the water column, or it may associate with particles. Processes that control the reactions of copper with particles include sorption, chelation, co-precipitation, and biological concentration. An important

factor controlling copper concentration in particulate materials is uptake by planktonic organisms. The kinds and amounts of dissolved organic material in the water are also important.

Humic substances make up a large percentage of the dissolved organic material in fresh water and include refractory organic molecules. These substances may scavenge copper ions and thus play a major role in its transformation. Humic substances are classified by solubility and include: 1) humic acid, which is soluble in base and insoluble in acid, and 2) fulvic acid, which is soluble in both acid and base. These molecules consist of long carbon chains or complex aromatic structures containing oxygen, nitrogen, sulphur, phosphorus functional groups and carboxylate groups. The affinity of copper for humic acid is quite high, but sorption on humic acid is dependent on Ph, metal concentration, and humic acid concentration.

Environmental factors other than dissolved organic carbon known to affect the speciation and thereby alter the availability and toxicity of copper to aquatic organisms include Ph, the presence of inorganic carbon and phosphorus, exchange reactions between suspended sediments and water, and the presence of other metals or toxicants (antagonistic, additive, and synergistic effects). Sensitivity to copper has been found to be inversely related to hardness and alkalinity. This may be due to the greater formation of copper carbonate complexes at the higher alkalinities that accompany higher hardness values (Chapman and McGrady 1977, Stiff 1971).

Copper complexes are principally formulated for aquatic plant and algae control and act as cell toxicants (Westerdahl and Getsinger 1988). A number of different formulations containing copper have been registered by EPA and by Washington Department of Agriculture for use in aquatic systems to control algae and aquatic macrophytes The active ingredient listed in these formulations is usually copper as copper sulfate pentahydrate or copper as elemental (in ethanolamine, triethanolamine, and ethylenediamine copper complexes).

Copper sulfate is probably the most widely used chemical for the control of planktonic algae, and its use as an algicide was first advocated in the United States by Moore and Kellerman (1904). However, copper sulfate has shown selectivity in its algal toxicity, which is considered by some to be due to the formation of insoluble copper complexes under certain conditions (Maloney and Palmer 1956). Generally, copper sulfate does induce reduction in primary production, but effects are short term because copper concentrations in the water column return to pretreatment levels within a few days.

Liquid formulations are applied using a hand or power sprayer or may be injected below the water surface (Westerdahl and Getsinger 1988). They are not subject to photolysis or volatilization. Once copper has been used for aquatic macrophyte control, it persists indefinitely due to its elemental nature. There are no restrictions concerning the use of treated water which may be used for domestic purposes, swimming, fishing, and irrigation immediately after treatment (Crafts 1975). EPA has established a 1 mg/l drinking water standard for copper.

Impact Analysis: Typical Use, Environmental Fate & Effects, Human Health Effects

Typical Use Several copper compounds are approved for use as aquatic herbicides, and in Washington State copper compounds are primarily used for algae control. Algae are an integral part of healthy aquatic ecosystems, and are an essential food source to fish and other aquatic animals. However, deleterious algae blooms can occur in waterbodies with excessive nutrients. Excessive algae adversely affect water quality, causing changes in water chemistry such as reduced dissolved oxygen. Certain types of algae can be harmful to human health.

Copper effectively controls algae and improves water quality in the short term. Long-term control is not normally achieved with copper treatments, therefore, repeat treatments are often required.

Environmental Impacts Potential significant adverse environmental impacts associated with the use of copper to control algae may include increased nutrients available for additional algae growth, accumulation of copper in sediments, reduced dissolved oxygen levels, and chronic and acute impacts on aquatic organisms (fish and invertebrates). The potential for impacts is dependent upon water chemistry, treatment concentration, and the number of applications to a water body over time, and as discussed in the "methods" section, mitigation measures could be designed to reduce or avoid some of these impacts.

1. Earth

Soils and Topography Use of copper compounds to control algae may result in increased water clarity. However, increased clarity often leads to increased plant growth. Greater densities of plant vegetation can reduce current speed in flowing water that may in turn increase siltation. In general, indirect impacts to soils or topography should be slight with the aquatic use of copper compounds. (See following section on Sediments.)

Sediments The ultimate sink for copper in the aquatic environment is deposition in sediments, which then form an important reservoir of copper in freshwater environments. High concentrations of copper in sediments have been reported near some industrial sources, such as discharge zones of some power stations. A long-term effect of 58 years of copper sulfate treatment of the numerous lakes in Minnesota includes copper accumulation in the sediments (Hanson and Stefan 1984).

Factors reported to affect the quantity of copper in sediments include the organic carbon content of the sediment and water, particle size distribution, Ph, and copper concentration in the water. These factors may account for the considerable variability in copper content among samples collected under different circumstances. The effect of organic matter on the binding of metal ions does not seem to be simple (Harrison 1986). Furthermore, increases in copper concentrations are correlated with decreasing particle size.

Numerous studies support the notion that retention of copper in sediment is strongly influenced by the presence of organic material (See review in Chu et al. 1978). Organic material may be bound to the surface of particulate material and from this site acts upon the metal (Murray 1973). Walter et al. (1974) determined the occurrence of copper and other trace elements in lake sediment cores and found significant enrichment for most metals, including copper, within the upper 30 cm of sediment. They speculated that the principal factors for this enrichment phenomenon were oxidation-reduction reactions resulting from decay of organic material under anaerobic conditions and induced biochemical reactions in microbes under stress. Other experiments demonstrated that heavy metals in sediments showed upward migration resulting from bacterial mechanisms. Thus, even with continual sedimentation, copper is likely to remain concentrated in the upper strata of sediments (Chu et al. 1978).

Residence time, which is defined as the length of time required for all of the element to be removed and replaced by materials of other origins, has been estimated as 5.0×10^5 years for copper (Horne 1969).

2. Air Adverse impacts to air quality are expected to be minor, such as a small amount of exhaust emissions associated with the use of application equipment. No aerial drift or overspray is expected since copper sulfate and copper complexes are not volatile.

3. Water

Surface Water Copper sulfate and the Cu Alkanolamine.$3H_2O^{++}$ and Cu Alkanolamine.$2H_2O^{++}$ (Cutrine-Plus) complexes (i.e. triethanolamine [$CuN(CH_2CH_2OH)_3.H_2O$], and ethylenediamine [$Cu(H_2NCH_2CH_2NH_2)2(H_2O)_2]^{++}SO_4^{-}$]) are highly water soluble (Westerdahl and Getsinger 1988). However, once copper has been applied for algal or plant control, it persists indefinitely due to its elemental nature. The major processes affecting the persistence of copper in aquatic systems are sediment sorption and physical export from the system (Westerdahl and Getsinger 1988). Both processes reduce the amount of copper in the aqueous phase; however sorption does not remove copper from the system. Copper has only been removed from the aqueous phase to the sediment phase and may remain in the system indefinitely.

Dissolved copper aqueous half-lives were observed in several Manitoba lakes (Wagemann and Barica 1979). For five out of six lakes, the half-lives were 1 to 2 days. The half-life in the sixth lake was 7 days. Up to pH6, dissolved free copper ion Cu^{++} is the dominant copper species, and it is the soluble copper form (not copper complexes and adsorbed species which are largely non-toxic) that is considered phytotoxic and bioavailable with most aquatic organisms (USEPA 1980, and Harrison 1985 in Westerdahl and Getsinger 1988).

Sporadic data on copper levels in the Pacific Northwest Basin show copper concentrations averaged 9 ug/l with a range of 1 to 37 ug/l. Copper concentrations ranged from 3 to 8 ug/l on the Yakima River (Richland, WA), 4 to 10 ug/l at Wawawai, WA, 10 to 19 ug/l at Ice Harbor Dam, and 1 to 28 ug/l on the Columbia river (Kopp and Kroner 1969 in Chu et al. 1978). Copper levels of 0.2 ug/l in Park Lake (Kittitas Co., WA), 0.4 ug/l in Rachel lake (Kittitas Co., WA), and 1.3 ug/l in Roosevelt Lake (Okanogan Co., WA) were observed by Burrell (1974). (See also sections on Description of Copper, Public Water Supply, and Habitat.)

A short-term effect of copper sulfate on surface water quality in some Minnesota lakes included dissolved oxygen depletion by decomposition of dead algae (Hanson and Stefan 1984). Repeated copper sulfate treatments also accelerated phosphorus recycling from the lake bed.

Ground Water No ground water contamination issue is associated with the use of copper compounds as aquatic algicides. There are no label restrictions against drinking, swimming, or fishing in waters treated with copper, but here is a 1 mg/l drinking water standard for copper.

Some copper concentrations in interstitial waters (aqueous solutions that occupy pore spaces between particles in rocks and sediments) are available for a few locations:

Copper

Interstitial Water (ug/L)	Water (ug/L)	Sediments (ug/g dry)	Location
1.0	--	30-90	Houghton Lake, MI Lake Michigan, MI
6.3-9.8	1.2-1.6	--	Beaver Bay
2.4-4.1	1.2-1.5	--	Hovland
38-71	--	--	Black Creek, SC

(From: Harrison 1986)

Trace metal concentrations are frequently higher in interstitial waters from surficial sediments than in water above the sediments. Copper concentrations in interstitial waters frequently change with sediment depth, and enrichment factors in interstitial waters are generally limited to a two- to five-fold enrichment (Harrison 1986).

Public Water Supplies Trace amounts of copper are essential to human life and health, and like all heavy metals, is also potentially toxic. Physiological mechanisms have evolved to control the absorption and excretion of copper which operate to offset the effects of temporary deficiency or excess of the metal in the diet. EPA has set 1.0 mg/l copper as a criteria for domestic water supplies.

The US Public Health Service issued a study in 1969 of 969 urban water supply systems which revealed that 11 supplies contained copper in concentrations above the drinking standard of 1.0 mg/l (US Department of Health, Education, and Welfare 1970 in Chu et al. 1978). The maximum concentration found was 8.35 mg/l. Of thirteen sources of drinking water in Washington analyzed for copper during 1984 and 1985, none contained copper above the detection limit of 0.25 ppm (Department of Social and Health Services, 1988). Copper levels in public water supplies have not been considered a significant problem. In some areas, copper is intentionally added to water supplies at a concentration of 59 ug/l in order to control algal growth (Klein et al. 1974 in Chu et al. 1978).

Almost all copper retained in the body plays a physiological role in a dozen specific copper proteins such as cytochrome c oxidase and tyrosinase. Only extremely small concentrations of free copper ions are normally found in body fluids. The toxicity of any heavy metal cation is sharply diminished when bound to proteins or other macromolecules; thus, toxicosis from dietary copper is extremely rare in humans.

Only very large amounts of orally ingested copper are toxic. For example, acidic foods or beverages which have been in contact for a long time with copper metal may cause acute gastrointestinal disturbances. When copper enters the body following inhalation, absorption from burned skin, or absorption from a contraceptive device in the uterine cavity, toxicosis may result from amounts of copper that would not cause a problem when eaten.

EPA's Office of Pesticide Programs does not have laboratory toxicological data meeting their standards, therefore, they consider available information from literature sources. They report that "Oral ingestion of copper compounds is irritating to the gastric mucosa and emesis [vomiting] occurs

promptly, thereby reducing the amount of copper available for absorption into the body....Only a small percentage of copper ingested is absorbed, and most of the absorbed copper is excreted. EPA is requiring additional human-health related data for only a few copper products.

Information provided by EPA, Office of Pesticide Programs is supplemented by a document prepared for EPA, Office of Drinking Water entitled, Review of the Drinking Water Criteria Document for Copper. The Science Advisory Board found reasonable a health-based drinking water standard of one mg/L (milligram per liter) . We feel this is germane even where recommended label rates are below 1 mg/L because scientists who reviewed the proposed standard found relevant the possibility of an increased sensitivity of 13 percent of the black population with G6PD deficiency.

The Science Advisory Board also recommended that the dietary intake of copper from food be considered if establishing a Maximum Contaminant Level Goal (MCLG), because this route comprises more that 80% of the total copper intake. We do not know if EPA, Office of Pesticide Programs, has determined the total amount of copper expected to be retained by an individual who ingests copper from various sources (both natural and artificial), or determined the potential effects of the total load. We also do not know if the two offices (Pesticide Programs and Drinking Water) coordinated their review of the potential health effects related to copper.

Hypersensitivity and sensitization are additional factors to consider when evaluating potential health effects of copper. The registration document for products containing copper sulfate notes that, "Ocular exposure to the granular material, however, can cause severe eye damage (Toxicity Category I). Hypersensitivity or sensitization can result from copper contact with the skin." For these reasons, EPA required registrants to include precautionary statements on the labels of manufacturing-use and end-use products containing copper sulfate.

Among the unknowns of copper formulations are "inert" ingredients. We do not know what inerts are used in various copper compounds and most inerts used in pesticides have not been tested to determine health and environmental effects. Inert ingredients constitute a major portion (as much as 92%) of many herbicides with copper as the active ingredient.

4. Plants and Animals

Plant Habitat Copper has been widely used as an algicide and herbicide for nuisance aquatic plants. It is known as an inhibitor of photosynthesis and plant growth; however, toxicity data on individual species are not numerous (USEPA 1980). Copper appears to affect basic physiological processes such as growth and nitrogen fixation as well as photosynthesis and can produce distinct morphological changes in algae.

Uptake of trace metals by algae is primarily a passive process, although uptake can be influenced directly by metabolism. Copper is necessary for plastocyanin synthesis and functions in photosynthetic electron transport. Copper is also involved in the enzymatic oxidation of ascorbate and polyphenolic compounds (Bidwell 1974).

The optimal concentration range for essential trace elements in aquatic environments may be very narrow. Copper inhibits photosynthesis and growth of sensitive algal species at concentrations often found in pristine waters (as low as 1-2 ug/l total Cu) (Steemann Nielsen and Wium-Andersen 1970).

The effect of pH on the toxicity of copper to algae can be important. Peterson et al. (1984) demonstrated that changes in metal toxicity with pH resulted from competition between H^+ and Cu^{+2} for cellular binding sites at the lower Ph range, but at higher pH, copper was still toxic because of the

decreased competition by H^+. H^+ affects toxicity directly by competing with free metal ions for cellular uptake sites and indirectly by determining the chemical speciation of copper (i.e., the size of the free metal pool).

The response of primary producers to copper is dependent on species, life stage, and most importantly, the chemical form of copper in the water (Harrison 1986). Recovery of the algal population was observed within 7 to 21 days of copper sulfate treatment of several lakes in Minnesota (Hanson and Stefan 1984). Copper releases can have both direct and indirect effects on food-chain organisms because algae concentrate copper to a high degree. Direct effects result when the overall productivity of an ecosystem is reduced because decreased quantities of the primary producers are available for consumption by higher food-chain organisms. Indirect effects result when algae concentrate copper to high concentrations and are consumed by higher trophic levels, resulting in sublethal or lethal effects on sensitive species.

Some cyanobacteria produce more copper-complexing extracellular material when stressed with copper than under usual growth conditions, thereby demonstrating a metabolic change that can increase their tolerance to copper. Stokes et al. (1973) found that growth inhibition occurs at very low concentrations (until concentrations reached 0.200 mg/l Cu). They found that algae from isolated, copper-polluted lakes grew better in laboratory media containing copper than did laboratory cultures of algae. However, the laboratory species of Scenedesmus and Chlorella were different from the species of these genera isolated from the lake.

Whitton (1970) sampled 20 discrete populations of algae to determine if either Cladophora glomerata or Stigeoclonium was able to adapt to streams with higher concentrations of copper. No evidence of any adaptation was found (i.e. populations from streams with different copper concentrations exhibited similar sensitivity to copper). However, Hanson and Stefan (1984) observed tolerance adjustments of certain species of algae to higher copper sulfate dosages, and a shift of phytoplankton species from green to blue-green algae following repeated copper sulfate treatments. They also observed the disappearance of macrophytes after years of weekly treatments.

Animals

Freshwater Invertebrates (Acute). In general, the sensitivity of invertebrates to acute copper exposure is highly variable (Chu et al. 1978). Acute toxicity data (48- to 96-hr LC_{50} or EC_{50}) of copper for certain phyla used as freshwater test organisms show a wide range of results. Concentrations for arthropoda (crustaceans) ranged from 5 to 3000 ug/l, for annelida ranged from 6 to 900 ug/l, and mollusca ranged from 40 to 9000 ug/l (Leland and Kuwabara 1985). Harrison (1986) reports that acute toxicity LC_{50} values for crustaceans ranged from <10 to 9000 ug/l and for mollusca ranged from 39 to 2600 ug/l.

Data on the gastropod Potamopyrgus jenkinsi and the bivalve Corbicula manilensis indicate that early life stages are more sensitive than adults. Generally, insects exhibit high tolerance to copper, although flies are among the more sensitive insect groups (Warnick and Bell 1969).

The largest amount of information available for any one group of crustaceans is on the acute toxicity of copper to daphnids. Daphnids are used as test organisms because they are a major component of freshwater zooplankton, are easily cultured, and are sensitive to contaminants. The same Daphnia species has demonstrated considerable differences in response to copper in numerous studies, perhaps due to experimental factors such as differing diet, water chemistry, species age, and loading density. Interspecific differences in four species of Daphnia in 72-hr LC_{50} values ranged from 68 to 87 ug/l copper (Spear and Pierce 1979 in Harrison 1986). D. magna individuals are capable of

developing tolerance to copper toxicity but D. magna pulex individuals are not (LeBlanc 1982 in Harrison 1986). Preexposure of D. pulex to 10 ug/l copper increased its sensitivity when exposed to 30 ug/l copper (LeBlanc 1985).

The relationship between copper speciation and toxicity is complex; it is not possible to predict toxicity to D. magna in the presence of organic complexing agents from knowledge of the free metal ion concentration alone. However, copper-amino acid complexes are less toxic than free copper ions. Borgman and Ralph (1984) showed that the free copper concentration needed to immobilize 50% of the daphnid population in 48 hr was strongly dependent on the type and concentration of complexing agents present.

Macrocrustaceans are tolerant to high concentrations of copper in water, although reductions of benthic macroinvertebrates were observed in Minnesota lakes following 58 years of copper sulfate treatment (Hanson and Stefan 1984). Copper is present in copper-containing enzymes and hemocyanin (a respiratory pigment) in crayfish, and copper is normally stored in the midgut reservoir for future use (Harrison 1986). Copper is concentrated in the viscera of crayfish transplanted to areas of high- and low-copper contamination (Stinson and Eaton 1983).

Part of the wide variability demonstrated by invertebrates to acute copper exposure may be due to behavioral or physiological adaptation to short-term stress. For example, Campeloma decisium usually closed its operculum at copper concentrations greater than 0.1 mg/l and did not move in the test tank at concentrations above 0.030 mg/l (Arthur and Leonard 1970). Adaptations such as these interfere with normal life support activities like feeding and respiration.

Freshwater Invertebrates, (Chronic/ Sublethal) Studies of the effects of chronic exposures of invertebrates to copper are limited (Chu et al. 1978). Biesinger and Christensen (1972) observed a 3-week LC_{50} of 0.044 mg/l for Daphnia magna, and a 50% loss of reproduction at 0.035 mg/l. A concentration less than 0.035 mg/l was the highest continuous concentration that did not significantly decrease survival, growth, and reproduction. Winner and Farrell (1976) exposed four species of Daphnia to copper in the laboratory using a static method, water with 100-119 mg/l alkalinity, 130-160 mg/l hardness, 8.2-9.5 mg/l oxygen. The four species of Daphnia had decreased survivorship when exposed to 0.040 mg/l copper.

Arthur and Leonard (1970) studied three species of invertebrates in a continuous-flow bioassay (44 mg/l hardness, pH 7.7, and 43 mg/l alkalinity) and found that survival of snail (Physa integra), amphipod (Gammarus pseudolimnaeus) and operculate snail (Campeloma decisum) was reduced at 0.0148 and 0.028 mg/l copper. No growth inhibition was observed at 0.008 mg/l copper or less.

A copper gradient was maintained in a chronic stream study (pH 8.0, total alkalinity 195.5 mg/l, and saturated oxygen) for 2.5 years (Winner et al. 1975). Zygopterans and members of the genera Psephenus, Baetis, Lirceus, and Stenoma disappeared from the benthic community at 0.120 mg/l copper and/or 0.066 mg/l copper. Chironomids, Stenelmis, and Chematopsyche contributed the most to total community numbers when exposed to copper. At the lowest concentration of copper (0.023 mg/l), three of four measures of community structure differed significantly from the control station.

Vertebrates (Acute). Trace metal toxicity to aquatic organisms is manifested in a wide range of effects, from slight reductions in growth rate to death. Occasional fish kills and a shift from game fish to rough fish were observed following copper sulfate treatment of lakes in Minnesota (Hanson and Stefan 1984). Large differences are seen in the sensitivity of different species of fishes to copper. Acute toxicity (48-to 96-hr LC_{50} or EC_{50}) data for copper for freshwater fish range from 10-

900 ug/l for salmonidae, 700-110,000 ug/l for centrachidae, and 20-2000 ug/l for cyprinidae (Leland and Kuwabara 1985).

It appears that the cupric ion is the chemical species that is toxic to fish, although $CuOH^+$ might also be involved (Pagenkopf et al. 1974). pH is an important factor in determining cupric ion activity and hence copper toxicity (Chapman 1977). This relationship suggests that the acute lethal level of copper for a given species of fish for a given pH corresponds to cupric ion activity rather than total copper concentrations. A number of studies have demonstrated that copper toxicity is related to concentrations of about 0.040 mg/l are reported to be toxic to salmonid eggs, fry, fingerlings, juveniles, and adults (Chu et al. 1978). As expected, fish tested in water harder than 20 mg/l were less sensitive to copper, with copper toxicity roughly inversely proportional to water hardness.

In general, cold-water species such as salmonids are more sensitive to copper than warm-water species (Chu et al. 1978). Most toxicity studies on salmonids have been performed with early life-stages ranging from eggs to juveniles while fewer studies have been performed to determine the relative sensitivity of older life stages.

Response to copper is not only dependent on species but on stage of development and sex. As fish develop, they undergo weight changes that affect their response to copper. Sac fry and early juveniles of eight freshwater fish were more sensitive than embryos to continuous exposures to copper (McKim et al. 1978). However, developing fish embryos are particularly sensitive to heavy metals during early embryogenesis (Weis and Weis 1977, Sabodash 1977). Permeability of the egg decreases and the chorion hardens during the first few hours after release, allowing the egg to become more resistant with time (Lee and Gerking 1980).

Shaw and Brown (1970) observed that rainbow trout eggs (Oncorhynchus mykiss, formerly Salmo gairdneri) could hatch following fertilization in a solution of copper (1000 mg/l), but hatching rate was significantly lower than unexposed controls. Grande (1967) demonstrated a reduction in egg hatching with copper exposure for rainbow, brown (Salmo trutta), and Atlantic salmon (Salmo salar). Brown trout were slightly more tolerant than the other two species. Copper inhibited egg development at the same concentration that was toxic to fry. However, concentrations as low as 0.02 mg/l had a sublethal effect (anorexia).

Hazel and Meith (1970) also concluded that chinook salmon (Oncorhynchus tshawytscha) eggs were more resistant to copper than fry (acute toxicity to fry was observed at 0.04 mg/l, with inhibition of growth and increased mortality at 0.02 mg/l). McKim and Benoit (1971) observed that 0.185 mg/l had no effect on hatchability of brook trout eggs (Salvelinus fontinales), but the same concentration drastically reduced survival and growth of alevin-juveniles. Thus, eggs appear to be more resistant to copper than other early stages.

Chapman (1977) tested the relative resistance of various life stages of chinook salmon and steelhead trout (O. mykiss) to a number of metals and found that steelhead were consistently more sensitive than chinook. Newly hatched alevins in both species were less resistant to copper than later juvenile stages.

In a study on effects of copper on adaptation of coho salmon (O. kisutch) from freshwater to seawater, ATPase activity, and downstream migration, Lorz and McPherson (1976) showed that yearling coho salmon exposed to ionic copper for 144 hours exhibited depressed ATPase activity and decreased survival in seawater in proportion to copper concentration (range: 0 to 0.080 mg/l). The sensitivity of juvenile fish to copper increased from November to May (of the following year) corresponding to the smolting period. Increased sensitivity to copper in May is related to onset of

parr-smolt transformation. Smolts that are exposed to copper in freshwater often cannot survive in saltwater (copper concentration of 0.020 mg/l for 144 hours). Adult salmonids appear to be just as susceptible to copper as juveniles of the same species (Chapman 1977).

In the above study, decreased Na^+ and K^+ activated ATPase activity in gill microsomes may be one of the factors leading to loss of osmoregulation and death in seawater. Exposure to sublethal concentrations of 0.005 to 0.030 mg/l for 144 hours had little effect on ATPase activity. However, chronic exposures (up to 172 days at sublethal concentrations) resulted in depressed ATPase activity. In a more recent study, gill Na^+, K^+-ATPase activity in chinook salmon parr was unaffected by 18 hours of exposure to elevated copper concentrations in natural springwater, while significant inhibition was found in smolts (Beckman and Zaugg 1988). Under the same exposure conditions, significant increases in hematocrit and plasma glucose were found in both parr and ATPase enzyme associated with chloride cells in the gill of smolts is susceptible to inhibition by copper, thus explaining the lack of enzyme inhibition found in parr.

Death in fish from copper acute toxicity may be due to the disruption of the respiratory process caused by damage to gill epithelium. Furthermore, copper may have a profound effect on hormone activity in salmonids; studies by Donaldson and Dye (1974) indicate that yearling sockeye salmon (O. nerka) exhibit a marked corticosteroid stress response when exposed to potentially lethal and sublethal concentrations of copper.

Holland et al. (1960) studied effects of copper sulfate and copper nitrate on chinook salmon, where 50 percent mortality was observed between 42 and 96 hours at concentrations of 0.178 to 0.318 mg/l. Total kills occurred in 18 hours when fish were exposed to 1.00 mg/l copper and in less than 42 hours at 0.563 mg/l. At 0.563 mg/l, pink salmon (O. gorbuscha) showed significant mortality and loss of equilibrium. The minimum and maximum critical levels for coho salmon were 0.16 mg/l and 0.38 mg/l copper, respectively.

The toxicity of copper in soft water on Atlantic salmon was tested by Sprague (1964). An incipient lethal level of 0.050 mg/l was estimated below which fish could survive indefinitely.

The 48-hour LC_{50} for rainbow trout was 0.8 mg/l copper (Herbert et al. 1965). Brown (1968) also estimated 48-hour LC_{50} values for the same species and reported a range of 0.4 to 0.5 mg/l. Trout lethality was dependent on water quality conditions such as total hardness and dissolved oxygen. In another acute toxicity study (Brown and Dalton 1970), a 48-hr LC_{50} of 0.75 mg/l copper was reported for 1-year old rainbow trout (in hard water under semistatic conditions). Lloyd (1961) found a 72-hr LC_{50} of 1.1 mg/l for rainbow trout, also with hard water (320 mg/l as $CaCO_3$). With soft water (15-20 mg/l as $CaCO_3$) the 72-hour LC_{50} for rainbow trout was 0.44 mg/l. In another study, investigators found a 96-hr LC_{50} in hard water (290-310 mg/l as $CaCO_3$) of approximately 0.9 mg/l for rainbow trout and chinook salmon (Calamari and Marchietti 1973). Differences in results among the above experiments appear primarily related to water quality variables, especially total hardness.

Intraspecific variation in copper susceptibility of bluegill (Lepomis macrochirus) was studied by Tsai and Chang (1984) who found that copper toxicity decreased from small to large fish, from young to old, and from male to female. The 96-hr LC_{50} for bluegill was 12.5 mg/l (Patrick et al. 1968), 0.20 mg/l in soft water (Tarzwell and Henderson 1960), and 1.0 mg/l in hard water (Tarzwell and Henderson 1960). The 96-hr LC_{50} was 6.5 mg/l copper for pumpkinseed (Lepomis gibbosus) (Rehwoldt et al. 1971).

Copper speciation and toxicity were investigated by Zitko et al. (1973), who found that the incipient lethal concentration of copper to Atlantic salmon increased with increasing concentrations of humic acid. Brown (1974) observed that the median survival time of rainbow trout exposed to 2000 ug/l copper more than doubled when the fish were also in the presence of 4.5 mg/l humic acid.

Various combinations of copper and hydrogen ion concentrations have been examined on toxic responses of rainbow trout. At a pH <5.4, toxicities of pH and copper were antagonistic; at a pH of 5.4, synergism between pH and copper toxicities were observed (Miller and MacKay 1980). Fish exposed to low pH secreted significantly more mucus than did fish exposed to copper; those exposed to copper did not secrete more mucus than controls (Miller and MacKay 1982).

Vertebrates (Chronic/Sublethal) Effects of chronic exposure to copper in rainbow trout have been investigated by Calamari and Marchetti (1973) who reported a 14-day LC_{50} value of 0.87 mg/l copper, slightly lower than their 96-hr LC_{50}. Chapman (1977) reported a 200-hr LC_{10} (lethal concentration for 10 percent of the population) to range from 0.007 to 0.019 mg/l copper for rainbow trout. In waters of intermediate hardness (100 mg/l as $CaCO_3$), Goettleet et al. (1971) found the maximum acceptable concentration (reflecting little or no mortality) to rainbow trout in chronic bioassays to be between 0.012 and 0.019 mg/l copper.

Spawning, growth, and long-term survival of freshwater fish species are apparently affected at total copper concentrations between 5 and 40 ug/l in waters low in organic complexing matter (Hodson et al. 1979). Lett et al. (1976) studied the effects of copper on appetite, growth, and proximate body composition of the rainbow trout. The initial effect of copper was a cessation of feeding, with a gradual return to control levels. The higher the copper concentration, the slower the return of appetite. Growth rates were depressed by copper but recovered with appetite to approach those of control fish after 40 days. Assimilation efficiency was unchanged, indicating that depressed growth represented a response to appetite suppression rather than a decreased ability to digest. Waiwood and Beamish (1978) also found growth to be suppressed by copper when appetite was normal because of a lower gross conversion efficiency of copper-exposed fish.

McKim and Benoit (1974) exposed brook trout to sublethal concentrations of copper from yearling through spawning to 3-month old juveniles over a 1.5 year period to determine a "no effect" concentration. No adverse effect on survival, growth, or reproductive capacity was detected in the second generation of fish from the parental stock which had previously been exposed to concentrations of 0.0094, 0.0061 and 0.0045 mg/l copper.

Salmonids have been observed in both laboratory and field situations to avoid copper (Chu et al. 1978); a threshold concentration of 0.0023 mg/l copper was estimated for Atlantic salmon. Furthermore, the olfactory response of rainbow trout to copper sulfate was shown to be depressed (Hara et al. 1976). Concentrations of less than half of the 96-hr lethal threshold value (about 0.024 mg/l) caused a marked increase in the number of spawning adult coho salmon migrating downstream without spawning. Lorz and McPherson (1976) also found reduction in the downstream migration of juvenile coho salmon after a long-term exposure of 0.005 mg/l copper, or short-term exposure to 0.030 mg/l copper.

Both marine and freshwater fishes respond to copper with periodic involuntary spasms which are similar to those of Wilson's disease (symptoms: spasmodic muscle contractions and quivering in mammals)(Benoit 1975, Baker 1969, Rice and Harrison 1976). Wilson's disease is characterized by an excess of unbound copper in the blood stream. Copper was not shown to have an adverse effect on the immune response of rainbow trout (Snarski 1982, Viale and Calamari 1984).

Adult bluegills accumulated copper in the liver at concentrations lethal to larvae, the most sensitive life stage of this species. In brown bullheads (Ictalurus nebulosa), gill and liver tissue concentrated copper when fish were exposed to 0.027 to 0.035 mg/l for 20 months.

Threatened and Endangered Species Treatment with copper compounds is not expected to affect submersed or emersed plant species federally listed as rare, threatened or endangered. Applications for short-term modifications to water quality standards are reviewed on a site-specific basis for rare, threatened, or endangered species listed by US Fish and Wildlife, and "proposed sensitive" plants and animals listed by Washington State National Heritage Data System.

5. Energy, Transportation, and Natural Resources.

Energy No impact anticipated.

Transportation No impact anticipated.

6. Environmental Health

Noise Adverse impacts due to noise are expected to be minor and associated with the use of applicator equipment.

Release of Toxic Materials Copper is not teratogenic or mutagenic. There are no irrigation restrictions on copper, so a spill would probably not cause significant damage to non-targeted vegetation.

7. Land and Shoreline Use

Aesthetics Use of copper would result in decreased phytoplankton concentrations, increased water clarity, and decreased populations of some species of zooplankton. However, fewer numbers of zooplankton and increased phosphorous recycling may result in subsequent rebound blooms of algae. Generally, decreased abundance of undesired algae would positively affect visual and olfactory aesthetics of the treated water body. (See Habitat section).

Recreation. There are no swimming restrictions associated with use of copper compounds. Copper treatment can temporarily increase water clarity which would improve conditions for swimming in some lakes.

Some fish may be affected at treatment concentrations. Copper treatment is not expected to affect wetlands used as fish and wildlife habitat. (See Habitat section.)

Agricultural Crops Copper has been known to be essential for certain fungi since 1927 and for the normal growth and development of green plants since 1931. The requirements of plants for copper are very low; however there are many instances of naturally occurring copper deficiency. Copper toxicosis in plants is almost never observed under natural conditions, but has occurred on mine spoils or where fungicides have been used excessively (NAS 1977).

Agricultural chemicals such as pesticides and chemical fertilizers are widely used for efficient crop production and are potential sources of copper in runoff or in sediments (Chu et al. 1978). Copper sulfate is widely used in orchards, and to control helminthiasis (worms) and infectious podermatitis

in cattle and sheep. Copper compounds are also used as fungicides, molluscicides, and in some insecticides (INCRA 1972).

Copper is generally added to the soil as a micronutrient at 2-50 lbs/acre for fruit trees, onions, leafy vegetables, forage grasses, corn, sorghum, and small grains. Dosages as high as 3 kg copper/ha (copper sulfate, copper EDTA, copper lignin sulfonate, or copper flavonoids) have been sprayed on soils to correct for copper deficiency.

8. Public Services and Utilities

Parks and Recreational Facilities Copper compounds have no swimming or fishing restrictions. Treatment with copper compounds may temporarily improve water clarity for swimming by decreasing phytoplankton densities. However, recreational areas may be closed for a few hours during treatment.

Communications Use of any aquatic herbicide requires notification of affected shoreline owners. In some cases, the applicator is required to place a newspaper notice of treatment. Otherwise, no impacts are anticipated.

Water/Stormwater Stormwater drainage facilities such as extended detention ponds are not expected to use copper compounds for the control of phytoplankton, therefore no impacts are anticipated.

Other Government Services Washington Departments of Wildlife, Fisheries, Agriculture, and/or Health may be requested to investigate or take enforcement action upon receiving complaints after treatment with copper compounds.

Additional Information The synergistic effects of copper and chemical pollutants on fish have been largely ignored with the exception of the effect of mixtures of copper and zinc. Most investigations have been restricted to laboratory studies where the effects of each metal can be evaluated. Lloyd (1961) investigated the toxicity of mixtures of copper and zinc sulfate in hard and soft water on the survival time of rainbow trout. At low concentrations, toxic effects of the mixture were additive, but at higher concentrations a synergistic effect was observed.

Bioconcentration factors (BCF) for copper (only) range from 88 for the hard-shelled clam (Mercenaria mercenaria) to 2,000 for the green alga (Chlorella vulgans) (Westerdahl and Getsinger 1988). A BCF of 290 was measured for the fathead minnow (Pimephales promelas) (USEPA 1980). Winner (1985) observed BCF values for the zooplankton Daphnia magna ranging from 1,200 to 7,100 (a value of 100 is usually regarded as a significant factor). Thus, there is a high probability that copper will bioaccumulate in aquatic organisms. Increased body burdens of metals would be of special interest to those involved with harvesting of aquatic resources for human consumption (Chu et al. 1978).

The significance of biological accumulation is probably greatest if copper is further concentrated by successive trophic levels of organisms (biomagnification). For example, the movement of copper from plant through primary herbivore, carnivore, and detrital feeders may result in further concentration. However, measurements of copper accumulation suggest that biological magnification of copper through the food chain does not occur (Krummholz and Foster 1957, Mathis and Cummings 1973, Leland and Kuwabara 1985). They noted decreasing copper concentrations among higher trophic levels and state that the classic idea of food chain enrichment, where the

highest trophic levels contain the highest toxicant concentrations, does not hold for most heavy metals.

Sprague and Ramsey (1965) tested copper and zinc mixtures on juvenile Atlantic salmon. With softwater (hardness = 14 mg/l as CaCO) the incipient level for copper was 0.032 mg/l. When concentrations of the mixture were increased, the combined effects acted 2 to 3 times more rapidly than the individual metals.

Results of investigations into the combined toxic effects of metals included findings that "the LC_{50} and EC_{50} of the mixtures were 1.8 and 1.6 toxic units [TUs - used to express expected toxicities] respectively, indicating an additive chronic toxicity of the metals with respect to individual survival as well as population growth of *Daphnia magna*" (Enserink, et.al. 1991). Metals tested both singly and in equitoxic mixtures included arsenic, cadmium, chromium, copper, mercury, lead, nickel and zinc.

3. Mitigation, Aquatic Herbicides, Copper

Copper herbicides are available in two different types of formulations: copper sulfate compounds and chelated or complexed copper compounds. The EPA label for Kocide (a copper sulfate formulation) recommends a copper concentration for treating algae ranging from 1/4 ppm (.25 ppm) to 2 ppm copper. A Cutrine-Plus (chelated copper) fact sheet states that Cutrine-Plus controls algae at 0.2 to 0.4 ppm copper.

Both copper sulfate and chelated copper compounds have been shown to be acutely and chronically toxic to invertebrates and vertebrates at the recommended application rates specified above. Additionally, copper only temporarily reduces algae populations and may alter algae composition from green to blue-green. Also, nutrients from decaying algae become available for new algae growth and repeat copper sulfate treatments have been shown to accelerate phosphorous recycling from a lake bed.

Both this technical review and the EPA registration label reveal that copper sulfate at the treatment concentration may cause significant reduction in populations of aquatic invertebrates and plants. The EPA label also states that trout and other fish species may be killed at recommended application rates. Copper is more toxic both in soft water, as determined by the content of calcium carbonate in water, and in acid (low pH) waters. According to EPA (1985), at a water hardness of 290 ppm, the LC_{50} for rainbow trout was 3.6 ppm; an LC_{50} of 0.032 ppm was noted when hardness was maintained at 40-48 ppm.

Though copper toxicity generally decreases as water hardness increases, Ecology does not have adequate information to determine the level of water hardness that would totally buffer adverse effects of copper. Generally, water in lakes in Eastern Washington is harder, providing a greater buffering effect than the softer waters of Western Washington.

Temperature has also been shown effect copper toxicity. EPA reports that "at 7 degrees centigrade copper sulfate was moderately toxic (LC_{50} = 1.5 ppm) to rainbow trout, while at 12 degrees centigrade, copper sulfate became highly toxic (LC_{50}=0.2 ppm)."

Registration labels for chelated (complexed) copper bear warnings similar to those for copper sulfate. They also provide a hardness threshold of 50 parts per million (mg/l) of calcium carbonate (i.e. the labels state that copper shall not be applied to water with a hardness less than 50 mg/l). Even with this restriction the label states that the product may be toxic to fish at treatment concentrations.

The following mitigation measures should provide some level of protection to aquatic systems.

Copper – Mitigation Measures:

1. As noted in the "impacts" section of this EIS, copper at very low concentrations has been shown to effect trout and salmon during various life stages. Even in waters of intermediate hardness (100 mg/l as $CaCO^3$) the maximum acceptable concentration reflecting little or no mortality to rainbow trout in chronic bioasssays ranged from 0.012 to 0.019 mg/l (ppm) of copper.

In general, information indicates that it is not advisable to use copper in waters where salmon or trout are present in any life stage (including eggs, fry, smolt, or adults). Permits may be denied if impacts to fisheries cannot be avoided. Permits may also restrict application of copper compounds to a period of time when fish are not present in the waterbody proposed for treatment.

Permits may also be conditioned to limit the size and/or location of the treatment area. Special precautions must be taken if it is determined that treatment is necessary in waters where sensitive species are present. The area of application should be limited so that the overall concentration in the water body (assuming total mixing) would be less than 0.012 ppm (the lowest concentration at which we know that impacts to fisheries occur). For example, at a treatment concentration of 1.0 ppm copper, less than 10% of the total volume of the water body should be treated (this would reduce the whole-lake concentration to a level below 0.012 ppm).

In some deep lakes, treatment could be staged to provide 100% coverage of surface waters. Staging would allow treatment of one/half (or some percentage less than one half) the surface area so that sensitive species could escape to the untreated portion of the lake. After waiting an appropriate length of time, other portions of the lake could be treated.

2. Water hardness measured in milligrams per liter as calcium carbonate (CaC03), must be submitted with the permit application. Per the EPA registration label, use of copper compounds will not be permitted in water with a calcium carbonate hardness less than 50 mg/l. The potential for impacts to occur at a hardness greater than 50 mg/l may be evaluated during the permit review process, and a permit may be conditioned or denied based on this evaluation.

3. The pH of water proposed for treatment must be submitted with the permit application. According to Westinger (1980) copper complexes should not be used "where pH of water or spray environment is below 6, because of copper ion formation and subsequent toxicity to fish". Copper will not be permitted for use in waters with a pH of 6 or less if waters are fish bearing or are considered environmentally significant. Of the 25 lakes surveyed through Ecology's Volunteer Lakes Program, several had a pH below 6 at some point in the year (Ecology, 1990).

The permit may also limit the allowable change in pH resulting from use of copper herbicides, and may stipulate that the pH be measured before and after treatment.

4. As noted previously, copper has been shown to be more toxic at higher water temperatures than at lower temperatures. For this reason, the permit applicant may be required to submit information about waterbody temperature and this information may be factored into the permit decisions. Use of copper products may be restricted if water temperature exceeds a certain threshold, recognizing that temperature within a waterbody may be highly variable depending on depth and season.

5. Unless removed from a system, copper may precipitate and become incorporated into the sediment regardless of the formulation used (copper sulfate or chelated copper). Upon receipt of a request to apply copper-based herbicides, Ecology will evaluate the proposal for potential sediment impacts. Based on this review, Ecology may require that sediment in the

water body proposed for treatment be tested to determine the concentration of copper in sediment. Ecology will review results of the sediment analysis to determine if addition of copper herbicides to the system would be inconsistent with Ecology's sediment anti-degradation policy.

A permit may be denied if Ecology determines that the use of copper would be inconsistent with this policy or other provisions of Chapter 173-204 WAC, or if existing copper concentrations in sediment are determined to be biologically significant. Chemical and/or biological testing before or after copper herbicides are used may also be required to establish impacts associated with this discharge.

In evaluating copper sediment levels, in lieu of adopted criteria, Ecology will consider existing criteria, studies, and ongoing research. For example, the marine sediment criteria for copper is 390 mg/kg dry weight [parts per million (ppm) dry]. Agencies in Canada and the U. S. have established freshwater-sediment copper criteria that were derived through various mechanisms and range from 16 ppm to 110 ppm.

6. In consideration of copper toxicity in aquatic environments and persistence in sediment, Ecology may elect to limit the number of times copper may be used per season and over time, e. g. only once per season and no more than three consecutive seasons. Segmented treatment that resulted in one full coverage of a waterbody would be considered "one treatment".

7. To reduce the potential for impacts to the aquatic environment, Ecology may limit treatments to lakes with an algae problem that exceeds a "severity" threshold. The severity of an algae problem can be determined, in part, by the depth of light penetration (water clarity) as measured by secchi disc readings, measurement of epilimnetic chlorophyll a, and phytoplankton abundance and composition.

8. Ecology, in cooperation with applicators and other interested parties, will evaluate whether chelated copper compounds can achieve results desired by the applicator at a lesser concentration than copper sulfate. Depending on the results of this evaluation, the permitter may choose to encourage the use of chelated copper compounds instead of copper sulfate. Further research may result in additional restrictions on the use of copper sulfate.

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Appendix E

1992 SEIS Appendices:

Fluridone Aquatic Risk Assessment

INTRODUCTION

Impact on the aquatic environment may occur from herbicide use which kills or inhibits the growth or reproduction of certain species of aquatic plants. Herbicides used for watermilfoil control also possess the potential to adversely affect other species of aquatic life, including fish and invertebrates. This appendix is a summary of aquatic ecological risk procedures and assessments used by METRO (1986) for the herbicide fluridone. Ecological risk assessment is used to provide data for management decisions despite data gaps which require assumptions to be made.

In order to quantify ecological risks of such effects, estimates are made of concentrations of herbicides that can be used while protecting most resident aquatic life. These estimates are called criteria concentrations. The criteria concentrations are then compared to estimated environmental concentrations (EEC) expected to occur in the water after application of the herbicides at recommended rates. The ecological risk assessment is accomplished by determining if the estimated environmental concentration is lower than the criterion concentration for aquatic toxicity.

A METRO study (1986) employed two assessment methodologies to seek estimates of herbicide concentrations that can be used while protecting most aquatic life from both acute (brief and severe) and chronic (long and low level) toxicity:

(1) OPP (EPA Office of Pesticide Program's aquatic ecological risk assessment methodology)(EPA 1986c), and

(2) OCS (EPA Office of Criteria and Standards, water quality criteria approach)(EPA 1985d).

The OPP aquatic ecological risk assessment methodology:

- Is used before an herbicide is registered for use, and
- Seeks to protect most important species and their uses.

The OSC water quality criteria approach:

- Is used for compliance monitoring in receiving waters after the herbicides are widely used,
- Is more rigorous than EPA's OPP approach because it requires a larger and more ecologically representative database and generates criteria for more uses of aquatic life,
- Attempts to protect 95% of aquatic species, endangered species, and those that are economically important.

EPA OPP AQUATIC ECOLOGICAL RISK ASSESSMENT

Procedure. The aquatic ecological risk assessment procedure of EPA's OPP (Office of Pesticide Programs) compares:

- o EEC (estimated environmental concentrations) to measures of acute toxicity (such as the median lethal concentration or LC50; in this case the lowest LC50 determined from the required tests (EPA 1984) is multiplied by 0.10, a safety factor that is intended to protect all the species without test data), and
- o EEC to measures of chronic toxicity (such as the no observed effect concentration, NOEC, from chronic tests).

OPP distinguishes three risk levels for acute toxicity:

(1) No risk,
(2) Risk that can be mitigated by restricted use,
(3) Unacceptable risk of impacting aquatic life;

and only two risk levels for chronic toxicity:

(1) No risk,
(2) Unacceptable risk.

The METRO report (1986) states that assessments based on the OPP approach overestimate the risk from acute toxicity and may underestimate the risk from chronic toxicity. In this case, databases for acute toxicity were much larger than those required by EPA and therefore were probably more representative of the herbicide's acute toxicity to aquatic life. However, some of the chronic tests failed to investigate reproductive success, one of the more sensitive indices, which would underestimate the NOECs (no observed effect concentration) and hence underestimate chronic toxicity.

Assessment. For ecological risk assessment, the first step compares laboratory toxicological data with the EECs. For acute toxicity evaluation, OPP multiplies the lowest LC50 from tests of its standard species (here the lowest EC50 or LC50 reported from the data set was used) by a safety factor of 0.10 to protect sensitive species that have not been tested. This value was compared to a time averaged EEC for a 4-day period, the duration most species are exposed in acute toxicity tests.

The EEC for fluridone does not exceed the acute criteria concentration, although it is just below the criterion value (Table 1).

A good chronic database was available for fluridone. The EEC for several weeks following herbicide application was compared with the criterion concentration for chronic toxicity; it did not exceed the criterion (Table 2).

EPA's OCS NATIONAL WATER QUALITY CRITERIA

Procedure. The second aquatic ecological risk assessment, based on EPA Office of Criteria and Standard's procedure for deriving national water quality criteria, specifies concentrations that cannot be exceeded in natural waters without potentially adversely impacting more than 5 percent of the species of aquatic life. The risk assessment procedure

followed but did not adhere strictly to the EPA procedure for the following reason:

o Not all of the fluridone data were reviewed as carefully as EPA recommends for meeting data quality requirements.

Consequently, the criteria developed should be considered estimates (Appendix C3).

Five criteria values were developed by application of the national water quality criteria guidelines:

(1) Final Acute Value (FAV), designed to ensure protection of 95% of the species of fish and invertebrates from acute toxicity, defined by an LC50;
(2) Final Residue Value, designed to ensure protection of both the public health and wildlife that prey on aquatic life from biomagnification of residues up the food chain;
(3) Final Chronic Value, designed to ensure protection of fish and invertebrates from chronic toxicity;
(4) Criterion Maximum Concentration, is one-half the final acute value (FAV);
(5) Criterion Continuous Concentration is an estimate of the threshold for an unacceptable effect from long term, chronic exposure, and is equal to the lowest concentration obtained for either the Final Residue Value or the Final Chronic Value.

After determining which data were suitable for calculating the criteria, a Final Acute Value (FAV) was calculated to ensure protection of 95% of the species from acute toxicity using the lowest four mean acute values (Erickson and Stephan 1985). Each mean acute value was calculated by averaging the acute toxicity values according to the taxonomic groupings of the organisms (by genera). The fit of all data on a plot of mean acute values against probabilities was examined to add insight as to whether the lowest four points were truly representative of the data set.

Acute-chronic ratios were obtained by dividing the acute toxicity value by the corresponding chronic toxicity value. The final acute-chronic ratio is the geometric mean of all the ratios. A Final Chronic Value was obtained by dividing the Final Acute Value by the geometric mean of the final acute-chronic ratio.

Assessment. The risk assessment performed using EPA's water quality criteria approach compares the estimated EECs to criteria calculated for different types of exposure which are derived under stringent guidelines in terms of acceptable data quality, the types of tests that must be run, and the types and number of species that must be tested (Stephan et al. 1985). The database for fluridone came close to fulfilling the requirements of the guidelines.

None of the criteria values are exceeded for fluridone (Table 3). Therefore, it should be possible to use this herbicide without significant risk to 95% or more of the aquatic animal species; however,

up to 5% of the aquatic species could be impacted adversely.

COMPARISON OF ASSESSMENTS

Results of the water quality-based risk assessment compare favorably with those made by EPA OPP's ecological risk assessment approach. Although the two approaches differ substantially in terms of data requirements, the rigor of the calculations, and the aquatic life uses explicitly protected, the approaches are conceptually the same.

The question of sediment toxicity to aquatic life is of concern only with herbicides that possess three properties in the following order of importance: high affinity for particulate matter, slow rate of degradation (i.e. persistence), and significant toxicity. Fluridone has a high affinity for particulates, a slow rate of degradation, and moderate toxicity.

Fluridone could potentially accumulate and persist in the sediments. However, the prediction of sediment toxicity to aquatic life is complex, primarily because only a fraction of the fluridone occurring in the seidments will be available to bottom-dwelling organisms in a form they can assimilate. Some species will only be able to take up dissolved fluridone via their skin and gills, while others may ingest sediments. Exposure concentrations will decline progressively after herbicide application due to leaching of sediment-bound fluridone into the water column and degradation of fluridone. It is suggested that trial applications in the field be conducted in order to confirm that sediment toxicity is not expected to occur, given the characteristics of herbicide application. water quality, and aquatic animals considered.

Another problem concerning risk assessment posed to aquatic life stems from use of granular formulations of the herbicides, because of significant uncertainties about estimates of exposure concentrations and hazard to bottom-dwelling organisms. Little information was available concerning the rapidity at which the herbicides leached from the granules. Granular formulations are designed to concentrate the herbicide at the bottom, in close proximity to the roots of aquatic plants. Calculations for EECs were based on the assumption that the herbicide would completely mix in the entire water column upon release from the granule. Mixing will not occur this rapidly. Data on leaching rates and more sophisticated models for EEC prediction would be needed in order to separately predict EECs for bottom and water column-dwelling organisms. At that time, risk assessments can be accomplished easily by comparing the more accurate EECs for granular formulations to the appropriate criterion concentrations already calculated in this report.

SUMMARY AND CONCLUSIONS

The risk to aquatic life from the use of fluridone was assessed using two methodologies developed by EPA: the Office of Pesticide Programs and the Office of Criteria and Standards. The OPP approach is used in the registration of herbicides, and the OCS approach is used in

deriving water quality criteria for chemicals. The estimated environmental concentration for fluridone was below those known to be acutely and chronically toxic to most organisms. However, all organisms are not protected; herbicide concentrations identified here as not causing significant adverse impacts may still adversely impact 5 percent of the aquatic species. Economically important and endangered/threatened species are expected to be protected at the forecast herbicide application rates and estimated exposure concentrations.

The risk assessments may have underestimated impacts to bottom-dwelling species from use of granular formulations because they are designed to initially create the highest herbicide concentrations on the bottom near the plant roots. The estimates assumed complete, instantaneous mixing of all granular formulations. With additional information, the degree of risk to aquatic life imposed by use of granular formulations can be determined.

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TABLE 1.

Comparison of acute toxicity criteria to the estimated environmental concentrations (EECs) based on EPA's OPP risk assessment procedure.

Compound	Lowest LC50 (ppm)	Criterion Concentration 1/10*LC50 (ppm)	4-day Geometric Mean EEC (ppm) *	Exceedance
Fluridone	1.3	0.13	0.126	No

* Geometric mean concentration averaged over the first four days following application, calculated using the initial concentrations and most representative half-lives.

TABLE 2.

Comparison of chronic toxicity criteria to the estimated environmental concentrations (EECs) based on the EPA's OPP risk assessment procedure.

Compound	Criterion Concentration Lowest NOEC (ppm)	Chronic EEC (ppm)	Exceedance
Fluridone	0.20	0.08 #*	No

Geometric mean concentration for the first 21 days following application, calculated using the initial concentrations and most representative half-lives.

* Duration is equivalent to the duration of the test of the most sensitive species subjected to chronic toxicity testing.

TABLE 3.

Risk assessment results concerning acute toxicity, chronic toxicity and biomagnification of herbicides in freshwater using EPA's OCS water quality criteria approach.

Criterion	EEC (ppm)	Criterion Concentration (ppm) 95% of species	Exceedance of 95% Criterion
Fluridone			
Final Acute Value	<0.13	0.70	No
Acute-Chronic Ratio	N/A	6.9	N/A
Final Residue Value	<0.13	350	No
Final Chronic Value	0.08	0.10	No
Criterion Max. Conc.	<0.13	0.35	No
Criterion Continuous Conc.	0.08	0.10	No

APPENDIX D1

APPENDIX D1

TABLE D1-1.

DATABASE USED FOR EVALUATING THE ACUTE TOXICITY OF FLURIDONE TO AQUATIC LIFE

Species	Compound	Toxic Concentration ppm (mg/l)	Exposure Time, Hours	Type of Test	Test Medium	Type of Response	Life Stage	Frequency of Concentration Measurements	Test Accepted[1/]	Reference
Amphipod *Gammarus pseudolimnaeus*	Fluridone[2/]	>32	96 hr	Static	FW[3/]	Mortality (LC50)	N.G.[4/]	Nominal	Yes	Hamelink et al. (1986)
Amphipod *Gammarus pseudolimnaeus*	Fluridone[2/]	>32	96 hr	Static	FW	Mortality (LC50)	N.G.[4/]	Nominal	Yes	Hamelink et al. (1986)
Fathead minnow *Pimephales promelas*	Fluridone	15.0	96 hr	Static	FW	Mortality (LC50)	N.G.[4/]	Nominal	Yes	Hamelink et al. (1986)
Channel catfish *Ictalurus punctatus*	Fluridone	14.0	96 hr	Static	FW	Mortality (LC50)	N.G.[4/]	Nominal	Yes	Hamelink et al. (1986)
Channel catfish *Ictalurus punctatus*	Fluridone	13.5	96 hr	Static	FW	Mortality (LC50)	N.G.[4/]	Nominal	Yes	Hamelink et al. (1986)
Channel catfish *Ictalurus punctatus*	Fluridone	13.2	96 hr	Static	FW	Mortality (LC50)	N.G.[4/]	Nominal	Yes	Hamelink et al. (1986)
Channel catfish *Ictalurus punctatus*	Fluridone	13.0	96 hr	Static	FW	Mortality (LC50)	N.G.[4/]	Nominal	Yes	Hamelink et al. (1986)
Bluegill *Lepomis macrochirus*	Fluridone	13.0	96 hr	Static	FW	Mortality (LC50)	N.G.[4/]	Nominal	Yes	Hamelink et al. (1986)
Bluegill *Lepomis macrochirus*	Fluridone	12.1	96 hr	Static	FW	Mortality (LC50)	N.G.[4/]	Assayed	Yes	Hamelink et al. (1986)
Bluegill *Lepomis macrochirus*	Fluridone	12.0	96 hr	Static	FW	Mortality (LC50)	N.G.[4/]	Assayed	Yes	Hamelink et al. (1986)
Rainbow trout *Salmo gairdneri*	Fluridone	11.7	96 hr	Static	FW	Mortality (LC50)	N.G.[4/]	Nominal	Yes	Hamelink et al. (1986)
Channel catfish *Ictalurus punctatus*	Fluridone	10.0	96 hr	Static	FW	Mortality (LC50)	N.G.[4/]	Nominal	Yes	Hamelink et al. (1986)
Channel catfish *Ictalurus punctatus*	Fluridone	10.0	96 hr	Static	FW	Mortality (LC50)	N.G.[4/]	Nominal	Yes	Hamelink et al. (1986)
Channel catfish *Ictalurus punctatus*	Fluridone	10.0	96 hr	Static	FW	Mortality (LC50)	N.G.[4/]	Nominal	Yes	Hamelink et al. (1986)

TABLE D1-1(Continued)

DATABASE USED FOR EVALUATING THE ACUTE TOXICITY OF FLURIDONE TO AQUATIC LIFE

Species	Compound	Toxic Concentration ppm (mg/l)	Exposure Time, Hours	Type of Test	Test Medium	Type of Response	Life Stage	Frequency of Concentration Measurements	Test Accepted[1/]	Reference
Rainbow trout Salmo gairdneri	Fluridone	8.0	96 hr	Static	FW	Mortality (LC50)	N.G.[2/]	Nominal	Yes	Hamelink et al. (1986)
Channel catfish Ictalurus punctatus	Fluridone	8.2	96 hr	Static	FW	Mortality (LC50)	N.G.[2/]	Nominal	Yes	Hamelink et al. (1986)
Rainbow trout Salmo gairdneri	Fluridone	8.1	96 hr	Static	FW	Mortality (LC50)	N.G.[2/]	Assayed	Yes	Hamelink et al. (1986)
Rainbow trout Salmo gairdneri	Fluridone	7.7	96 hr	Static	FW	Mortality (LC50)	N.G.[2/]	Nominal	Yes	Hamelink et al. (1986)
Rainbow trout Salmo gairdneri	Fluridone	7.6	96 hr	Static	FW	Mortality (LC50)	N.G.[2/]	Nominal	Yes	Hamelink et al. (1986)
Rainbow trout Salmo gairdneri	Fluridone	7.6	96 hr	Static	FW	Mortality (LC50)	N.G.[2/]	Nominal	Yes	Hamelink et al. (1986)
Rainbow trout Salmo gairdneri	Fluridone	7.6	96 hr	Static	FW	Mortality (LC50)	N.G.[2/]	Nominal	Yes	Hamelink et al. (1986)
Rainbow trout Salmo gairdneri	Fluridone	7.1	96 hr	Static	FW	Mortality (LC50)	N.G.[2/]	Nominal	Yes	Hamelink et al. (1986)
Daphnia magna	Fluridone	6.3	48 hr	Static	FW	Mortality (LC50)	N.G.[2/]	Nominal	Yes	Hamelink et al. (1986)
Rainbow trout Salmo gairdneri	Fluridone	5.7	96 hr	Static	FW	Mortality (LC50)	N.G.[2/]	Nominal	Yes	Hamelink et al. (1986)
Rainbow trout Salmo gairdneri	Fluridone	5.6	96 hr	Static	FW	Mortality (LC50)	N.G.[2/]	Nominal	Yes	Hamelink et al. (1986)
Rainbow trout Salmo gairdneri	Fluridone	4.5	96 hr	Static	FW	Mortality (LC50)	N.G.[2/]	Nominal	Yes	Hamelink et al. (1986)
Daphnia magna	Fluridone	4.4	48 hr	Static	FW	Mortality (LC50)	N.G.[2/]	Nominal	Yes	Hamelink et al. (1986)
Rainbow trout Salmo gairdneri	Fluridone	4.2	96 hr	Static	FW	Mortality (LC50)	N.G.[2/]	Nominal	Yes	Hamelink et al. (1986)

TABLE D1-1 (Continued)

DATABASE USED FOR EVALUATING THE ACUTE TOXICITY OF FLURIDONE TO AQUATIC LIFE

Species	Compound	Toxic Concentration ppm (mg/l)	Exposure Time, Hours	Type of Test	Test Medium	Type of Response	Life Stage	Frequency of Concentration Measurements	Test Accepted[1/]	Reference
Amphipod *Gammarus pseudolimnaeus*	Fluridone	4.1	96 hr	Static	FW	Mortality (LC50)	N.G.[4/]	Nominal	Yes	Hamelink et al. (1986)
Daphnia magna	Fluridone	3.9	48 hr	Static	FW	Mortality (LC50)	N.G.[4/]	Nominal	Yes	Hamelink et al. (1986)
Daphnia magna	Fluridone	3.9	48 hr	Static	FW	Mortality (LC50)	N.G.[4/]	Nominal	Yes	Hamelink et al. (1986)
Daphnia magna	Fluridone	3.6	48 hr	Static	FW	Mortality (LC50)	N.G.[4/]	Nominal	Yes	Hamelink et al. (1986)
Amphipod *Gammarus pseudolimnaeus*	Fluridone	2.1	96 hr	Static	FW	Mortality (LC50)	N.G.[4/]	Nominal	Yes	Hamelink et al. (1986)
Midge *Chironomus plumosus*	Fluridone	1.3	48 hr	Static	FW	Mortality (LC50)	N.G.[4/]	Nominal	Yes	Hamelink et al. (1986)
Midge *Chironomus plumosus*	Fluridone	1.3	48 hr	Static	FW	Mortality (LC50)	N.G.[4/]	Nominal	Yes	Hamelink et al. (1986)
Midge *Chironomus plumosus*	Fluridone	1.3	48 nr	Static	FW	Mortality (LC50)	N.G.[4/]	Nominal	Yes	Hamelink et al. (1986)
Midge *Chironomus plumosus*	Fluridone	1.3	48 hr	Static	FW	Mortality (LC50)	N.G.[4/]	Nominal	Yes	Hamelink et al. (1986)

1/ Refers to whether there were data of sufficient quality to meet the requirements of the EPA guidelines for criteria derivation (Stephan et al. 1985).

2/ Fluridone formulation used was a field formulation containing 48 percent active ingredient of fluridone. This is the only species in which the toxicity of the field formulation was significantly different than the technical grade, and hence mentioned here.

3/ FW = Freshwater.

4/ Life stage of the animal was not given (N.G.) in reference.

TABLE L.-2.

DATABASE USED FOR EVALUATING THE CHRONIC TOXICITY OF FLURIDONE TO AQUATIC LIFE

Species	Compound	Toxic Concentration ppm (mg/l)	Exposure Time, Hours	Type of Test	Test Medium	Type of Response	Life Stage	Frequency of Concentration Measurements	Test Accepted[1]	Reference
Amphipod *Gammarus pseudolimnaeus*	Fluridone	1.2	60 days	Flow-through	FW[2]	Development and survival	Lifecycle	Weekly	Yes	Hamelink et al. (1986)
Midge *Chironomus plumosus*	Fluridone	1.2	30 days	Flow-through	FW	Emergence	Larvae to Adult	Weekly	Yes	Hamelink et al. (1986)
Channel catfish *Ictalurus punctatus*	Fluridone	1.0	60 days	Flow-through	FW	Development and survival	Fry to Adult	Weekly	Yes	Hamelink et al. (1986)
Fathead minnow *Pimephales promelas*	Fluridone	0.98	90 days	Flow-through	FW	Survival	Lifecycle	Weekly	Yes	Hamelink et al. (1986)
Daphnia magna	Fluridone	0.2	21 days	Flow-through	FW	Survival and Reproduction	Lifecycle	Weekly	Yes	Hamelink et al. (1986)

1/ Refers to whether there were data of sufficient quality to meet the requirements of the EPA guidelines for criteria derivation (Stephan et al. 1985).

2/ FW = Freshwater.

APPENDIX D2

APPENDIX D2
Summary of Toxicity Data

Available toxicity data are summarized along with the results of data analyses. Fluridone's acute toxicity to aquatic life lies in the range of 1.3 to greater than 32 ppm. When the acute toxicity values were averaged according to the taxonomic grouping of the organism (to genera), the mean acute values ranged roughly along a straight line from 1.3 to 22 ppm (Fig. D2-1).

Fluridone's chronic toxicity ranged from 0.2 to 1.2 ppm. Most of the chronic toxicity tests encompassed reproductive stages and were tied to acute toxicity tests, which permitted estimates of the acute-chronic ratios. Although the geometric mean acute-chronic ratio was 6.9, individual ratios were so variable that the 95 percent confidence limits for fluridone's acute-chronic ratio ranged from 0.2-307. Because of this variability, there is a greater chance that aquatic life are being either under or overprotected from chronic toxicity (Table D2-1).

Table D2-1. Acute-Chronic Rations for Fluridone-

Species	Acute Value ppm	Chronic Value ppm	Acute-Chronic Ratio
Fathead minnow	22	0.96	22.9
Daphnia magna	4.3	0.2	21.5
Channel catfish	11.7	1.0	11.7
Gammarus pseudolimnaeus	2.9	1.2	2.4
Midge	1.3	1.2	1.1
	Geometric Mean Acute-Chronic Ratio = 6.9		
	95 Percent Confidence Limits = 0.20 - 307		

APPENDIX D3

APPENDIX

Limits Concerning EPA's OCS Water Quality Criteria Risk Assessment

The rationale concerning what percentage of the species to protect is discussed by Stephan (1985), who indicates that EPA believed that protecting 99% of the species produced a criterion that was too stringent, and that protecting 90% of the species produced a criterion that was too lenient. The compromise was protecting 95% of the species. Statistically there is substantially more uncertainty in a criterion protecting 99% of the species than in one protecting 95%. It is very difficult to detect significant impacts to 25% or even 10% of the species; thus detecting impacts to a lesser proportion of the species is even more difficult. The program of Erickson and Stephan (1985) was modified to determine the criteria protecting, theoretically, 90%, 80%, and 70% of the species in balanced populations. This modification was made in order to determine whether exceedance of a criterion protecting 95% of the species would have the potential for impacting a much larger percentage of the species in a population. It may also be of interest to determine whether decisions regarding the use of herbicides would change if it was considered acceptable to reduce the percentage of aquatic organisms to be protected. The concentration protecting 99% of the organisms was not estimated because (1) this appeared to constitute an unprecedented level of protection with respect to the EPA water quality criteria, and (2) would be highly uncertain in the statistical sense because of the relatively small sizes of the toxicity databases.

Stephan et al. (1985) provide several options for evaluating the available data depending upon its characteristics. For example, they state: "depending on the data that are available concerning chronic toxicity to aquatic animals, the Final Chronic Value might be calculated in the same manner as the Final Acute Value or by dividing the Final Acute Value by the Final Acute-Chronic Ratio. In some cases it may not be possible to calculate a Final Acute-Chronic Value." This allowance provides some flexibility for developing a criterion in response to the available data's character.

When the available data were evaluated for acceptability for this assessment according to criteria in the Guidelines and ASTM (1985a), many studies could not be used for estimating water quality criteria. Some of the

reasons for rejecting toxicity data, as well as exceptions made to data requirements, were as follows:

- o A number of the studies were conducted with species not indigenous to the United States.
- o Acute tests that were not of 96 hr duration were not used, except for (1) daphnids and other cladocerans (for which 48 hr tests were used) or (2) tests with embryos or larvae (for which tests ranging from 48 to 96 hr are appropriate).
- o For acute tests with older life stages, the 96-hr EC50 was used if available. If the EC50 was unavailable, then the 96-hr LC50 was used.

TABLE 3

BIOCONCENTRATION FACTORS FOR AQUATIC LIFE EXPOSED TO FLURIDONE

Species	Bioconcentration[a] Factor
	FLURIDONE
Brown bullhead *Ictalurus nebulosus*	2.46
Rainbow Trout *Salmo gairdneri*	2.30
Chub Sucker *Erimyzon sucetta*	1.92
Black bullhead *Ictalurus melas*	1.76
Green Sunfish *Lepomis cyanellus*	1.61
Warmouth Sunfish *Chaenobryttus gulosus*	1.42
Largemouth bass *Micropterus salmoides*	1.23
Tilapia *Tilapia sp.*	0.96
Bluegill *Lepomis macrochirus*	0.94

[a]References: Fluridone, West et al. (1983)

TABLE 4

COMPARISON OF INITIAL HERBICIDE CONCENTRATIONS WITH MAXIMUM ACCEPTABLE CONCENTRATIONS FOR FISH INGESTION EXPOSURE 1/

Chemical	Exposure Period	Initial Concentration (ppm)	BCF 2/	Fish Ingestion Exposure MAC (ppm)	Exceedance
Fluridone-liquid	chronic	0.14	2.46	350	No
Fluridone-pellets	chronic	0.07	2.46	350	No

1/ MAC in water based AD calculated by METRO (1986) for chronic exposure.

2/ Bioconcentration factor = BCF.

APPENDIX A1
SUMMARY OF TOXICITY DATA

Potential human health effects of fluridone are briefly described below and results of mammalian toxicity studies reviewed by METRO (1986) are summarized in Appendix A2. Much of this information was obtained via Freedom of Information Office requests. The objective of the toxicity evaluation performed during the METRO study was to calculate an acceptable dose (AD) (defined as an average lifetime intake rate that is unlikely to cause adverse effects on human health) and identify the resulting potential for adverse effects. Emphasis in identification of potential adverse effects was placed upon regulatory guidance available for fluridone. AD values determined by METRO (1986) for fluridone are summarized in Table A1 while the basis for METRO's AD determinations is detailed below.

At extremely high doses, fluridone has been shown to affect growth and survival rates, organ weights and function, and blood chemistry. In general, fluridone exhibits low toxicity, as evidenced by the high concentrations required to induce an effect. Studies performed to date have found no evidence of carcinogenicity, teratogenicity, or mutagenicity for this herbicide.

Health risk assessment information for fluridone has been compiled in EPA's Integrated Risk Information System (IRIS) (EPA 1986a). The Risk Reference Dose (RfD) for oral exposure recommended by EPA is 0.08 mg/kg/day. This value is based upon a NOEL level for glomerulonephritis (kidney effects) of 8 mg/kg/day in studies in rats and an uncertainty factor of 100. The EPA RfD was used in this study as the AD with which to evaluate the potential for harm to human health. In 1988, EPA's RfD work group completed a reevaluation of fluridone data (EPA 1988) in which the oral RfD remained the same and was given a high confidence rating. No data gaps were noted. An assessment of the carcinogenic potential of fluridone was recently completed by EPA's cancer risk assessment work group (R. Engler, 1988) which concluded that fluridone is not carcinogenic. They classified the weight of evidence as "E"; i.e. no evidence for carcinogenicity in at least two adequate animal tests.

EPA (1986a) reports that the critical study design upon which the RfD is based exceeded minimal requirements and that the NOEL for both kidney and liver effects was supported by other reviewed Confidential Business Information (CBI). The CBI information reviewed by EPA was also reviewed during this evaluation; a summary of available data is included as Appendix A2.

Again, data were not available to estimate a short-term AD. The chronic AD value represents a very conservative approach for evaluating potential risks resulting from occasional fluridone application.

TABLE A-1

ACCEPTABLE DOSE (AD) VALUES FOR FLURIDONE

	Exposure Period	AD (mg/kg/day)	AD for 70 kg Adult (mg/day)	AD for 10 kg Child (mg/day)
Fluridone	Chronic	0.08	5.6	0.8

APPENDIX A2
SUMMARY OF FLURIDONE MAMMALIAN TOXICITY DATA REVIEW

Author	Species	Sex and No. per Dose Group	Chemical	Dose	Exposure Time	Type of Test	Route of Administration	Type of Response	Comments
Ringer et al. 1981	Bobwhite Quail *Colinus virginius*	M,F (50:500)	11237] EL 111	range = 0.00-0.1% in diet	24 weeks	Chronic (1 generation)	Oral	NOEL	No observed effect
	Mallard Duck *Anas platyrhynchos*	sex unknown (28) M,F (2:5)	11237] EL 121	0.1 % in diet	27 weeks	Chronic	Oral	NOEL	No observed effect
Meyerhoff and Brannon 1982	Rats			8.5 mg/kg/day	2 years	Chronic	Oral	NOEL	No observed effect
	Bobwhite Quail			2,000 mg/kg	14 days	Acute	Oral	No mortalities	
	Mallard, Bobwhite			5,000 ppm	8 days	Subacute	Oral (dietary)	No mortalities	
	Mallard, Bobwhite			1,000 ppm	24, 27 weeks	Chronic	Oral	NOEL	24 wks - Bobwhite 27 wks - Mallards
Ferson et al. 1981a	Rabbits (White New Zealand)	M,F (5:5)	11237]	2 ml/kg Equivalent dose in mg/kg: 768(80% formulation), 384(40%), 192(20%	3 weeks (5 days/ week)	Subchronic	Dermal	See Comments	Fluridone 4AS (80% in water): caused moderate-severe erythema, epidermal fissures, edema, slight desquamation. Fluridone 4AS (40%): caused well defined erythema, slight edema and desquamation. Fluridone 4AS (20%) caused transient erythema. Fluridone (80%, no water) caused a slight decrease in kidney weights for males. No other systemic toxicity was apparent
Ferson et al. 1981b	Guinea Pig (Albino Hartley Strain)	F (10) (Induction or Challenge) 5/group for Challenge Controls	Fluridone (Aqueous Suspension, AS)	See comments (Dose group A)	24 days		Dermal		Induction: dosed 3x/wk for 2 wks) Challenge: Dosing Commenced 10 days post final induction. (continued next page)

APPENDIX A2(Continued)
SUMMARY OF FLURIDONE MAMMALIAN TOXICITY DATA REVIEW

Author	Species	Sex and No. per Dose Group	Chemical	Dose	Exposure Time	Type of Test	Route of Administration	Type of Response	Comments
Pierson et al. 1981b (continued)									Group A: Dinitrochlorobenzene (DNCB): 0.2 ml of 0.1% DNCB in 70% ethanol for induction and challenge groups
	Guinea Pig (Albino Hartley Strain)	F (10) Induction or Challenge 5/group for Challenge Controls	Fluridone (Aqueous suspension, AS)	See Comments (Dose Group B)	72 hrs		Dermal	See Comments	Group B DNCB challenge control: 0.2 ml of 0.1% ethanol. No response evident (i.e., sensitization or irritation.
				See Comments (Dose Group C)	24 days		Dermal		Group C fluridone 4AS induction and challenge: 0.2 ml undiluted. No response evident.
				See Comments (Dose Group D)	72 hrs		Dermal		Group D fluridone 4AS challenge control; 0.2 ml undiluted. No response evident.
Adams 1980a	Rabbit (Dutch Belted)	F (5)	EL-171 (112371)	0 mg/kg/day 250 mg/kg/day 500 mg/kg/day 750 mg/kg/day 1000 mg/kg/day	Gestation days (6-18) Gestation days (6-18) Gestation days (6-18) Gestation days (6-18) Gestation days (6-18)		Oral (gavage)		No observed effect at 0, 250 mg/kg/day doses Increased incidence of abortion at 500, 750, 1000 mg/kg (500: 1/4; 750: 1/5; 1000: 3/5). At the 3 highest doses there was a dose-related reduction of food consumption. Weight gain was depressed at 750 and 1000 mg/kg/day.

APPENDIX A2 (Continued)
SUMMARY OF FLURIDONE MAMMALIAN TOXICITY DATA REVIEW

Author	Species	Sex and No. per Dose Group	Chemical	Dose	Exposure Time	Type of Test	Route of Administration	Type of Response	Comments
Adams 1980b	Rabbit (Dutch Belted)	F (15)	112371	0 mg/kg/day 125 mg/kg/day 300 mg/kg/day 750 mg/kg/day	Gestation days (6-18) Gestation days (6-18) Gestation days (6-18) Gestation days (6-18)		Oral (gavage)	See Comments	No effect at 0, and 125 mg/kg/day doses. Abortions, death and increased absorptions at 300, 750 mg/kg/day though no evidence of teratogenic effects. Dose-related reduction of food consumption at 300 and 750 mg/kg/day.
Adams 1980c.	Rat (Fisher 344)	F (25)	112371	0 mg/kg/day 20 mg/kg/day 65 mg/kg/day 200 mg/kg/day	Gestation days 6-15	Subacute	Oral (gavage)	See comments	No effect on reproduction. No evident teratogenic effects. No maternal toxicity.
Adams 1980d	Rat (Fisher 344)	M,F (25:25)	112371	Average % in diet: 0%, 0.02%, 0.065%, 0.2%. Equivalent average doses in mg/kg/day: Male: 0, 11, 36, 112 Female: 0, 13, 42, 130	3 generations.	Chronic	Oral (Diet)	See comments	No apparent treatment related effects except a slight reduction in mean pregnancy weight at day 21 postpartum at the 0.2% dose.
Probst 1981a	Mouse (Strain ICR)	M,F (15:15)	EL-171	0.003%, 0.03%, 0.01% in diet. Equivalent dose (mg/kg/day): Male: 3.2, 10.8, 30.9 Female: 3.6, 12.0, 34.1	1 year	Chronic	Oral (diet)	See comments	Increased in vitro activity of liver microsomal p-nitroanisole-o-demthylase. Relative liver weight increases for females at the 0.03% dose. Otherwise no effects on growth survival, physical signs, hematology, clinical chemistry, or pathology.

APPENDIX A2 (Continued)
SUMMARY OF FLURIDONE MAMMALIAN TOXICITY DATA REVIEW

Author	Species	Sex and No. per Dose Group	Chemical	Dose	Exposure Time	Type of Test	Route of Administration	Type of Response	Comments
Probst 1981b	Beagle Dogs	M,F (4:4)	EL-171	75 mg/kg/day 150 mg/kg/day 400 mg/kg/day	1 year	Chronic	Oral (Capsule)	See comments	At 400 mg/kg/day: Dogs showed a slight decrease in body weight near end of study. Females: Elevated alkaline phosphatase from 5th week on and increased absolute liver weights. Otherwise no treatment effects related to hematology, urinalysis, liver enzyme induction, opthamology, or pathology.
Probst 1981c.	Mouse (ICR Strain)	M,F, (40:40)	EL 171	0.0033, 0.01, 0.033% in the diet. Equivalent dose in mg/kg/day: Males: 3.5, 10.9, 30.7. Females: 4.0, 12.3, 34.5	2 year	Chronic	Oral	See Comments	Males at 0.033% exhibited increased in vitro activity of liver microsomal p-nitrosnisole O-demethylase. Otherwise, no tumors or effects on survival, growth, hematology, clinical chemistry, organ weights, or pathology
Probst 1980a	Rat (Fischer 344)	M,F (3:3)	EL-171	0.02, 0.065, 0.2% in diet. Equivalent dose (mg/kg/day): Male: 7.7, 25.2, 80.8 Female: 9.2, 30.1, 97.0	2 years	Chronic	Oral (diet)	See comments	At 0.2% (male and female): decreased survival, growth, and food consumption. Increased absolute weights for liver, kidneys. Increased incidence of renal tubular degeneration. Elevated blood urea nitrogen (BUN) and creatinine levels. (continued next page)

APPENDIX A2(Continued)
SUMMARY OF FLURIDONE MAMMALIAN TOXICITY DATA REVIEW

Author	Species	Sex and No. per Dose Group	Chemical	Dose	Exposure Time	Type of Test	Route of Administration	Type of Response	Comments
Probst 1980a (continued)									At 0.2% (females): Decreased erythrocyte count, hemoglobin and hematocrit. Dose related increase in the incidence and severity of progressive glomerulonephritis (kidney inflamation). Decrease in incidence of benign tumors.
Probst 1980b	Rat (Fisher 344)	M,F (15:15)	112371	Average % in the diet: 0, 0.02, 0.065, 0.20. Equivalent dose in mg/kg/day: 0, 9.4, 30.9, 95.9	1 year	Chronic	Oral	See comments	At 0.06% and 0.02% in diet (females): Initial growth retardation observed. Elevated in vitro microsomal p-nitroanisole O-demethylase activity. Elevated bilirubin levels. Initial growth enhancement also observed for some females at this dose. Decreased food consumption and decreased efficiency of food utilization. Decreased weight of adrenal; elevated liver, kidney, spleen and brain weights. At 0.2% in the diet (male and female): Decreased erythocyte count. Progressive glomerulonephritis. At 50.2% in the diet (male and female): Increased BUN levels. (continued next page)

APPENDIXA2 (Continued)
SUMMARY OF FLURIDONE MAMMALIAN TOXICITY DATA REVIEW

Author	Species	Sex and No. per Dose Group	Chemical	Dose	Exposure Time	Type of Test	Route of Administration	Type of Response	Comments
Probst 1980b (continued)									At 0.2% in the diet (males): Increased liver and kidney weights (absolute). Relative weights of liver, kidney, spleen and thyroid observed.
Hill 1981	Primary cultures from an adult male rat (Fischer 344)	-----	125670	500 moles/ml 1,000 moles/ml	20 hours	Acute	In vitro assay	Cytotoxicity	No induction of UNA repair synthesis by 1-meth/l-3-(4-hydroxyphenyl)-5-[3-(trifluoromethyl) phenyl]-6-(1H)-pyridinone (possibly a fluridone degradation product.)
Ansley & Levitt 1981	Rat (Fischer 344)	M,F (5:5)	112371, EL-171 Sonar 5p	500 mg/kg (Mixture)	Single dose with 7-day observation.	Acute	Oral (gavage)		No mortality or signs of toxicity. Normal mean body weights.
	Rabbit (New Zealand White)	M,F (3:3)	112371 EL-171 Sonar 5p	2000 mg/kg (Mixture)	Single application with 7-day observation.	Acute	Dermal	See comments	No mortality or signs of toxicity. No dermal irritation.
	Rabbit (New Zealand White)	M,F (3:3)	112371 EL-171 Sonar 5p	2000 mg/kg (Mixture)	Single application with 7-day observation.	Acute	Ocular	See comments	Corneal dullness, slight iritis, at 1 hour post treatment in 2 animals (cleared within 24 hrs). Slight conjunctivitis in all eyes (cleared in 3-7 days). One male lost weight; all others gained weight.

APPENDIXA2 (Continued)
SUMMARY OF FLURIDONE MAMMALIAN TOXICITY DATA REVIEW

Author	Species	Sex and No. per Dose Group	Chemical	Dose	Exposure Time	Type of Test	Route of Administration	Type of Response	Comments
Probst et al. 1978a	House (ICR/SPF Strain)	M,F (15:15)	EL-171 112371	0.033, 0.056, 0.10, 0.14, 0.20% in diet. Equivalent dose (mg/kg/day): 49.5, 84, 150, 210, 300.	92-94 (days)	Subchronic	Oral (diet)	See comments	At top 3 dose levels (males and females): Increased liver weights. Females: Slight increase in leukocyte count and an increase in relative weight. Increase in hepatic microsomal activity (p-nitroanisole o-demethylase). At top 2 dose levels (males): Increased hepatic microsomal activity (see above). At all doses (male): Increase in relative weights. Dose-related increase in hepatic hypertrophy. Otherwise, no effect on survival or weight gain.
	House (ICR/SPF Strain)	M,F (15:15)	EL-171 112371	0.0062, 0.011, 0.02, 0.033, 0.056% in diet. Equivalent dose (mg/kg/day): 9.3, 16.5, 30, 49.5, 84.	91-93 (days)	Subchronic	Oral (diet)	See comments	Doses above 9.3 mg/kg/day resulted in dose dependent hepatic hypertrophy. Otherwise, no effects on liver weights, survival or weight gain.
robst et al. 1978b	Beagle dog	M,F (1:1)	EL-171	100, 200 mg/kg/day	2 weeks	Subacute	Oral	See comments	Females at both doses showed slight anorexia. At 200 mg/kg/day: Emesis, and slight reduction in body weight. No effects on survival.

APPENDIX A2 (Continued)
SUMMARY OF FLURIDONE MAMMALIAN TOXICITY DATA REVIEW

Author	Species	Sex and No. per Dose Group	Chemical	Dose	Exposure Time	Type of Test	Route of Administration	Type of Response	Comments
Probst et al. 1978b (continued)	Beagle dog	M,F (1:1)	112371	100 mg/kg/day 200 mg/kg/day	2 weeks	Subacute	Oral (capsule)	See comments	Slight anorexia of females at both doses. Emesis and slight reduction in body weight in both sexes at 200 mg/kg/day.
Probst et al. 1978c	Beagle dog	M,F (4:4)	112371	50 mg/kg/day 100 mg/kg/day 200 mg/kg/day	91 days	Subchronic	Oral (capsules)	See comments	For male and female at 200 mg/kg/day: lowered erythrocyte count, hemoglobin and hematocrit; BUN and alkaline phosphatase slightly elevated. For females at 100 mg/kg/day, relative liver weights increased.
Ansley & Arthur 1980	Rat (Wistar)	M,F (5:5)	Sonar 5p	500 mg/kg (pellet form)	2-week observation.	Acute	Oral (gavage)	See comments	No mortality or signs of toxicity.
	Rabbit (New Zealand Albino)	M,F (3:3)	Sonar 5p	3 g/kg	2-week observation.	Acute	Dermal	See Comments	No mortality, signs of toxicity or dermal irritation.
	Rabbit (New Zealand Albino)	M,F (3:3)	Sonar 5p	138 mg/kg	1-week observation.	Acute	Ocular	See comments	Slight conjunctival redness 1 hr. post-treatment (cleared within 24-72 hours).
Arthur et al. 1978a	Rabbits (Albino)	M,F (3:3)	112371 (wettable powder)	2 g/kg	Single application, with 14 days observation.	Acute	Dermal	See comments	No toxicity or dermal irritation.
Arthur et al. 1978b	Rats (Harlan Wister)	M,F (5:5)	112371 (wettable powder)	2.45 mg/l (air)	1 hour with 14 day observation.	Acute	Inhale	See comments	No signs of toxicity.

APPENDIX A2 (Cont'd)
SUMMARY OF FLURIDONE MAMMALIAN TOXICITY DATA REVIEW

Author	Species	Sex and No. per Dose Group	Chemical	Dose	Exposure Time	Type of Test	Route of Administration	Type of Response	Comments
Thur et al. 1978c	Rats (Wister)	M,F (5:5)	112371 (Aqueous Suspension)	0.5 ml/kg	Single dose with 14 day observation.	Acute	Oral (gavage)	See comments	Ptosis and hyperactivity observed within 3 hours (disappeared within 24 hours).
Thur et al. 1978d	Rabbits (New Zealand Albino)	M,F (3:3)	112371 (Aqueous Suspension)	0.1 ml	Single dose with 7 day observation.	Acute	Ocular	See comments	All animals developed slight conjunctival hyperemia within 1 hour. Three had slight chemosis. Symptoms disappeared within 24-48 hours.
Thur et al. 1978e	Rabbits (Albino)	M,F (3:3)	112371 (Aqueous Suspension)	2 ml/kg	1 application with 14 day observation.	Acute	Dermal	See comments	Mild erythema & edema at treatment sights (all animals). Symptoms disappeared by day 6.
Thur et al. 1978f	Rats (Wister)	M,F (5:5)	112371 (Aqueous Suspension)	9.6ml/L air	1 hour exposure with 14 day observation.	Acute	Inhale	See comments	Slight chromorhinorrhea and chromodacryorrhea (symptoms disappeared within 1 hour).
Thur et al. 1978g	Wistar-derived rats (fasted over night)	(F) (10)	112371	2,000 mg/kg 3,000 mg/kg 4,500 mg/kg 7,000 mg/kg 10,000 mg/kg	Single exposure with 14 days observation.	Acute	Oral (gavage)	See comments	Animals fasted pre-treatment. At 1-6 hours post treatment: diursis, leg weakness, hyperactivity, loss of righting reflex, ptosis and dyspnea. Most rats recovered 24 hours post-treatment. No deaths. Weight gain was normal.
Thur et al. 1978h	Rabbits (New Zealand Albino)	M,F (1:3)	112371	27 mg	Single application with 7 day observation.	Acute	Occular	See comments	Slight conjunctivitis within 1 hour. Recovery within 72 hours.

APPENDIXA2 (Continued)
SUMMARY OF FLURIDONE MAMMALIAN TOXICITY DATA REVIEW

Author	Species	Sex and No. per Dose Group	Chemical	Dose	Exposure Time	Type of Test	Route of Administration	Type of Response	Comments
Kehr et al. 1978a	Bobwhite quail	M,F, (5:5)	112371	2,000 mg/kg	Single dose 14 days observation.	Acute	Oral (gavage)	See comments	8 month-old animals utilized (fasted). No treatment-related effects (i.e., mortality or abnormal behavior).
Kehr et al. 1978b	Bobwhite quail	Unknown	112371	0.125, 0.250, 0.500% in diet	5-day exposure with 3 days Observation	Acute	Oral (Diet)	See comments	Ten day-old chicks utilized. At 0.25 and 0.50% in the diet statistically significant depression in body weight gain during days 0-3.
Kehr et al. 1978c	Mallard ducks	Unknown	112371,	0.125, 0.250, 0.500% in diet	5-day exposure with 3 days observation	Acute	Oral (Diet)	See comments	16 day-old chicks utilized. At 0.025 and 0.50% in the diet reduced food consumption for days 0-5. At 0.125% some dietary rejection. Reduction in weight gain for all tested animals.
Krobst et al. 1979	Rat (Fischer 344)	M (10)	EL 171	2.0 g/kg	Single exposure	Acute	Oral (gavage)	See comments	Reproductive performance of male rats not affected. No mortalities or weight change. No effect on mean litter size, resorption, or implantation. Fetuses all appeared normal.
Krobst & Neal 1980a	Rat hepatocyte primary cultures (Fisher 344)	---	112371	Range 0.5 - 1,000 nmoles/ml	20 hours	Acute	In vitro Assay	See comments	No induction of DNA repair synthesis, as measured by autoradiography of unscheduled DNA synthesis (uds). Cytotoxicity observed.

APPENDIX A2(Continued)
SUMMARY OF FLURIDONE MAMMALIAN TOXICITY DATA REVIEW

Author	Species	Sex and No. per Dose Group	Chemical	Dose	Exposure Time	Type of Test	Route of Administration	Type of Response	Comments
Neal 1981	Chinese Hamsters	F (3)	112371	Range 62.5 - 500 mg/kg	Single exposure	Acute	Intraperitoneal	See comments	Fluridone did not induce SCE in vivo in bone marrow of Chinese hamsters. Cytotoxicity was observed at doses of 250, 350 mg/kg.

APPENDIX A3
WORST CASE CALCULATIONS FOR NMF

No Effects Level for NMF. A no effects level (NOEL) for humans was originally calculated for NMF by Merkle and Zeller (1980). They concluded that the NOEL for NMF was 10 mg/kg. Their experiments were repeated in 1988 by a contractor to Elanco Company, and results were the same; the NOEL for rabbits was 10 mg/kg/dy, and the NOEL for rats was 10 mg/kg/dy.

NMF Concentrations. Next, potential NMF concentrations in the field were calculated. Under worst case calculations based on theoretical conditions:

(0.15 ppm fluridone) (36%) (18%) = 0.01 ppm NMF.

EPA approved tolerance limit for fluridone in water	Conversion of fluridone to NMF in laboratory conditions	Molecular weight ratio of NMF/fluridone

In conclusion, worst case NMF concentrations are 0.01 ppm = 0.01 mg/l.

Under more realistic conditions based on actual experiments in Florida ponds where NMF was not detected after use (detection limit = 0.002 ppm), the realistic case NMF concentrations in water would equal <0.002 ppm = <0.002 mg/l.

Assumptions. Six assumptions were made for the following safety assessment of NMF:

1. Concentrations of NMF in water:

   - o Worst case concentration of 0.01 ppm = 0.01 mg/l, and a
   - o Realistic case concentration of <0.002 ppm = <0.002 mg/l.

2. NMF NOEL (no effects level from above) for teratogenesis = 10 mg/kg.

3. Average human body weight = 60 kg.

4. Average human body surface area at 60 kg = 17,000 cm2.

5. Average daily drinking water = 2l.

6. Penetration rate of water through skin = 0.4 mg/cm2/hr.

Drinking Water Worst Case. Calculations for a drinking water scenario

follow:

$$\frac{(0.01 \text{ mg/l water}) \ 21}{60 \text{ kg body weight}} = 0.00033 \text{ mg NMF/kg}$$

$$\frac{10}{0.00033} = 30{,}303 \text{ X Safety Factor}$$

In conclusion, the safety factor for NMF in drinking water was 30,303 X the worst case concentration.

Percutaneous Absorption During 8 hour Exposure. Calculations for absorption through the skin while swimming follow:

(0.4 mg/cm2/hr) (17,000 cm2) (8 hours) = 54.400 mg water.

Using the worst case concentration of 0.01 ppm = 0.01 mg/l:

$$\frac{(0.01 \text{ mg NMF/l}) \ (0.0544 \text{ l water})}{60 \text{ kg}} = 0.000009 \text{ mg NMF/kg}$$

10/0.000009 = 1,111,111 X Safety Factor.

In conclusion, the safety factor for NMF being absorbed through the skin was 1,111,111 X the worst case concentration.

In summary, safety factors for drinking water and percutaneous absorption are very large:

Safety Factors	Worst Case	Realistic Case
Drinking Water	30,303 X	>149,254 X
Percutaneous Absorption	1,111,111 X	>5,555,555 X

Exposure needed to equal the no effects level (NOEL)	Worst Case	Realistic Case
Drinking water	15,852 gal/day	>78,077 gal/day
Percutaneous Absorption	1,014 years	>5,070 years

We conclude that the use of fluridone according to label instructions does not pose any effect to human health. To put it in perspective, these are very large margins of safety, and the amount of water that a person would have to drink to reach the no effects level for NMF is very unrealistic.

APPENDIX A3
WORST CASE CALCULATIONS FOR NMF

No Effects Level for NMF. A no effects level (NOEL) for humans was originally calculated for NMF by Merkle and Zeller (1980). They concluded that the NOEL for NMF was 10 mg/kg. Their experiments were repeated in 1988 by a contractor to Elanco Company, and results were the same; the NOEL for rabbits was 10 mg/kg/dy, and the NOEL for rats was 10 mg/kg/dy.

NMF Concentrations. Next, potential NMF concentrations in the field were calculated. Under worst case calculations based on theoretical conditions:

(0.15 ppm fluridone) (36%) (18%) = 0.01 ppm NMF.

EPA approved tolerance limit for fluridone in water	Conversion of fluridone to NMF in laboratory conditions	Molecular weight ratio of NMF/fluridone

Thus, worst case NMF concentrations are calculated to be 0.01 ppm = 0.01 mg/l.

Under more realistic conditions based on actual experiments in Florida ponds where NMF was not detected after use (detection limit = 0.002 ppm), the realistic case NMF concentrations in water would equal <0.002 ppm = <0.002 mg/l.

Assumptions. Six assumptions were made for the following safety assessment of NMF:

1. Concentrations of NMF in water:
   - o Worst case concentration of 0.01 ppm = 0.01 mg/l, and a
   - o Realistic case concentration of <0.002 ppm = <0.002 mg/l.
2. NMF NOEL (no effects level from above) for teratogenesis = 10 mg/kg.
3. Average human body weight = 60 kg.
4. Average human body surface area at 60 kg = 17,000 cm2.
5. Average daily drinking water = 2l.
6. Penetration rate of water through skin = 0.4 mg/cm2/hr.

Drinking Water Worst Case. Calculations for a drinking water scenario follow:

$$\frac{(0.01 \text{ mg/l water})\ 21}{60 \text{ kg body weight}} = 0.00033 \text{ mg NMF/kg}$$

$$\frac{10}{0.00033} = 30{,}303 \text{ X Safety Factor}$$

In conclusion, the safety factor for NMF in drinking water was 30,303 X the worst case concentration.

Percutaneous Absorption During 8 hour Exposure. Calculations for absorption through the skin while swimming follow:

(0.4 mg/cm2/hr) (17,000 cm2) (8 hours) = 54.400 mg water.

Using the worst case concentration of 0.01 ppm = 0.01 mg/l:

$$\frac{(0.01 \text{ mg NMF/l})\ (0.0544 \text{ l water})}{60 \text{ kg}} = 0.000009 \text{ mg NMF/kg}$$

10/0.000009 = 1,111,111 X Safety Factor.

In conclusion, the safety factor for NMF being absorbed through the skin was 1,111,111 X the worst case concentration.

In summary, safety factors for drinking water and percutaneous absorption are very large:

Safety Factors	Worst Case	Realistic Case
Drinking Water	30,303 X	>149,254 X
Percutaneous Absorption	1,111,111 X	>5,555,555 X

Exposure needed to equal the no effects level (NOEL)	Worst Case	Realistic Case
Drinking water	15,852 gal/day	>78,077 gal/day
Percutaneous Absorption	1,014 years	>5,070 years

We conclude that the use of fluridone according to label instructions does not pose any effect to human health. To put it in perspective, these are very large margins of safety, and the amount of water that a person would have to drink to reach the no effects level for NMF is very unrealistic.

Appendix E

1992 SEIS Appendices:

Fluridone Human Health Risk Assessment

The basis for all the models involves quantifying the intake rate to determine a MAC in water for each route of exposure:

$$\text{Maximum Acceptable Concentration (MAC)} = \frac{\text{Acceptable Dose (AD)}}{\text{Intake Rate (IR)}}$$

Equations used for each of the potential exposure routes are described below.

WATER INGESTION

Procedure

A maximum acceptable water concentration for the water ingestion route was calculated by assuming that all of the acceptable dose is received in ingested water as follows:

$$MAC = \frac{AD}{IR}$$

where:

MAC = Maximum acceptable concentration (mg/l or ppm)
AD = Acceptable dose (mg/day) for 70 kg adult or 10 kg child
IR = Water ingestion rate (l/day).

Two different ingestion rates were used. The first was selected to represent the total amount of water that would be ingested on a daily basis (i.e., as if treated waters were the primary drinking water supply source). The second ingestion rate was selected to represent a more realistic water intake that could occur as incidental ingestion during swimming.

For water supply intake rates, standard intake values used by EPA for water quality criteria development were selected. For an adult, daily intake is equal to 2.0 l/day, for a child, intake is equal to 1.0 l/day. Incidental ingestion values were assumed to be equal to one tenth of the daily ingestion. Incidental intake is therefore equal to 0.2 and 0.1 l/day for adults and children, respectively.

Assessment

Based on the risk assessment by METRO (1986), maximum acceptable concentrations determined for ingestion exposure are compared to initial ambient herbicide concentrations in Table 1. No exceedances of the fluridone water supply MAC are predicted. Similarly, no exceedances of the short-term incidental ingestion MAC values are observed for fluridone.

The short-term exposure for fluridone was evaluated using the same AD as

INTRODUCTION

Potential risks to human health as a result of fluridone application in Washington lakes were evaluated by METRO (1986). The population that could be exposed to lake water includes individuals of both sexes and sensitive subgroups such as infants, the ill or the elderly. Risks to applicators were not included in the assessment. This report is a summary of the procedures and results of the METRO risk assessment.

Three potential routes of human exposure were evaluated in the METRO study. These included:

- o water ingestion
- o dermal contact during swimming
- o ingestion of aquatic organisms.

Two other routes of exposure were considered but not included in the assessment since the potential for adverse effects by those routes was judged to be minimal. During degradation of fluridone some volatile compounds are formed (Saunders and Mosier 1983), but according to METRO (1986) are unlikely to cause adverse effects due to the low toxicity of fluridone (Appendix A1). The breakdown products themselves have apparently not been tested, however n-methyl formamide is one breakdown product of concern. A worst-case analysis for fluridone was conducted by Elanco in 1988 (Appendix A3). Ingestion of crops irrigated with water containing herbicides was also not included in the assessment for the following reasons:

1) Product labels contain use restrictions and warnings about effects on non-target plants.
2) Damage to plants by herbicides in irrigation water would decrease the likelihood of human ingestion.
3) Intermittent use of herbicides, and their dissipation and degradation, would preclude continuous use of irrigation water containing herbicides at significant concentrations.

To evaluate the potential for adverse effects, estimated environmental concentrations (EECs) calculated from herbicide application rates and persistence data were compared to criteria concentrations for human health. Next, acceptable doses (AD) for all three exposure routes were determined after review of toxicity information (Appendix A1, A2); the ADs used were derived from chronic oral studies in animals.

To relate an acceptable dose (AD) to a water concentration, models were developed which simulate the transport of the substance from the source to the receptor population for each of the exposure pathways of interest. Each pathway is expressed as an algebraic equation which is solved to calculate the Maximum Allowable Concentration (MAC) in water which results in an acceptable dose.

for chronic exposure (Appendix A1). Results of the above analyses indicate that applications of fluridone should not pose a long-term threat to human health. Initial concentrations of fluridone would not interfere with water usage. For incidental ingestion during recreation, fluridone would not lead to increased risk to human health.

DERMAL EXPOSURE

Procedure

The potential for harm resulting from dermal exposure was evaluated using a procedure which is recommended by EPA (1986b). The approach is based on the assumptions that contaminants are carried through the skin as a solute in water (rather than being preferentially absorbed independently of the water) and that the contaminant concentration in the water being absorbed is equal to the ambient concentration. Thus, the flux rate of water across the skin boundary is assumed to be the factor controlling the contaminant absorption rate. According to Scheuplein and Blank (1971) (as reported in EPA 1979), the flux rate of water through human skin ranges from 0.2 to 0.5 mg/cm2/hr.

$$MAC = \frac{AD}{D \times SA \times Flux} \times \frac{1{,}000\ mg}{cc} \times \frac{1{,}000\ cc}{1}$$

where:

MAC - Maximum Acceptable Concentration (mg/l or ppm) of contaminant in water

D - duration of exposure event (hours) for swimming (1 hr per day is assumed)

SA - skin surface area available for contact (cm2)

SA - 18,150 cm2 for an average adult 20-30 years old (EPA 1986b)

SA - 9,400 cm2 for an average child 3-12 years old (EPA 1986b)

Flux - flux rate of water across skin (0.5 mass/cm2/hr)

AD - Acceptable dose (mg/day) determined from ingestion studies, for 70 kg adult or 10 kg child

The AD as determined from ingestion studies is based upon the assumption that all of the ingested material is absorbed and is toxicologically available in the bloodstream. For dermal exposure, this AD is used to estimate the ambient concentration that will result in this same dose to the bloodstream from flux across the skin.

Assessment

As shown in Table 2, initial ambient concentrations of fluridone do not result in exceedances of the MAC values computed on the basis of the ingestion AD. Recall that this procedure is based upon a toxicologically available dose of herbicide (i.e., absorption to the bloodstream). On this basis, a toxic response that would harm or impair human health is not indicated.

Studies by Ansley and Levitt 1981, Arthur et al. 1978a, and Probst et al. 1982, indicate that fluridone is not irritating to skin. Application of undiluted fluridone formulations to the eyes of rabbits resulted in slight conjunctivitis (inflammation of the eyelid membrane) and corneal dullness. All treated eyes were normal within two to seven days (Ansley and Arthur 1980, Ansley and Levitt 1981, Arthur et al. 1978a and 1978b). Ambient exposure concentration while swimming will be very dilute compared to direct product exposure. Therefore, serious or long-term irritation as a result of dermal or ocular fluridone exposure is not expected to occur and swimming in treated waters is not expected to cause an observable increased risk of irritation.

INGESTION OF AQUATIC ORGANISMS

Procedure

The MAC value calculated for ingestion of aquatic organisms is equivalent to the concentration commonly called the Final Residue Value in guidelines for developing EPA water quality criteria (Stephan et al. 1985). The MAC is calculated from the fish ingestion rate and bioconcentration factor as shown below:

$$MAC = \frac{AD}{FI \times BCF}$$

where:

MAC = Maximum Acceptable Concentration of contaminant in water
AD = Acceptable dose (mg/day) for 70 kg adult
FI = Fish Ingestion Rate (kg/day)
= 6.5 g/day for adults = 0.0065 kg/day (EPA, 1980b)
BCF = Bioconcentration Factor (l/kg) (highest reported values used).

Assessment

Bioconcentration data available for fluridone (Table 3) indicated that bioconcentration factors were 2.46 for fluridone, far too low to be of concern in terms of bioaccumulation and biomagnification. The bioconcentration factor is a measure of the extent to which a chemical accumulates in the aquatic animal solely as a function of exposure to the chemical in the water. Bioaccumulation reflects uptake from water and from food. Biomagnification represents the increased concentration of a

chemical as predators eat prey in a food chain. ASTM (1985b) indicates that chemicals with bioconcentration factors less than approximately 100 have low potential for causing harm to wildlife and human health via biomagnification of residues up food chains. Kimerle et al. (1978) suggest that studies of impacts arising from biomagnification need only be performed when bioconcentration factors in muscle tissue exceed 1,000. Fluridone's bioconcentration factor averaged 1.5; 95 percent confidence limits ranged from 0.5 to 5.3.

As expected, calculation of the fluridone MAC or Final Residue Values for ingestion of aquatic organisms confirmed that this exposure route does not endanger human health. The residue values are compared to ambient exposure concentrations in Table 4.

SUMMARY AND CONCLUSIONS

A 1986 METRO study of risks to human health from application of fluridone to Washington lakes has been summarized. Three potential routes of human exposure were evaluated. These included:

- water ingestion
- dermal contact during swimming
- ingestion of aquatic organisms.

To evaluate the potential for adverse effects, estimated environmental concentrations calculated from herbicide application rates and persistence data were compared to criteria concentrations for human health. For each route of exposure, an acceptable dose (AD) was determined after review of toxicity information and EPA's risk assessment data base (integrated risk information system or IRIS). EPA's chronic risk reference dose (RfD) for ingestion exposures was used as the AD for all three exposure routes evaluated. A model was used for each route of exposure to derive a maximum acceptable concentration (MAC) of the herbicide in water by dividing the AD by an intake rate.

For water ingestion, two intake rate scenarios were used: a worst-case analysis assuming the herbicide-treated water was used as the drinking water supply, and a more likely exposure scenario assuming incidental water ingestion while swimming. The incidental ingestion scenario is still conservative because it was assumed that people were exposed daily for a prolonged time period (chronic exposure) to initial herbicide concentrations. Potential exposures would actually be much more limited. Application of herbicides is expected to occur once per year at most, and degradation half-lives reported in field studies range from five to 20 days for fluridone.

Estimated initial water concentrations did not exceed either the water supply MAC or the incidental ingestion MAC for adults or children. For the dermal exposure route and ingestion of aquatic organisms, estimated initial concentrations did not exceed calculated MACs for fluridone. For

dermal exposure, the model used to calculate a MAC was based on the assumption that contaminants are carried through the skin as a solute in water. Thus, the flux rate of water across the skin boundary was assumed to be the factor controlling contaminant absorption rate. For ingestion of aquatic organisms, contaminant intake rate was calculated from a daily fish ingestion rate (6.5 grams/day) multiplied by a bioconcentration factor for accumulation of the contaminant in fish tissue.

In addition to potential risks from systemic absorption of the herbicides, there is a potential for effects from direct contact of herbicides with skin and eyes. Fluridone is not irritating to the skin and only minor effects were noted after application of undiluted fluridone to the eyes of rabbits. Thus, no adverse effects are expected from contact with dilute solutions.

In summary, no adverse effects are anticipated due to exposure to fluridone under the expected conditions of use.

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TABLE 1

COMPARISON OF INITIAL HERBICIDE CONCENTRATIONS WITH MAXIMUM ACCEPTABLE CONCENTRATIONS FOR WATER INGESTION EXPOSURE 1/

Chemical	Initial Concentration (ppm)	Water Supply Ingestion MAC (ppm) Adult	Child	Exceedances	Incidental Ingestion MAC (ppm) Adult	Child	Exceedances
Fluridone-liquid	0.14	2.8	0.8	No	28	8	No
Fluridone-pellets	0.07 2/	2.8	0.8	No	28	8	No

1/ MAC in water based on AD calculated by METRO (1986) for chronic (lifetime) exposure (Appendix A).

2/ Maximum concentration after application calculated using longest half-life.

TABLE 2

COMPARISON OF INITIAL HERBICIDE CONCENTRATIONS WITH MAXIMUM ACCEPTABLE CONCENTRATIONS FOR DERMAL EXPOSURE 1/

Chemical	Initial Concentration (ppm)	Dermal Exposure MAC		Exceedance
		Adult (ppm)	Child (ppm)	
Fluridone-liquid	0.14	617	170	No
Fluridone-pellets	0.07 2/	617	170	No

1/ MAC in water based on AD calculated by METRO (1986) for chronic (lifetime) exposure (Appendix A).

2/ Maximum concentration after application calculated using longest half-life.

Appendix E

1992 SEIS Appendices:

Glyphosate Risk Assessment

APPENDIX E.

RISK ASSESSMENT FOR GLYPHOSATE

from:

WORST CASE ANALYSIS STUDY

ON FOREST PLANTATION HERBICIDE USE

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Chapter 5

Risk Assessment for Glyphosate

5.1 Chemical and Use Properties

Glyphosate, N-(phosphonomethyl) glycine, is a non-selective, non-residual, post-emergence herbicide effective against deep-rooted perennial species and against annual and biennial species of grasses, sedges and broadleaf weeds. It is used primarily in agricultural applications with only recent limited forestry use (U.S. Department of Agriculture (USDA), 1984a; Weed Science Society of America, 1983). First registered by the Monsanto Company in 1974, glyphosate is commercially available under the trade names Roundup herbicide and Rodeo herbicide. Roundup is a formulation of the isopropylamine salt of glyphosate (41%), water and surfactants; Rodeo consists of the isopropylamine salt (53.5%), water and other materials, with no surfactants (USDA, 1984a).

Glyphosate is readily absorbed through photosynthetically active structures of plants, primarily foliage (Weed Science Society of America, 1983). Some absorption by roots is possible under proper soil conditions (USDA, 1984a). Foliar absorption is increased substantially under conditions of increased humidity or by the presence of surfactants (Gottrup *et al.*, 1976 in USDA, 1984a). Glyphosate is not metabolized by plants (Gottrup *et al.*, 1976 in USDA, 1984a). Translocation throughout the plant is rapid, with resultant inhibition of regrowth from underground propagation structures in perennial species. The precise mode of action is unknown, though glyphosate is believed to inhibit the synthesis of essential aromatic amino acids and to degrade photosynthetic pigments in plants (Weed Science Society of America, 1983; Shoner and Lyon, 1980 and Hoagland, 1980 in USDA, 1984a).

Residue and metabolism studies indicate that glyphosate absorption across gastrointestinal membranes and subsequent tissue retention is minimal. In rats and rabbits, orally administered radiolabeled glyphosate is readily excreted (Monsanto 1973a, 1973b in Monsanto, 1984a). In rats, approximately 85-95% of the administered dose was excreted within 48 hours of dosing primarily in the feces. Unchanged glyphosate was the major radioactive component identified in the feces and urine of rats, indicating that glyphosate is not readily metabolized (Monsanto, 1973c). There were no detectable glyphosate residues (<0.05 ppm) in the muscle and fat of several animal species fed diets containing up to 75 ppm glyphosate (Monsanto, 1984a). Calculated bioconcentration factors in a variety of fish species ranged from 0.1 to <2.0, indicating that glyphosate has little tendency to bioaccumulate (Monsanto, 1984a).

Under standard conditions, pure glyphosate has a solubility in water of 1.2% and is insoluble in other solvents (Weed Science Society of America, 1983). The isopropylamine salt formulations are chemically stable and completely miscible in water (USDA, 1984a). Glyphosate has a low partition coefficient, indicating its low solubility in lipids or fats (USDA, 1984a).

Glyphosate undergoes complete microbial degradation rapidly in soil and water with an experimentally determined half-life of 28 days (Rueppel *et al.*, 1977). The major soil metabolite, amino methyl-phosphonic acid, undergoes relatively rapid degradation in soil with approximately 35% completely degraded in 63 days (Rueppel *et al.*, 1977). In soil, glyphosate is resistant to chemical degradation and stable to sunlight (Rueppel *et al.*, 1977). It adsorbs strongly to soil particles, is relatively nonleachable, and has a low tendency for run off (Rueppel *et al.*, 1977). Glyphosate adsorbs strongly to organic and mineral matter in aquatic systems where it also undergoes microbial degradation. Generally, environmental persistence of glyphosate is very low (Weed Science Society of America, 1983; USDA, 1984a).

5.2 Toxicology

5.2.1. Introduction

The toxicity of glyphosate and its potential as a human health hazard have been evaluated in standard acute, subchronic, chronic, reproductive, and teratogenicity toxicity tests in several species of laboratory animals by a variety of routes of administration. The majority of the testing has been done with the active ingredient, glyphosate or N-(phosphonomethyl) glycine. The major formulation containing glyphosate, Roundup, has been evaluated in acute toxicity and selected subchronic studies. Technical grade glyphosate contains 95% or more of the active ingredient, N-(phosphonomethyl) glycine. Roundup contains 41% isopropylamine salt of N-(phosphonomethyl) glycine (IPA-G).

The glyphosate experimental data discussed in this report were obtained primarily from experimental studies conducted by the manufacturer, Monsanto Company. Monsanto provided a comprehensive summary of the toxicological data on glyphosate and Roundup. In addition, Monsanto provided access to data from the most recent experiments that evaluated reproductive, teratogenic, and carcinogenic effects. These data included experimental protocols, raw data, and summary analyses of the reproductive, teratogenic, and carcinogenic studies discussed in this report. Although these data have been provided to the EPA for analysis, much of this information still remains proprietary. Some of the descriptions of study protocols and experimental results, i.e. dosage levels or incidence of a response, were limited by Monsanto to data already made public; however, our qualitative conclusions based on the experimental results were not hindered by these restrictions. A number of the earlier studies on glyphosate conducted by Industrial

Biotest were judged to be unacceptable by the EPA and were repeated by the manufacturer. Only those studies judged to be valid by an EPA audit were included in the discussion of potential health hazards from exposure to glyphosate.

Details of the experimental protocols and results of available mammalian toxicity data are presented in Table 5-1.

5.5.2. Noncarcinogenic Effects

5.2.2.1. Acute Effects

Oral. The acute oral toxicity from ingestion of a single dose of glyphosate or the isopropylamine salt of glyphosate (IPA-G) is low in all experimental species tested. The acute oral LD50 of glyphosate in rats ranged from 4,300 mg/kg (Weed Science Society of America, 1983) to 5,600 mg/kg (Monsanto, 1979a in Monsanto, 1984a), while that of IPA-G was greater than 5,000 mg/kg (Monsanto, 1978a in Monsanto, 1984a). In rabbits, the oral LD50 of glyphosate was 3,800 mg/kg (U.S. Department of Energy, 1983). The acute oral LD50 in rats of the glyphosate formulation, Roundup (41% IPA-G), was 5,400 mg/kg (Monsanto, 1979b in Monsanto, 1984a).

At lethal doses, dyspnea, ataxia and occasional convulsive movements preceded death. Discoloration in the lungs, liver, and kidneys was observed in animals that died.

Intraperitoneal. Single intraperitoneal injections of glyphosate technical mixed in saline resulted in acute LD50s ranging from 134 to 281 mg/kg in rats (Bababunmi et *al.*, 1978 and Monsanto, 1978b in Monsanto, 1984a) and 388 to 740 mg/kg in mice (Bababunmi et *al.*, 1978 and Monsanto, 1975a in Monsanto, 1984a). The acute toxicity of glyphosate appears to be route and species dependent (Bababunmi et *al.*, 1978). The large difference in oral versus intraperitoneal LD50s, coupled with high fecal excretion of unchanged glyphosate, suggests that oral bioavailability is very low perhaps on the order of 5% or less.

Dermal. Acute percutaneous absorption studies conducted on rabbits and rats indicate that glyphosate and formulations containing glyphosate are not readily absorbed through the skin. No signs of toxicity were observed in rabbits following a 24-hour occluded dermal exposure to 5,000 mg/kg of glyphosate (Monsanto, 1979c in Monsanto, 1984a), IPA-G (Monsanto, 1981a in Monsanto, 1984a), or Roundup (Monsanto, 1979d in Monsanto, 1984a); therefore, the LD50 values for acute dermal exposure in rabbits are greater than 5,000 mg/kg for glyphosate, IPA-G, and Roundup. The acute dermal LD50 value in rats resulting from a single dermal exposure to undiluted Roundup was greater than 17,600 mg/kg (Monsanto, 1978c in Monsanto, 1984a).

In primary skin irritation studies, glyphosate and IPA-G were practically nonirritating to intact and abraded rabbit skin (Monsanto, 1979e, 1981b in Monsanto, 1984a), while Roundup produced moderate skin irritation (Monsanto, 1979f in Monsanto, 1984a). This difference suggests that the surfactant present in Roundup may be responsible for the moderate skin irritation noted in the commercial formulation.

Eye Irritation. In standard eye irritation tests, 0.1 ml of a 25% wt/vol aqueous suspension of glyphosate or IPA-G was instilled into the conjunctival sac of the rabbit eye. Glyphosate was slightly irritating, resulting in corneal opacity and ulceration in one of six rabbits tested (Monsanto, 1979g in Monsanto, 1984a), while IPA-G was essentially nonirritating (Monsanto, 1981c in Monsanto, 1984a). All ocular irritation disappeared within seven days. The average Draize scores of the 24-, 48- and 72-hour readings were 6.9 and 0 on a scale of 110 for glyphosate and IPA-G, respectively.

Application of undiluted Roundup to the conjunctival sac of rabbit eyes resulted in moderate irritation (Monsanto, 1975b in Monsanto, 1984a). All ocular irritation was transient and all irritation disappeared within ten days. The Draize score of the 24-, 48-, and 72-hr average has been variously reported as 18.6/110 (Monsanto, 1982a in USDA, 1984a) and 4.1/110 (Monsanto, 1975b in Monsanto, 1984a). In a summary of a primary eye irritation study in rabbits, the maximum Draize score was reported to be 26.6/110 at 24 hours, accompanied by severe erythema, slight to moderate edema, and copious discharge (EPA, 1984). All ocular irritation was transient and all irritation disappeared within ten days. Both glyphosate and IPA-G have a relatively low irritation potential for skin and eyes, but the EPA requires precautionary labeling for Roundup use (Monsanto, 1984a).

Inhalation. The acute toxicity of Roundup has been evaluated in inhalation studies. In an acute rat inhalation study, the four-hour nominal LC50 value was 25 mg/l of air, while an LC50 value based upon the analytical (chemical) determination was 3.18 mg/l of air (Monsanto, 1982b in Monsanto, 1984a). No signs of toxicity were observed in rats exposed to a Roundup spray mix solution (Monsanto, 1981d in Monsanto, 1984a). Rats were exposed for four hours to a 2% vol/vol spray dilution of Roundup, resulting in a nominal concentration of 4.89 mg solution/l of air.

5.2.2.2. Subchronic Effects

Dermal. Glyphosate was administered dermally to rabbits for a total of 15 days in a 21-day period at dosage levels of 0, 100, 1,000, or 5,000 mg/kg/day (Monsanto, 1982c in Monsanto, 1984a). No evidence of systemic toxicity was observed in any of the treated rabbits. Adverse effects were limited to localized skin irritation, slight erythema and edema in the 5,000 mg/kg/day dosage group only. The NOEL was determined to be 1,000 mg/kg/day for dermal effects and 5,000 mg/kg/day for

systemic effects by the dermal route.

Roundup and its components have been evaluated in 21-day dermal subchronic toxicity tests. When applied to rabbit skin five days per week for three weeks at a concentration five times (5x) the intended spray mix concentration (6.4% aqueous solution by volume), Roundup produced both severe local irritation and signs of systemic toxicity, which included reduced food consumption, body weight loss, testicular atrophy and death (Monsanto, 1972 in Monsanto, 1984a). No signs of systemic effects and only moderate local irritation were observed in rabbits treated dermally with three times (3x) the intended spray mix (Monsanto, 1973d in Monsanto, 1984a). When tested using the same study design, the surfactant in Roundup and another surfactant produced marked local irritation and adverse systemic effects similar to those seen with Roundup at the 5x spray mix level (Monsanto, 1973e in Monsanto, 1984a). The authors stated that systemic toxicity has been observed in rabbits subjected to severe stress; therefore, the authors concluded that the toxicity observed at the 5x spray mix concentration level was a stress-induced response caused by severe dermal irritation, rather than the result of direct systemic toxicity of Roundup. No other experimental data were available to resolve the cause of the observed systemic effects.

Roundup was not a primary irritant or skin sensitizer to human skin (Monsanto, 1973f in Monsanto, 1984a). No skin irritation was produced in patch test experiments with human volunteers. Roundup was applied to shaved human skin at 5x the spray mix level daily for 15 days. No irritation or skin sensitization resulted when the skin was challenged with another application at a later time. The human studies indicate that the severe adverse reaction in rabbits from a dermal exposure to Roundup at the 5x spray mix level would not be expected in humans.

Neither Roundup nor glyphosate produced signs of allergic contact dermatitis or dermal sensitization in guinea pigs (Monsanto, 1984a). In dermal sensitization tests, glyphosate was initially applied to the shaved skin of guinea pigs for 6-hours per day, three days per week for three weeks during the induction phase. After a two week exposure-free interval, animals were then topically challenged with another dermal application of glyphosate. Glyphosate produced no irritation following initial exposure, moderate to severe edema and/or necrosis in some animals with subsequent exposures in the induction phase, but no dermal sensitization upon challenge.

Inhalation. In a subchronic inhalation study, male and female rats were exposed to aerosol concentrations of up to 0.36 mg of an aqueous solution of Roundup (1:2 Roundup formulation: water) per liter of air for six hours daily, five days per week for 30 days (Monsanto, 1983a in Monsanto, 1984a). Adverse effects were limited to minor nasal irritation.

Oral. Glyphosate subchronic toxicity has been evaluated in rats and mice. Five groups of rats were maintained on diets containing 0, 200, 2,000, 5,000, or 12,500 ppm glyphosate for 90 days (Monsanto, 1979h in Monsanto, 1984a). These doses were equivalent to 0, 13.5, 135, 340, or 820 mg/kg/day as calculated from food consumption data (Street, 1985). No deaths occurred and no treatment-related changes in hematology, clinical chemistry, urinalysis, or gross and microscopic pathology were reported. Both absolute and relative lung weight of male rats fed 5,000 ppm and males and females at the 12,500 ppm dosage level were significantly increased over control values. For purposes of this worst case analysis, the NOEL for this study was determined to be 2,000 ppm or 135 mg/kg/day.

In a 90-day oral subchronic study, mice were fed diets containing up to 50,000 ppm glyphosate (Monsanto, 1979i in Monsanto, 1984a). Adverse effects were limited to depressed growth, as indicated by reduced body weight gains at the 50,000 ppm dosage level. No gross or histopathological tissue changes observed in any of the treated animals were considered to be treatment-related. The NOEL was established at 10,000 ppm. The dose was equivalent to 2,305 mg/kg/day, calculated from food consumption data (Street, 1985).

5.2.2.3. Reproductive Effects

In a three-generation reproduction study, male and female rats were fed diets containing 0, 3, 10 or 30 mg glyphosate/kg/day (Monsanto, 1981e). Treatment began prior to mating and continued through the production of two litters for each of three generations. No adverse effects in any of the parameters that evaluate reproductive capability, such as fertility, gestation, viability, or lactation indexes, were observed in treated parental animals or offspring. Appearance, body weight gains, behavior, and survival of the test animals were not affected by treatment. Therefore, the NOEL for reproductive effects was determined to be greater than 30 mg/kg/day. The NOEL of 30 mg/kg/day will be used in the calculation of margins of safety for reproductive effects from a single exposure to glyphosate.

In general, three-generation reproduction studies have been used to evaluation impaired reproductive capability or teratogenicity. Since animals in a three-generation reproduction study are exposed throughout a major portion of their lifetimes, systemic effects other than those affecting reproductive capability may be manifested. In the three-generation reproductive study discussed above (Monsanto, 1981e), renal focal tubular dilation in males of the F_{3b} generation was observed at the 30 mg/kg/day level. In an EPA review (EPA, 1984) this effect was describes as a systemic effect rather than a teratogenic effect. The systemic NOEL for this study is then 10 mg/kg/day, while the NOEL for reproductive effects was established at 30 mg/kg/day. Therefore, a NOEL of 10 mg/kg/day was selected for use in calculating margins of safety for systemic effects (Table 5-5), and a NOEL of 30 mg/lg/day was used to

calculate margins of safety for reproductive effects (Table 5-6).

5.2.2.4. Teratogenic Effects

The teratogenic potential of glyphosate was evaluated in rats and rabbits. Maternal toxicity, fetotoxicity and teratogenicity were evaluated in each study.

Groups of 25 Charles River CD female rats were given glyphosate by gavage at dosage levels of 0, 300, 1,000 or 3,500 mg/kg/day from day 6 through 19 of the gestation period (Monsanto, 1980a). All surviving rats were sacrificed on day 20. The number and location of viable and nonviable fetuses, and the number of resorptions, implantations, and corpora lutea were evaluated. One-half of the fetuses from surviving dams were examined for internal anomalies and the other half for skeletal malformations. Maternal toxicity consisting of reduced body weight gains, stomach hemorrhages, soft stools, diarrhea, and nasal discharge occurred in the 3,500 mg/kg/day dosage group. Some maternal deaths occurred in the high dose group. The NOEL for maternal toxicity was determined to be 1,000 mg/kg/day. A significant increase in delayed ossification of sternebrae occurred in the 3,500 mg/kg/day group; therefore, the NOEL for fetotoxic effects was established at 1,000 mg/kg/day. No significant teratogenic effects were reported, and the NOEL for teratogenicity was 3,500 mg/kg/day. However, 6 fetuses of the 197 in the high dose group examined exhibited major structural malformations. Although several of these malformations were not present in the concurrent or historical control groups, all occurred in the same litter and were not considered by the authors to be related to treatment. However, for this worst case analysis, the presence of these malformations will be considered as possibly treatment-related.

Glyphosate was administered by gavage to groups of 16 pregnant rabbits at dosage levels of 0, 75, 175, or 350 mg/kg day from day 6 through 27 of gestation (Monsanto, 1980b). All survivors were sacrificed at day 28. At 350 mg/kg/day some deaths occurred and most of the does exhibited signs of adverse effects including soft stools, diarrhea, and nasal discharge. The NOEL for maternal toxicity was 175 mg/kg/day. No impairment of embryonic or fetal development was evident at any dose tested. The parameters indicative of developmental effects that were evaluated included number of viable fetuses, corpora lutea, implantations and resorptions. Only those fetuses of rabbits surviving treatment were examined for visceral and skeletal defects. No significant increases in fetotoxicity or teratogenicity occurred at any dose tested. The NOEL established in this study for fetotoxic and teratogenic effects was 350 mg/kg/day. However, major structural malformations were observed in two fetuses in the 175 mg/kg/day dose group and one fetus in the 350 mg/kg/day dose group. Although these structural malformations were not present in the concurrent control group, the incidences were not statistically significantly greater than control. Therefore, these defects were not considered by the authors to

be related to treatment. For this worst case analysis the presence of major development effects in a total of three fetuses will be considered to be possibly treatment-related.

However, for a worst case analysis, a NOEL for fetotoxic effects of 350 mg/kg/day, and a NOEL for teratogenic effects of 75 mg/kg/day derived from the teratogenic study with rabbits will be used for evaluation of margins of safety (Table 5-7).

5.2.2.5. Mutagenic Effects

Glyphosate has been evaluated for mutagenic or genotoxic activity in a variety of *in vivo* and *in vitro* systems. No evidence of mutagenicity was observed in several microbial assays including the Ames assay with five *Salmonella typhimurium* strains (Monsanto, 1978d in Monsanto, 1984a), an *Escherichia coli* reverse mutation assay (Monsanto, 1978e in Monsanto, 1984a), and a *Bacillus subtilis* recombination assay (Monsanto, 1978e in Monsanto, 1984a). Glyphosate did not induce mutagenic responses in two *in vitro* studies conducted in mammalian cell test systems, the Chinese hamster ovary cell point mutation assay (Monsanto, 1983b in Monsanto, 1984a) and a rat hepatocyte primary culture/DNA repair assay (Monsanto, 1983c in Monsanto, 1984a). No evidence of mutagenicity was observed in several *in vivo* mammalian tests including host mediated assays with *S. typhimurium* conducted in both rats and mice (Monsanto, 1975c in Monsanto, 1984a), a mouse dominant lethal, an *in vivo* cytogenetics study in rats, and a sex-linked recessive lethal assay in *Drosophila* (Monsanto, 1984a).

In a study in which glyphosate was first reacted with high concentrations of sodium nitrite *in vitro* to induce nitrosoglyphosate formation and then tested for mutagenicity in a *S. typhimurium* assay, evidence of neither mutagenicity nor the presence of nitrosoglyphosate were detected (Seiler, 1977).

The mutagenicity of Roundup has been evaluated. Roundup has been reported to significantly increase the induction of sister-chromatid exchanges in human lymphocytes *in vitro* (Vigfusson and Vyse, 1980). The validity of this experiment has been questioned due to limitations in both the number of test subjects and statistical analysis of the data (Brusick, 1983).

5.2.3. Carcinogenic Effects

Early long term bioassays of chronic effects and carcinogenicity in mice, rats, or dogs (Monsanto, 1973g, 1973h, 1974) were judged to be invalid in an audit by the EPA.

Replacement lifetime carcinogenicity studies in rats and mice have been completed, and one in dogs is currently being evaluated. In the

rat study, groups of 50 Charles River Sprague-Dawley rats/sex/dose group were fed glyphosate in the diet at dosages of up to 31 mg/kg/day for 26 months (Monsanto, 1981f). The highest dose tested was equivalent to approximately 600 ppm glyphosate in the diet. Evaluation of mortality, food and water consumption, hematology, clinical chemistry, urinalysis, and terminal organ and body weights failed to reveal any treatment-related effects. Hematology, clinical chemistry and urinalysis values, evaluated at specific times throughout the study, exhibited occasional deviations from control values, but none were consistently different or dose-related. The most frequent chronic toxic changes were age-related respiratory disease and progressive nephropathy, neither of which appeared to alter the mortality patterns in control or treated groups. No significant differences in total tumor-bearing animals or total number of animals with malignant tumors were observed. However, two individual tumor types showed a statistically significant increase as compared to controls. Interstitial cell tumors (Leydig cell tumors of the testes) were significantly increased in high dose males. This was not considered to be treatment-related because interstitial cell tumors are common to aging male rats, and the incidence in this study was within the range of incidences in historical controls. Thyroid C-cell carcinomas were significantly increased in high dose female rats. An independent review by two pathologists concluded that this tumor was incidental and not treatment-related. The rationale stated that conditions indicative of a carcinogenic effect of the thyroid C-cell type (dose-related increased incidences in thyroid hyperplasia, adenomas, and lung metastasis) were absent. In addition, it was stated that in this tissue, adenomas and carcinomas are difficult to distinguish and that the incidence was within the range of historical controls. The authors concluded that no adverse chronic or carcinogenic treatment-related effects occurred at any dose tested; therefore a NOEL for systemic effects and carcinogenic effects was established at 31 mg/kg/day, the highest level tested.

Charles River CD-1, COBS mice, 50 animals per sex per dose groups, were fed glyphosate at dietary levels of 0, 1,000, 5,000 or 30,000 ppm for 24 months (Monsanto, 1983d). Glyphosate dosages were equivalent to time-weighted averages of 0, 157, 814 or 4,841 mg/kg/day for males and 0, 190, 955 or 5,874 mg/kg/day for females. No physical or behavioral signs of treatment-related toxicity were observed. Neither the percentage of total tumor-bearing animals nor number of animals with malignant tumors showed dose-dependent increases, or were significantly different from the control values. The majority of tumors observed in the control and the treated groups were bronchiolar-alveolar adenomas and adenocarcinomas, hepatocellular adenomas and adeno-carcinomas, and tumors of the lymphoreticular system, none of which were considered to be treatment-related.

A possible treatment-related increased incidence of renal tubule adenomas in male mice was observed. In male mice, the incidence of renal tubule adenomas was 1/49 in concurrent controls, 0/49 in the low dose (1,000 ppm), 1/50 in the mid dose (5,000 ppm), and 3/50 in the high

dose (30,000 ppm). No renal tubule adenomas were observed in female mice. Initially no renal tubule adenomas were reported in the control group, however on re-examination of the relevant slides, one tumor was observed in a control animal. The incidence of this tumor type in each treated group is not statistically significant when compared to the concurrent control group and there is not a statistically significant dose-response trend (p-value = 0.059 by the Cochran-Armitage test using the exact distribution). According to a review report (EPA, 1985b), this tumor type has rarely been found among untreated historical control mice of this strain and further, incidence of renal tubule adenomas in male treated mice was statistically significant when compared to historical controls. (The incidence in historical controls from seven other studies ranged from 0% to 3% with 1/54, 2/60, and 0/57 to 0/60 in five other studies.) The authors stated that no other renal lesions suggestive or supportive of a compound-related effect on the urinary system was present.

Carcinogenic potency estimates were not calculated using any of the other responses in rats or mice discussed in this report due to limitations placed by Monsanto on the use of data not yet made public. None of the responses reported in the rat or mice carcinogenicity assays were considered to be treatment-related. Only the renal tubule adenomas in mice were identified as possibly treatment-related (EPA, 1985b); therefore in the absence of additional available bioassay data, the response modeled will be that in male mice for renal tubule adenomas (Table 5-8).

5.3. Risk Characterization

For each exposure scenario described in Chapter 2, Tables 5-5, 5-6 and 5-7 contain more reasonable and worst case margins of safety corresponding to systemic, reproductive and teratogenic effects, respectively. Margins of safety represent ratios of estimated animal NOELs expressed in mg/kg body weight/day to estimated single-day human exposures expressed in µg/kg body weight/day.

All estimated margins of safety reported in Table 5-7 exceed 1000 even in the worst case, implying that the risk of teratogenic effects from exposure to glyphosate through a single spraying episode is negligible, if interpreted in terms of the traditional 100-fold safety factor. For systemic and reproductive effects, although margins of safety are smaller (Tables 5-5 and 5-6), they all exceed 100, with the smallest being 139 and 417 in the worst case for systemic and reproductive effects, respectively. These results indicate that with respect to noncarcinogenic risk, the primary cause for concern, if any, from exposure to glyphosate is related to possible systemic effects. It should be recognized, however, that these margins of safety are conservative in the sense that they compare single-day human exposures to average daily animal exposures over ninety days. In the worst case scenario, a worker would have to encounter 139 times the worst case

single-day exposure to reach a level equal to the NOEL, only above which are adverse effects considered to be likely (Table 5-5). A margin of safety of 298 corresponding to the worst case environmental scenario for exposure to glyphosate from eating wild berries means that an individual would have to consume approximately 160 pounds of contaminated wild berries in one day in order to reach an exposure equivalent to the NOEL for glyphosate.

For each exposure scenario described in Chapter 2, Table 5-8 contains more reasonable and worst case estimates of extra carcinogenic risk corresponding to each estimate of total exposure to glyphosate resulting from a single spraying episode. More reasonable estimates of extra carcinogenic risk are based on maximum likelihood estimates from the multistage model while worst case estimates are based on upper 95% confidence limits on extra risk. Animal-to-human dose conversion was made on the basis of average lifetime dose expressed in mg/kg body weight/day, with risk multiplied by a factor of 1.3 to adjust to a short-term human exposure at age 20 from exposure averaged over a 70-year human lifetime (see Chapter 3.3).

The estimated risks in Table 5-8 are all very small, with the largest worst case estimate (corresponds to the largest estimated environmental exposure from ingestion of wild berries) being only 8.76×10^{-10}, (*i.e.*, less than 9 in ten billion). Values for estimated risk corresponding to other routes of environmental exposure ranging down to 2 in 100 billion from inhalation exposures. Estimated risk from occupational exposure to glyphosate through a single spraying episode range from 9 in 100 billion to 1 in 100 billion.

This analysis suggests that the carcinogenic risk from exposure to glyphosate through a single spraying episode is negligible, both for occupationally exposed and for environmentally exposed individuals.

Table 5-1

Summary of Mammalian Toxicity Studies on Glyphosate, Glyphosate Isopropylamine (IPA-G) and Roundup

Type of Test / Formulation / Species	Nature of Exposure	Effects: NOEL	Effects: LEL	Effects: LD50	Comments	Reference
Acute, oral		mg/kg				
Glyphosate						
Rat	Ingestion of a single dose.	---[a]	---	4,300	---	Weed Science Society of America, 1983
Rat	Ingestion of a single dose.	---	---	5,600	At lethal doses dyspnea, ataxia and occasional convulsive movements preceded death. Discoloration in the lungs, liver, and kidneys were observed in animals that died.	Monsanto, 1979a in Monsanto, 1984
Rabbit	Ingestion of a single dose.	---	---	3,800	---	U S Dept of Energy, 1983
IPA-G						
Rat	Ingestion of a single dose	---	---	16,000	---	Monsanto, 1978a in Monsanto, 1984
Roundup						
Rat	Ingestion of a single dose	---	---	5,400	---	Monsanto, 1979b in Monsanto, 1984
Acute, intraperitoneal		mg/kg				
Glyphosate						
Rat	Single intraperitoneal injection, mixed in saline	---	---	134	---	Wobobunmi et al., 1978
Rat	Single intraperitoneal injection, mixed in saline	---	---	281	---	Monsanto, 1978b in Monsanto, 1984

Table 5-1 (continued)

Summary of Mammalian Toxicity Studies on Glyphosate, Glyphosate Isopropylamine (IPA-G) and Roundup

Type of Test / Formulation / Species	Nature of Exposure	Effects: NOEL	Effects: LEL	Effects: LD50	Comments	Reference
Mouse	Single intraperitoneal injection, mixed in saline.	---	---	740	---	Monsanto, 1975a in Monsanto, 1984
Acute, dermal		**mg/kg**				
Glyphosate						
Rabbit	Single dermal application to shaved skin at 5,000 mg/kg; occluded bandage for 24 hours.	---	---	>5,000	No deaths or signs of toxicity.	Monsanto, 1979c in Monsanto, 1984
IPA-G						
Rabbit	Single dermal application to shaved skin at 5,000 mg/kg; occluded bandage for 24 hours.	---	---	>5,000	No deaths or signs of toxicity.	Monsanto, 1981a in Monsanto, 1984
Roundup						
Rabbit	Single dermal application to shaved skin at 5,000 mg/kg; occluded bandage for 24 hours.	---	---	>5,000	No deaths or signs of toxicity	Monsanto, 1979d in Monsanto, 1984
Rat	Single dermal exposure to shaved skin, undiluted formulation (15 ml/kg body weight) held under an occluded bandage for 24 hours	---	---	>17,600	No deaths or signs of toxicity.	Monsanto, 1978c in Monsanto, 1984

Table 5-1 (continued)

Summary of Mammalian Toxicity Studies on Glyphosate, Glyphosate Isopropylamine (IPA-G) and Roundup

Type of Test / Formulation / Species	Nature of Exposure	Effects: NOEL	Effects: LEL	Effects: LD50	Comments	Reference
Skin Irritation						
Glyphosate Rabbit	Single application of 0.5 ml of 25% wt/vol aqueous solution to intact and abraded skin, covered for 24 hours and evaluated at 24 and 72 hours.	---	---	---	Practically nonirritating with a Draize score of 0.1/8.0.	Monsanto, 1979e in Monsanto, 1984
IPA-G Rabbit	Single application of 0.5 ml of 25% wt/vol aqueous solution to intact and abraded skin, covered for 24 hours and evaluated at 24 and 72 hours.	---	---	---	Practically nonirritating with a Draize score of 0.1/8.0.	Monsanto, 1981b in Monsanto, 1984.
Roundup Rabbit	Single application of 0.5 ml of 25% wt/vol aqueous solution to intact and abraded skin, covered for 24 hours and evaluated at 24 and 72 hours.	---	---	---	Moderate irritation with a Draize score of 4.3/8.0.	Monsanto, 1979f in Monsanto, 1984
Eye Irritation						
Glyphosate Rabbit	Single application of 0.1 ml of 25% wt/vol aqueous suspension into the conjunctival sac of the eye, evaluated at 24, 48 and 6 9/110	---	---	---	Slightly irritating resulting in corneal opacity and ulceration in 1 of 6 rabbits tested; all ocular irritation disappeared within seven days, the average Draize score was 72 hours	Monsanto, 1979g in Monsanto, 1984

Table 5-1 (continued)

Summary of Mammalian Toxicity Studies on Glyphosate, Glyphosate Isopropylamine (IPA-G) and Roundup

Type of Test / Formulation / Species	Nature of Exposure	Effects NOEL	Effects LEL	Effects LD50	Comments	Reference
IPA-G						
Rabbit	Single application of 0.1 ml of 25% wt/vol aqueous suspension into the conjunctival sac of the eye, evaluated at 24, 48 and 72 hours.	---	---	---	Essentially nonirritating with average Draize score of 0/110	Monsanto, 1981c in Monsanto, 1984
Roundup						
Rabbit	Single application of 0.1 ml of 25% wt/vol aqueous suspension into the conjunctival sac of the eye, evaluated at 24, 48 and 72 hours.	---	---	---	Moderate irritation resulting in ocular irritation that disappeared within 10 days.	Monsanto, 1975b in Monsanto, 1984
Roundup						
Rat	Rats exposed for four hours, details not specified	---	---	25 (3.18)	The four hour LC50 was 25 mg/l air based on nominal concentrations (3.18 mg/l air based on an analytical determination)	Monsanto, 1982b in Monsanto, 1984
Rat	Exposed for four hours to a 2% vol/vol spray mix solution resulting in a nominal concentration of 4.89 mg solution/l air.	4.89	---	---	No signs of toxicity observed	Monsanto, 1981d in Monsanto,
Subchronic, dermal		**mg/kg/day**				
Glyphosate						
Rabbit	Repeated dermal applications of 0, 100, 1,000 or 5,000 mg/kg/day for 15 days in a 21-day period	1,000	5,000	---	Adverse effects were limited to localized skin irritation, slight erythema and edema in the 5,000 mg/kg/day dosage group only. The NOEL was determined to be 1,000 mg/kg/day for dermal effects and 5,000 mg/kg/day systemic effects by the dermal route	Monsanto, 1982c in Monsanto, 1984

Table 5-1 (continued)

Summary of Mammalian Toxicity Studies on Glyphosate, Glyphosate Isopropylamine (IPA-G) and Roundup

Type of Test / Formulation / Species	Nature of Exposure	Effects NOEL	Effects LEL	Effects LD50	Comments	Reference
Roundup						
Rabbit	Repeated dermal applications at a concentration 5 times the intended spray mix concentration (6.4% vol/vol) for 5 days per week for three weeks.	---	---	---	Produced both severe local irritation and signs of systemic toxicity, which included reduced food consumption, body weight loss, testicular atrophy and death.	Monsanto, 1972 in Monsanto, 1984
Rabbit	Repeated dermal applications at a concentration 3 times the intended spray mix concentration for 5 days per week for three weeks.	---	---	---	No signs of systemic effects and only moderate local irritation were observed.	Monsanto, 1973d in Monsanto, 1984
Skin Sensitization						
Glyphosate						
Guinea pig	Glyphosate was initially applied to the shaved skin of guinea pigs 6 hr/day, 3 days/week for 3 weeks. After a 2-week exposure-free interval, animals were then topically challenged with another dermal application of glyphosate.	---	---	---	Glyphosate produced no irritation following initial exposure, moderate to severe edema and/or necrosis in some animals with subsequent exposures in the induction phase, but no dermal sensitization upon challenge.	Monsanto, 1984
Subchronic, Inhalation		mg/l				
Roundup						
Rat	Male and female rats were exposed to aerosol concentrations of up to 0.36 mg of an aqueous solution of Roundup (1:2 Roundup	No NOEL	36	---	Adverse effects were limited to minor nasal irritation	Monsanto, 1983a in Monsanto, 1984

Table 5-1 (continued)

Summary of Mammalian Toxicity Studies on Glyphosate, Glyphosate Isopropylamine (IPA-G) and Roundup

Type of Test / Formulation / Species	Nature of Exposure	Effects: NOEL	Effects: LEL	Effects: LD50	Comments	Reference
Subchronic, oral		mg/kg/day				
Glyphosate						
Rat	Four groups of rats were maintained on diets containing 0, 200, 2,000, 5,000 or 12,500 ppm glyphosate (equivalent to 0, 13, 135, 340, 825 mg/kg/day) for 90 days.	135	340	---	No deaths occurred and no treatment-related changes in hematology, clinical chemistry, urinalysis, or gross pathology were reported. Both absolute and relative lung weights of male rats fed 5,000 ppm and males and females at the 12,500 ppm dosage level were significantly increased over control values.	Monsanto, 1979h in Monsanto, 1984
Mouse	Groups of mice were fed diets containing up to 50,000 ppm glyphosate for 90 days (equivalent to 12,225 mg/kg/day).	2,305	12,225	---	Adverse effects were limited to depressed growth, as indicated by reduced body weight gains at the 50,000 ppm dosage level. No gross or histopathological tissue changes observed in any of the treated animals were considered to be treatment-related.	Monsanto, 1979i in Monsanto, 1984
Reproductive		mg/kg/day				
Glyphosate						
Rat	In a three-generation reproductive study, male and female rats were fed diets containing 0, 3, 10 or 30 mg glyphosate/kg/day. Treatment began prior to mating and continued through the production of the two litters for each of three generations. R = reproductive, S = systemic	R: 30	---	---	No adverse effects in any of the parameters that evaluate reproductive capability, such as fertility, gestation, viability, or lactation indexes, were observed in treated parental animals or offspring. Renal focal tubular dilation in males of the F1 generation was observed at the 30 mg/kg/day level	Monsanto, 1981e in Monsanto, 1984
		S: 10	30	---		

Table 5-1 (continued)

Summary of Mammalian Toxicity Studies on Glyphosate, Glyphosate Isopropylamine (IPA-G) and Roundup

Type of Test / Formulation / Species	Nature of Exposure	Effects: NOEL	Effects: LEL	Effects: LD50	Comments	Reference
Teratogenic		mg/kg/day				
Glyphosate						
Rat, Charles River CD	Groups of 25 female rats were given glyphosate by gavage at dosage levels of 0, 300, 1,000 or 3,500 mg/kg/day from day 6 through 19 of the gestation period, all surviving rats were sacrificed on day 20. M = maternal, F = fetotoxic, T = teratogenic.	M: 1,000 F: 1,000 T: 3,500	3,500 3,500 ---	--- --- ---	Maternal toxicity consisting of reduced body weight gains, stomach hemorrhages, soft stools, diarrhea, and nasal discharge occurred in the 3,500 mg/kg/day dosage group. A significant increase in delayed ossification of sternebrae occurred in the 3,500 mg/kg/day group. No significant teratogenic effects were reported at any dose tested, however, 6 fetuses of 187 fetuses (from one litter) at the high dose level exhibited major structural malformations.	Monsanto, 1980a in Monsanto, 1984
Rabbit	Administered by gavage to groups of 16 pregnant rabbits at dosage levels of 0, 75, 175 or 350 mg/kg/day from day 6 through 27 of gestation, all survivors were sacrificed at day 28. M = maternal, F = fetotoxic, T = teratogenic	M: 175 F: 350 T: 350	350 --- ---	--- --- ---	At 350 mg/kg/day most of the does exhibited signs of adverse effects including soft stools, diarrhea, and nasal charge. No impairment in reproductive capability was evident at any dose tested. No significant increases in fetotoxicity or teratogenicity occurred at any dose tested. Incidences of fetotoxic effects were not significantly different from control and were within the range of historical controls However, major structural malformations were observed in two fetuses in the 175 mg/kg/day dose group, and one fetus in the 350 mg/ kg/day dose group	Monsanto, 1980b in Monsanto, 1984

Table 5-1 (continued)

Summary of Mammalian Toxicity Studies on Glyphosate, Glyphosate Isopropylamine (IPA-G) and Roundup

Type of Test Formulation Species	Nature of Exposure	Effects NOEL	 LEL	 LD50	Comments	Reference
Carcinogenic		mg/kg/day				
Glyphosate Rat	Groups of 26 rats/sex/dose group were fed diets containing up to 31 mg/kg/day for 26 months.	31	---	---	No adverse treatment-related effects were reported. Adverse effects included age-related respiratory disease and progressive neuropathy. No significant differences in total tumor bearing animals or total number of animals with malignant tumors were observed. Increased incidence of two individual tumor types was within the range of historical controls, and not considered treatment-related.	Monsanto, 1981f in Monsanto, 1984
Mouse Charles River CD	50 animals/sex/dose groups, were fed glyphosate at dietary levels of 0, 1,000, 5,000 or 30,000 ppm for 24 months; were equivalent to time-weighted averages of 0, 157, 814 or 4,841 mg/kg/day for males and 0, 190, 965 or 5,874 mg/kg/day for females.	Males: 157 Females: 5,874	814 ---	--- ---	No physical or behavioral signs of treatment-related toxicity were observed. Neither the percentage of total tumor bearing animals nor the number of animals with malignant tumors showed dose-dependent increases, or were significantly different from the control. The majority of tumors observed in the control and the treated groups were bronchiolar-alveolar adenomas and adenocarcinomas, hepatocellular adenomas and carcinomas, and tumors of the lymphoreticular system, none of which were considered to be treatment-related. A possible treatment-related increased incidence of renal tubule adenomas in male mice was observed. In male mice, the incidence of renal tubule was 1/49 in concurrent controls, 0/49 in the low dose (1,000 ppm), 1/50 in the mid dose (5,000 ppm), and 3/50 in the high dose (30,000 ppm) No renal tubule adenomas were observed in female mice	Monsanto, 1983d in Monsanto, 1984

*Information unavailable or not applicable

Table 5-2

NOEL and LEL Used in Calculation of
Margin of Safety for Noncarcinogenic Effects
Resulting from Exposure to Glyphosate

Effect	Study	NOEL mg/kg/day	LEL mg/kg/day	Reference
Systemic Toxicity	Three generation reproduction male and female rats fed diets containing 0, 3, 10 or 30 mg/kg/day throughout life.	10	30[a]	Monsanto, 1981e
Reproductive	Three generation reproduction-rat. Male and females rats fed diets containing 0, 3, 10 or 30 mg/kg/day. Treatment began prior to mating and continued through the production of two litters for each of three generations.	30	--	Monsanto, 1981e
Teratogenic	Teratogenic-rabbit. Groups of 16 rabbits/dose administered by gavage 0, 75, 175 or 350 mg/kg/day from day 6 through 27.	75	175[b]	Monsanto, 1980b

[a]At 30 mg/kg/day, male rats of the F_{3b} generation exhibited renal focal tubular dilation.

[b]No significant incidence of teratogenic effects were reported at any dose tested in this study, however a non-significant occurrence structural defects were observed at 175 mg/kg/day and 350 mg/kg/day. Although not statistically significant, their presence was considered in this worst case analysis. The NOEL reported by the authors was 350 mg/kg/day.

Table 5-3

Tumor Incidence Data on Mice
Administered Glyphosate in the Diet

Sex	Tumor Type	Dose (mg/kg/day)[a] 0	157	814	4,841
Males	Renal Tubular Adenoma	1/50	0/49	1/50	3/50

[a]Doses in mg/kg/day derived from time-weighted averages based on dosage levels of 0, 1,000, 5,000 or 30,000 ppm in the diet.

Table 5-4

Results of Multistage Model Fitting to Glyphosate Carcinogenesis Dose-Response Data in Table 5-3[a]

Maximum Likelihood Estimates of Model Parameters[b]	Goodness-of-Fit Test Results: Chi-square	Degrees of Freedom	p-value
$q_0 = 1.14 \times 10^{-2}$ $q_1 = 5.47 \times 10^{-6}$ $q_2 = 1.04 \times 10^{-9}$ $q_3 = 0$	0.98	1	0.33

Carcinogenic potency parameter, q_1^*
(95% upper statistical confidence limit on q_1)[d]

$$q_1^* = 2.5656 \times 10^{-5} \text{ (mg/kg/day)}^{-1}$$

[a]Incidence of renal tubule adenoma in male Charles River CD-1, COBS mice.

[b]Maximum likelihood estimates of extra risk are obtained from these parameters using the formula

$$\frac{P(d) - P(0)}{1 - P(0)} = 1 - \exp(-q_1 d - q_2 d^2 - q_3 d^3),$$

where d is dose in mg/kg/day (see Chapter 3.3).

[c]Results of the goodness of fit test indicates how well the multistage model fits the animal data. A p-value of 1.0 indicates a perfect fit. Smaller p-values indicate poorer fits. A p-value of less than 0.01 is often considered to indicate an unacceptable fit.

[d]Worst case estimates of human risk are calculated by converting worst case estimates of total human exposure in mg/kg to an average lifetime exposure in mg/kg/day by dividing by 25,500 days (70 years) and then multiplying the average lifetime dose by 1.3 q_1^*. The factor 1.3 results from assuming exposure occurs when a person is 20 years old (see Chapter 3.3).

Table 5-5

Margin of Safety for Noncarcinogenic
Systemic Effects from Exposure to Glyphosate
through a Single Spraying Episode

Exposure Scenario	More Reasonable: Estimated Human Exposure[a] (µg/kg/day)	More Reasonable: Margin of Safety[b]	Worst Case: Estimated Human Exposure[a] (µg/kg/day)	Worst Case: Margin of Safety[b]
Occupational				
Pilot	10.00	1000.00	63.00	158.73
Loader	18.00	555.56	72.00	138.89
Mechanic	3.00	3333.33	15.00	666.67
Observer	2.00	5000.00	8.00	1250.00
Environmental				
Inhalation	0.483	20703.93	6.57	1522.07
Dermal Absorption	0.192	52083.33	4.83	2070.39
Ingestion-Water	0.0182	549450.55	10.10	990.10
Ingestion-Wild Meat	0.123	81300.81	5.19	1926.78
Ingestion-Fish	0.0091	109890.11	2.51	3984.06
Ingestion-Wild Berries	6.16	1623.38	33.60	297.62
Ingestion-Garden Vegetables	0.416	24038.46	1.12	8928.57

[a]Estimated single-day exposures in mg/kg/day, as calculated in Chapter 2, were converted to µg/kg/day by multiplying each value by 1000.

[b]Margin of safety calculated by dividing the NOEL in rats (10 mg/kg/day) by the estimated exposure. The margin of safety indicates the number of times lower the estimated exposure is than the NOEL.

[c]The observer refers to a local representative, district manager, forester, etc.

Table 5-6

Margin of Safety for Noncarcinogenic Reproductive Effects from Exposure to Glyphosate through a Single Spraying Episode

Exposure Scenario	More Reasonable: Estimated Human Exposure[a] (µg/kg/day)	More Reasonable: Margin of Safety[b]	Worst Case: Estimated Human Exposure[a] (µg/kg/day)	Worst Case: Margin of Safety[b]
Occupational				
Pilot	10.00	3000.00	63.00	476.19
Loader	18.00	1666.67	72.00	416.67
Mechanic	3.00	10000.00	15.00	2000.00
Observer	2.00	15000.00	8.00	3750.00
Environmental				
Inhalation	0.483	62111.80	6.57	4566.21
Dermal Absorption	0.192	156250.00	4.83	6211.18
Ingestion-Water	0.0182	1648351.65	10.10	2970.30
Ingestion-Wild Meat	0.123	243902.44	5.19	5780.35
Ingestion-Fish	0.0091	3296703.30	2.51	11952.19
Ingestion-Wild Berries	6.16	4870.13	33.60	892.86
Ingestion-Garden Vegetables	0.416	72115.38	1.12	26785.71

[a]Estimated single-day exposures in mg/kg/day, as calculated in Chapter 2, were converted to µg/kg/day by multiplying each value by 1000.

[b]Margin of safety calculated by dividing the NOEL in rats (30 mg/kg/day) by the estimated exposure. The margin of safety indicates the number of times lower the estimated exposure is than the NOEL.

[c]The observer refers to a local representative, district manager, forester, etc.

Table 5-7

Margin of Safety for Noncarcinogenic
Teratogenic Effects from Exposure to Glyphosate
through a Single Spraying Episode

Exposure Scenario	More Reasonable: Estimated Human Exposure[a] (µg/kg/day)	More Reasonable: Margin of Safety[b]	Worst Case: Estimated Human Exposure[a] (µg/kg/day)	Worst Case: Margin of Safety[b]
Occupational				
Pilot	10.00	7500.00	63.00	1190.48
Loader	18.00	4166.67	72.00	1041.67
Mechanic	3.00	25000.00	15.00	5000.00
Observer	2.00	37500.00	8.00	9375.00
Environmental				
Inhalation	0.483	155279.50	6.57	11415.53
Dermal Absorption	0.192	390625.00	4.83	15527.95
Ingestion-Water	0.0182	4120879.12	10.10	7425.74
Ingestion-Wild Meat	0.123	609756.10	5.19	14450.87
Ingestion-Fish	0.0091	8241758.20	2.51	29880.48
Ingestion-Wild Berries	6.16	12175.32	33.60	2232.14
Ingestion-Garden Vegetables	0.416	180288.46	1.12	66964.29

[a]Estimated single-day exposures in mg/kg/day, as calculated in Chapter 2, were converted to µg/kg/day by multiplying each value by 1000.

[b]Margin of safety calculated by dividing the NOEL in rabbits (75 mg/kg/day) by the estimated exposure. The margin of safety indicates the number of times lower the estimated exposure is than the NOEL.

[c]The observer refers to a local representative, district manager, forester, etc.

NOTE: Margins of safety for fetotoxic effects are calculated by dividing the NOEL in rabbits of 350 mg/kg/day by the estimated human exposures; therefore, all margins of safety in this table would be increased by a factor of 4.67.

Table 5-8

Lifetime Carcinogenic Risk to General Public from Exposure to Glyphosate through Single Spraying Episode

Glyphosate has not been shown to be a carcinogen. Estimates of risk in this table have been derived from negative data (no significantly increased incidence in tumors were reported), and are based on the assumption that a carcinogenic risk might exist.

Exposure Scenario	More Reasonable Exposure (mg/kg)[a]	More Reasonable Risk[b]	Worst Case Exposure (mg/kg)[a]	Worst Case Risk[b]
Occupational				
Pilot	1.0×10^{-2}	2.78×10^{-12}	6.3×10^{-2}	8.22×10^{-11}
Loader	1.8×10^{-2}	5.01×10^{-12}	7.2×10^{-2}	9.37×10^{-11}
Mechanic	3.0×10^{-3}	8.34×10^{-13}	1.5×10^{-2}	1.96×10^{-11}
Supervisor[c]	2.0×10^{-3}	5.56×10^{-13}	8.0×10^{-3}	1.04×10^{-11}
Environmental				
Inhalation	1.30×10^{-3}	3.61×10^{-13}	1.77×10^{-2}	2.31×10^{-11}
Dermal Absorption	1.19×10^{-3}	3.31×10^{-13}	1.79×10^{-1}	2.33×10^{-10}
Ingestion - Water	1.82×10^{-5}	5.06×10^{-15}	1.87×10^{-2}	2.45×10^{-11}
Ingestion - Wild Meat	2.46×10^{-3}	6.84×10^{-13}	1.97×10^{-2}	2.57×10^{-11}
Ingestion - Fish	1.82×10^{-4}	5.06×10^{-14}	5.02×10^{-2}	6.53×10^{-11}
Ingestion - Wild Berries	1.23×10^{-1}	3.42×10^{-11}	6.72×10^{-1}	8.77×10^{-10}
Ingestion - Garden Vegetables	8.32×10^{-3}	2.31×10^{-12}	2.24×10^{-2}	2.92×10^{-11}

Table 5-8 (continued)

Lifetime Carcinogenic Risk to General Public from Exposure to Glyphosate through Single Spraying Episode

[a]Exposure estimates from Chapter 2. More reasonable and worst case occupational exposures correspond to more reasonable and maximum expected exposures from Chapter 2. More reasonable and worst case environmental exposures correspond to more reasonable and worst case total exposures to general public from Chapter 2.

[b]Extra risk corresponding to given exposures, estimated from dose-response data on renal tubular adenoma in mice. Realistic and worst case estimates of extra risk are based on maximum likelihood estimates and upper 95% confidence limits, respectively, from the multistage model. Animal to human dose conversion is based on average doses in mg glyphosate/kg body weight/day over a lifetime. If conversion were based on mg glyphosate/m^2 surface area/day, then risk estimates would be increased by a factor of approximately 13. The risk estimates have been multiplied by a factor of 1.3 to reflect equivalent risk from short-term exposure at age 20 to a given total dose, as opposed to an average daily dose over a 70-year lifetime (see Chapter 3.3).

[c]Includes local representative, district manager and area forester.

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EPA **R.E.D. FACTS**

Glyphosate

Pesticide Reregistration

All pesticides sold or distributed in the United States must be registered by EPA, based on scientific studies showing that they can be used without posing unreasonable risks to people or the environment. Because of advances in scientific knowledge, the law requires that pesticides which were first registered years ago be reregistered to ensure that they meet today's more stringent standards.

In evaluating pesticides for reregistration, EPA obtains and reviews a complete set of studies from pesticide producers, describing the human health and environmental effects of each pesticide. The Agency imposes any regulatory controls that are needed to effectively manage each pesticide's risks. EPA then reregisters pesticides that can be used without posing unreasonable risks to human health or the environment.

When a pesticide is eligible for reregistration, EPA announces this and explains why in a Reregistration Eligibility Decision (RED) document. This fact sheet summarizes the information in the RED document for glyphosate.

Use Profile

Glyphosate is a non-selective herbicide registered for use on many food and non-food field crops as well as non-crop areas where total vegetation control is desired. When applied at lower rates, glyphosate also is a plant growth regulator.

Glyphosate is among the most widely used pesticides by volume. It ranked eleventh among conventional pesticides used in the U.S. during 1990-91. In recent years, approximately 13 to 20 million acres were treated with 18.7 million pounds of glyphosate annually. The largest use sites include hay/pasture, soybeans and field corn.

Three salts of glyphosate are used as active ingredients in registered pesticide products. Two of these active ingredients, plus technical grade glyphosate, are contained in the 56 products that are subject to this RED.

The isopropylamine salt, an active ingredient in 53 registered products, is used as a herbicide to control broadleaf weeds and grasses in many food and non-food crops and a variety of other sites including ornamentals, lawns and turf, residential areas, greenhouses, forest plantings and industrial rights-of-way. It is formulated as a liquid, solid or pellet/tablet, and is applied using ground or aerial equipment.

The sodium salt of glyphosate, an active ingredient in two registered pesticide products, is used as a plant growth regulator for peanuts and sugarcane, to modify plant growth and hasten the ripening of fruit. It is applied as a ground spray to peanut fields and as an aerial spray to sugarcane. Preharvest intervals are established for both crops.

The monoammonium salt of glyphosate is an active ingredient in an additional seven herbicide/growth regulator products. This form of glyphosate was initially registered after November 1984, so it is not subject to reregistration or included in this RED. However, in reassessing the existing glyphosate tolerances (maximum residue limits in or on food and feed), EPA included those for the monoammonium salt.

Regulatory History

EPA issued a Registration Standard for glyphosate in June 1986 (NTIS PB87-103214). The Registration Standard required additional phytotoxicity, environmental fate, toxicology, product chemistry and residue chemistry studies. All of the data required have been submitted and reviewed, or were waived.

Human Health Assessment

Toxicity

Glyphosate is of relatively low oral and dermal acute toxicity. It has been placed in Toxicity Category III for these effects (Toxicity Category I indicates the highest degree of acute toxicity, and Category IV the lowest). The acute inhalation toxicity study was waived because glyphosate is non-volatile and because adequate inhalation studies with end-use products exist showing low toxicity.

A subchronic feeding study using rats showed blood and pancreatic effects. A similar study with mice showed reduced body weight gains in both sexes at the highest dose levels. A dermal study with rabbits showed slight reddening and swelling of the skin, decreased food consumption in males and decreased enzyme production, at the highest dose levels.

Several chronic toxicity/carcinogenicity studies using rats, mice and beagle dogs resulted in no effects based on the parameters examined, or resulted in findings that glyphosate was not carcinogenic in the study. In June 1991, EPA classified glyphosate as a Group E oncogen--one that shows evidence of non-carcinogenicity for humans--based on the lack of convincing evidence of carcinogenicity in adequate studies.

In developmental toxicity studies using pregnant rats and rabbits, glyphosate caused treatment-related effects in the high dose groups including diarrhea, decreased body weight gain, nasal discharge and death.

One reproductive toxicity study using rats showed kidney effects in the high dose male pups; another study showed digestive effects and decreased body weight gain. Glyphosate does not cause mutations.

In one metabolism study with rats, most of the glyphosate administered (97.5 percent) was excreted in urine and feces as the parent compound; less than one percent of the absorbed dose remained in tissues and organs, primarily in bone tissue. Aminomethyl phosphonic acid (AMPA) was the only metabolite excreted. A second study using rats showed that very little glyphosate reaches bone marrow, that it is rapidly eliminated from bone marrow, and that it is even more rapidly eliminated from plasma.

Dietary Exposure

The nature of glyphosate residue in plants and animals is adequately understood. Studies with a variety of plants indicate that uptake of glyphosate or AMPA from soil is limited. The material which is taken up is readily translocated throughout the plant and into its fruit. In animals, most glyphosate is eliminated in urine and feces. Enforcement methods are available to detect residues of glyphosate and AMPA in or on plant commodities, in water and in animal commodities.

85 tolerances have been established for residues of glyphosate and its metabolite, AMPA, in or on a wide variety of crops and crop groups, as well as in many processed foods, animal feed and animal tissues (please see 40 CFR 180.364, 40 CFR 185.3500 and 40 CFR 186.3500). EPA has reassessed the existing and proposed tolerances for glyphosate. Though some adjustments will be needed, no major changes in existing tolerances are required. EPA also has compared the U.S. tolerances with international Codex maximum residue limits (MRLs), and is recommending certain adjustments to achieve greater compatibility.

EPA conducted a dietary risk assessment for glyphosate based on a worst-case risk scenario, that is, assuming that 100 percent of all possible commodities/acreage were treated, and assuming that tolerance-level residues remained in/on all treated commodities. The Agency concluded that the chronic dietary risk posed by glyphosate food uses is minimal.

A reference dose (RfD), or estimate of daily exposure that would not cause adverse effects throughout a lifetime, of 2 mg/kg/day has been proposed for glyphosate, based on the developmental toxicity studies described above.

Occupational and Residential Exposure

Occupational and residential exposure to glyphosate can be expected based on its currently registered uses. However, due to glyphosate's low acute toxicity and the absence of other toxicological concerns (especially carcinogenicity), occupational and residential exposure data are not required for reregistration.

Some glyphosate end-use products are in Toxicity Categories I or II for primary eye irritation or skin irritation. In California, glyphosate ranks high among pesticides causing illness or injury to workers, who report numerous incidents of eye and skin irritation from splashes during mixing and loading.

EPA is not adding any personal protective equipment (PPE) requirements at this time, but any existing PPE label requirements must be retained.

The Worker Protection Standard (WPS) for Agricultural Pesticides (please see 40 CFR 156 and 170) established an interim restricted entry interval (REI) of 12 hours for glyphosate. The Agency has decided to retain this REI as a prudent measure to mitigate risks to workers. During the REI, workers may reenter areas treated with glyphosate only in the few, narrow exceptions allowed in the WPS. The REI applies only to glyphosate uses within the scope of the WPS, so homeowner and commercial uses are not included.

Human Risk Assessment

EPA's worst case risk assessment of glyphosate's many registered food uses concludes that human dietary exposure and risk are minimal. Existing and proposed tolerances have been reassessed, and no significant changes are needed to protect the public.

Exposure to workers and other applicators generally is not expected to pose undue risks, due to glyphosate's low acute toxicity. However, splashes during mixing and loading of some products can cause injury, primarily eye and skin irritation. EPA is continuing to recommend PPE, including protective eye wear, for workers using end-use products that are in Toxicity Categories I or II for eye and skin irritation. To mitigate potential risks associated with reentering treated agricultural areas, EPA is retaining the 12 hour REI set by the WPS.

Environmental Assessment

Environmental Fate

Glyphosate adsorbs strongly to soil and is not expected to move vertically below the six inch soil layer; residues are expected to be immobile in soil. Glyphosate is readily degraded by soil microbes to AMPA, which is degraded to carbon dioxide. Glyphosate and AMPA are not likely to move to ground water due to their strong adsorptive characteristics. However, glyphosate does have the potential to contaminate surface waters due to its aquatic use patterns and through erosion, as it adsorbs to soil particles suspended in runoff. If glyphosate reached surface water, it would not be broken down readily by water or sunlight.

Ecological Effects

Glyphosate is no more than slightly toxic to birds and is practically non-toxic to fish, aquatic invertebrates and honeybees. Due to the presence of a toxic inert ingredient, some glyphosate end-use products must be labeled, "Toxic to fish," if they may be applied directly to aquatic environments. Product labeling does not preclude off-target movement of glyphosate by drift. EPA therefore is requiring three additional terrestrial plant studies to assess potential risks to nontarget plants.

EPA does not expect that most endangered terrestrial or aquatic organisms will be affected by the registered uses of glyphosate. However,

many endangered plants as well as the Houston toad (due to its habitat) may be at risk. EPA is deferring any use modifications or labeling amendments until it has published the Endangered Species Protection Plan and has given registrants guidance regarding endangered species precautionary labeling.

Ecological Effects Risk Assessment

Based on current data, EPA has determined that the effects of glyphosate on birds, mammals, fish and invertebrates are minimal. Under certain use conditions, glyphosate may cause adverse effects to nontarget aquatic plants. Additional data are needed to fully evaluate the effects of glyphosate on nontarget terrestrial plants. Risk reduction measures will be developed if needed, once the data from these studies are submitted and evaluated.

Additional Data Required

EPA is requiring three generic studies (Tier II Vegetative Vigor, Droplet Size Spectrum, and Drift Field Evaluation) which are not part of the target data base and do not affect the reregistration eligibility of glyphosate. The Agency also is requiring product-specific data including product chemistry and acute toxicity studies, as well as revised Confidential Statements of Formula and revised labeling.

Product Labeling Changes Required

All end-use glyphosate products must comply with EPA's current pesticide product labeling requirements. In addition:

- **Protection of Aquatic Organisms**

Non-Aquatic Uses - End-use products that are not registered for aquatic uses must bear the following label statement:

Do not apply directly to water, to areas where surface water is present or to intertidal areas below the mean high water mark. Do not contaminate water when disposing of equipment washwaters and rinsate.

Aquatic Uses - End-use products registered for aquatic uses must bear the following label statement:

Do not contaminate water when disposing of equipment washwaters and rinsate. Treatment of aquatic weeds can result in oxygen loss from decomposition for dead plants. This loss can cause fish kills.

- **Worker Protection Standard (WPS) Requirements**

Any product whose labeling permits use in the production of an agricultural plant on any farm, forest, nursery or greenhouse must comply with the labeling requirements of:

• PR Notice 93-7, "Labeling Revisions Required by the Worker Protection Standard (WPS)," and

- PR Notice 93-11, "Supplemental Guidance for PR Notice 93-7."

Unless specifically directed in the RED, all statements required by these two PR Notices must appear on product labeling exactly as instructed in the Notices. Labels must be revised by April 21, 1994, for products distributed or sold by the primary registrant or supplementally registered distributors, and by October 23, 1995, for products distributed or sold by anyone.

- **Personal Protective Equipment (PPE)**

No new PPE requirements must be added to glyphosate labels. However, any existing PPE requirements on labels must be retained.

- **Entry Restrictions**

Products Not Primarily Intended for Home Use:

o Uses Within the Scope of the WPS - A 12-hour restricted entry interval (REI) is required for all products with uses within the scope of the WPS, except products intended primarily for home use. The PPE for early entry should be that required for applicators of glyphosate, except any applicator requirement for an apron or respirator is waived. This REI and PPE should be inserted into the standardized statements required by PR Notice 93-7.

- Sole Active Ingredient End-Use Products - Labels must be revised to adopt the entry restrictions set forth in this section. Any conflicting entry restrictions on current labeling must be removed.
- Multiple Active Ingredient Products - Registrants must compare the entry restrictions set forth in this section to those on their current labeling and retain the more protective. A specific time period in hours or days is considered more protective than "until sprays have dried" or "dusts have settled."

o Uses Not Within the Scope of the WPS - No new entry restrictions must be added. However, any entry restrictions on current product labeling with these uses must be retained.

Products Primarily Intended for Home Use:

o No new entry restrictions must be added. However, any entry restrictions on current product labeling must be retained.

Regulatory Conclusion

The use of currently registered pesticide products containing the isopropylamine and sodium salts of glyphosate in accordance with the labeling specified in this RED will not pose unreasonable risks or adverse effects to humans or the environment. Therefore, all uses of these products are eligible for reregistration.

These glyphosate products will be reregistered once the required product-specific data, revised Confidential Statements of Formula and revised labeling are received and accepted by EPA.

Products which contain active ingredients in addition to glyphosate will not be reregistered until all their other active ingredients also are eligible for reregistration.

For More Information

EPA is requesting public comments on the Reregistration Eligibility Decision (RED) document for glyphosate during a 60-day time period, as announced in a Notice of Availability published in the Federal Register. To obtain a copy of the RED document or to submit written comments, please contact the Pesticide Docket, Public Response and Program Resources Branch, Field Operations Division (7506C), Office of Pesticide Programs (OPP), US EPA, Washington, DC 20460, telephone 703- 305-5805.

Following the comment period, the glyphosate RED document will be available from the National Technical Information Service (NTIS), 5285 Port Royal Road, Springfield, VA 22161, telephone 703-487-4650.

For more information about EPA's pesticide reregistration program, the glyphosate RED, or reregistration of individual products containing glyphosate, please contact the Special Review and Reregistration Division (7508W), OPP, US EPA, Washington, DC 20460, telephone 703-308-8000.

For information about the health effects of pesticides, or for assistance in recognizing and managing pesticide poisoning symptoms, please contact the National Pesticides Telecommunications Network (NPTN). Call toll-free 1-800-858-7378, between 8:00 am and 6:00 pm Central Time, Monday through Friday.