Human Health and Ecological Risk Assessment for Borax (Sporax®) FINAL REPORT

USDA, Forest Service

Forest Health Protection
USDA Forest Service
Rosslyn Plaza Building C, Room 7129C
1601 North Kent Street
Arlington, VA 22209

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Contributors

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WORKSHEETS

ACRONYMS, ABBREVIATIONS, AND SYMBOLS

ACGIH	American Conference of Governmental Industrial Hygienists
a.e.	acid equivalents
AEL	adverse-effect level
a.i.	active ingredient
ALS	acetolactate synthase
ATSDR	Agency for Toxic Substances and Disease Registry
B	boron
BCF	bioconcentration factor
bw	body weight
CBI	confidential business information
CI	confidence interval
cm	centimeter
CNS	central nervous system
DAA	days after application
DAT	days after treatment
d.f.	degrees of freedom
EC_x	concentration causing X% inhibition of a process
EC_{25}	concentration causing 25% inhibition of a process
EC_{50}	concentration causing 50% inhibition of a process
ExToxNet	Extension Toxicology Network
F	female
FH	Forest Health
FIFRA	Federal Insecticide, Fungicide and Rodenticide Act
FOIA	Freedom of Information Act
FQPA	Food Quality Protection Act
g	gram
ha	hectare
HQ	hazard quotient
IAA	indole-3-acetic acid
IARC	International Agency for Research on Cancer
IRIS	Integrated Risk Information System
k_a	absorption coefficient
k_e	elimination coefficient
kg	kilogram
$K_{o/c}$	organic carbon partition coefficient
$K_{o/w}$	octanol-water partition coefficient
K_p	skin permeability coefficient
L	liter
lb	pound
LC_{50}	lethal concentration, 50% kill
LD_{50}	lethal dose, 50% kill

ACRONYMS, ABBREVIATIONS, AND SYMBOLS *(continued)*

LOAEL	lowest-observed-adverse-effect level
LOC	level of concern
m	meter
M	male
MMAD	mass median aerodynamic diameter
MCS	multiple chemical sensitivity mg milligram
mg/kg/day	milligrams of agent per kilogram of body weight per day
mg B/kg/day	milligrams of boron per kilogram of body weight per day
mL	milliliter
mM	millimole
MOS	margin of safety
MRID	Master Record Identification Number
MSDS	material safety data sheet
MW	molecular weight
NCAP	Northwest Coalition for Alternatives to Pesticides
NCI	National Cancer Institute
NIOSH	National Institute for Occupational Safety and Health
NOAEL	no-observed-adverse-effect level
NOEC	no-observed-effect concentration
NOEL	no-observed-effect level
NOS	not otherwise specified
NRC	National Research Council
NTP	National Toxicology Program
OM	organic matter
OPP	Office of Pesticide Programs
OPPTS	Office of Pesticide Planning and Toxic Substances
OSHA	Occupational Safety and Health Administration
ppm	parts per million
RBC	red blood cells
RED	re-registration eligibility decision
RfD	reference dose
SERA	Syracuse Environmental Research Associates
SGOT	serum glutamic oxaloacetic transaminase
SGPT	serum glutamic pyruvic transaminase
SRC	Syracuse Research Corporation
UF	uncertainty factor
U.S.	United States
USDA	U.S. Department of Agriculture
U.S. EPA	U.S. Environmental Protection Agency
USGS	U.S. Geological Survey
WCR	water contamination rate
WHO	World Health Organization
µ	micron

COMMON UNIT CONVERSIONS AND ABBREVIATIONS

To convert ...	Into ...	Multiply by ...
acres	hectares (ha)	0.4047
acres	square meters (m^2)	4,047
atmospheres	millimeters of mercury	760
centigrade	Fahrenheit	1.8 °C+32
centimeters	inches	0.3937
cubic meters (m^3)	liters (L)	1,000
Fahrenheit	centigrade	0.556 °F-17.8
feet per second (ft/sec)	miles/hour (mi/hr)	0.6818
gallons (gal)	liters (L)	3.785
gallons per acre (gal/acre)	liters per hectare (L/ha)	9.34
grams (g)	ounces, (oz)	0.03527
grams (g)	pounds, (oz)	0.002205
hectares (ha)	acres	2.471
inches (in)	centimeters (cm)	2.540
kilograms (kg)	ounces, (oz)	35.274
kilograms (kg)	pounds, (lb)	2.2046
kilograms per hectare (hg/ha)	pounds per acre (lb/acre)	0.892
kilometers (km)	miles (mi)	0.6214
liters (L)	cubic centimeters (cm^3)	1,000
liters (L)	gallons (gal)	0.2642
liters (L)	ounces, fluid (oz)	33.814
miles (mi)	kilometers (km)	1.609
miles per hour (mi/hr)	cm/sec	44.70
milligrams (mg)	ounces (oz)	0.000035
meters (m)	feet	3.281
ounces (oz)	grams (g)	28.3495
ounces per acre (oz/acre)	grams per hectare (g/ha)	70.1
ounces per acre (oz/acre)	kilograms per hectare (kg/ha)	0.0701
ounces fluid	cubic centimeters (cm^3)	29.5735
pounds (lb)	grams (g)	453.6
pounds (lb)	kilograms (kg)	0.4536
pounds per acre (lb/acre)	kilograms per hectare (kg/ha)	1.121
pounds per acre (lb/acre)	mg/square meter (mg/m^2)	112.1
pounds per acre (lb/acre)	µg/square centimeter ($\mu g/cm^2$)	11.21
pounds per gallon (lb/gal)	grams per liter (g/L)	119.8
square centimeters (cm^2)	square inches (in^2)	0.155
square centimeters (cm^2)	square meters (m^2)	0.0001
square meters (m^2)	square centimeters (cm^2)	10,000
yards	meters	0.9144

Note: All references to pounds and ounces refer to avoirdupois weights unless otherwise specified.

CONVERSION OF SCIENTIFIC NOTATION

Scientific Notation	Decimal Equivalent	Verbal Expression
$1 \cdot 10^{-10}$	0.0000000001	One in ten billion
$1 \cdot 10^{-9}$	0.000000001	One in one billion
$1 \cdot 10^{-8}$	0.00000001	One in one hundred million
$1 \cdot 10^{-7}$	0.0000001	One in ten million
$1 \cdot 10^{-6}$	0.000001	One in one million
$1 \cdot 10^{-5}$	0.00001	One in one hundred thousand
$1 \cdot 10^{-4}$	0.0001	One in ten thousand
$1 \cdot 10^{-3}$	0.001	One in one thousand
$1 \cdot 10^{-2}$	0.01	One in one hundred
$1 \cdot 10^{-1}$	0.1	One in ten
$1 \cdot 10^{0}$	1	One
$1 \cdot 10^{1}$	10	Ten
$1 \cdot 10^{2}$	100	One hundred
$1 \cdot 10^{3}$	1,000	One thousand
$1 \cdot 10^{4}$	10,000	Ten thousand
$1 \cdot 10^{5}$	100,000	One hundred thousand
$1 \cdot 10^{6}$	1,000,000	One million
$1 \cdot 10^{7}$	10,000,000	Ten million
$1 \cdot 10^{8}$	100,000,000	One hundred million
$1 \cdot 10^{9}$	1,000,000,000	One billion
$1 \cdot 10^{10}$	10,000,000,000	Ten billion

EXECUTIVE SUMMARY

OVERVIEW

The primary focus of this risk assessment is use of sodium tetraborate decahydrate to treat annosum root disease. Sodium tetraborate decahydrate, also know as borax, is the active ingredient and sole constituent in Sporax, the commercial formulation used by the Forest Service. While this risk assessment nominally concerns Sporax or borax, the agent of toxicologic concern is boron and exposures as well as toxicity information are expressed as boron equivalents in the analysis of risk.

Unlike most other risk assessments on pesticides used by the Forest Service, the agent of toxicologic concern in Sporax – i.e., boron – occurs naturally and exposures to boron are unavoidable. Except for the most extreme exposure scenario considered in this risk assessment – i.e., the direct consumption of Sporax from a tree stump by a child – the use of Sporax in Forest Service programs will not substantially contribute to boron exposures in humans. In addition, the use of Sporax in Forest Service programs will not typically or substantially contribute to concentrations of boron in water or soil.

The use of Sporax in the control of annosum root disease does not present a significant risk to humans or wildlife species under most conditions of normal use, even under the highest application rate. Given the highly focused application method for Sporax, application of granular product to cut tree stump surfaces, exposures considered for both the human health and environmental risk assessments are limited to those which are expected to result in significant exposure. Thus, the exposure scenarios evaluated in this risk assessment are as follows. For the human health risk assessment, the exposures considered are worker exposure via spill of granular product to the lower legs and hands, ingestion of applied Sporax by a child, and exposure via consumption of water contaminated by an accidental spill or by run-off. For exposure of wildlife species, the scenarios considered are the direct consumption of applied Sporax and ingestion of contaminated water by terrestrial vertebrates, exposure of aquatic species by water contaminated by an accidental spill or by runoff, and exposure of terrestrial plants to soil contaminated by runoff. The most significant risk of toxicity in both humans and wildlife species results from the direct consumption of Sporax applied to tree stumps.

For a child that consumes Sporax applied to a tree stump, hazard quotients exceed the level of concern for small children (HQ range of 2 to 16). Based on the highest exposure value modeled for this scenario, the estimated exposure to a child ingesting applied Sporax is less than the lowest reported lethal dose in children by factors of about 11 to 135. For workers and the general public, none of the other exposure scenarios considered yield hazard quotients that exceed the level of concern. Thus, based on this analysis, there is no basis for asserting that systemic toxic effects to workers or the general public will result from either acute or longer-term exposures, except by direct consumption. Borax can cause eye irritation. Quantitative risk assessments for irritation are not derived; however, from a practical perspective, eye irritation is likely to be the only overt effect as a consequence of mishandling Sporax. This effect can be minimized or avoided by prudent industrial hygiene practices during the handling of the compound.

For terrestrial species, risk associated with the application of Sporax to tree stumps appear to be very low. Most risk quotients are range from 0.000003 to 0.005 and are below the level of concern by factors of about 200 to over 330,000. There also does not appear to be a risk to terrestrial plants exposed to boron through runoff of Sporax applied to tree stumps; however, this assessment is based on relatively limited toxicity data. Since borax is used effectively in the control of fungi and insects, adverse effects of environmental exposures to nontarget insects and microorganisms are possible. However, given the atypical application method for Sporax, widespread exposures are not likely.

For aquatic animals and plants, hazard quotients marginally exceed the level of concern for amphibians for the worst-case accidental spill of 25 pounds of Sporax into a small pond (HQ, 1.3) and for the sensitive species of microorganisms for all accidental spill scenarios (HQs ranging from about 1 to 4). None of the other exposure scenarios results in hazard quotients that exceed the level of concern in any aquatic species. These results indicate that aquatic animals and plants are not at risk under the exposure scenarios considered; however, an accidental spill of large quantities of Sporax into a small pond may result in toxicity in amphibians and sensitive species of aquatic microorganisms.

PROGRAM DESCRIPTION

The primary focus of this risk assessment is sodium tetraborate decahydrate (Sporax®), also called borax decahydrate or borax. The Forest Service uses Sporax to limit the development of annosum root disease in conifer stands. Annosum root disease is caused by the fungus *Heterobasidion annosum*, which infects cut conifer stumps following thinning or cutting operations. Treatment of tree stumps with borax prevents annosus spores from establishing infections in tree stumps. The commercial borate sodium salt formulation currently used by the Forest Service is Sporax, which contains 100% sodium tetraborate decahydrate.

Sporax is applied to tree stump surfaces by dry application of the solid material. For this risk assessment, the typical application rate for Sporax will be taken as 1 lb/acre, with a range of 0.1 lb/acre to 5 lbs/acre to reflect plausible ranges that the Forest Service may use. That is, for the typical application rate of 1 lb/acre, given the density of stumps to be treated in a 1 acre conifer stand, a total of 1 lb of Sporax will be applied to cut tree stumps in the 1 acre plot. For this risk assessment, exposures are based on the typical application rate of 1 lb/acre rather than the full range of application rates. The consequences of varying application rates within the range of 0.1 lb/acre to 5 lbs/acre are considered in the risk characterization for human health and ecological effects. The Forest Service reported yearly application rates for borax ranging from about 0.111 lb/acre to 1.869 lbs/acre. Thus, the range of application rates calculated from actual use data encompasses the range of application rates used for this risk assessment (0.1 lb Sporax/acre to 5 lbs Sporax/acre).

HUMAN HEALTH RISK ASSESSMENT

Hazard Identification **–** The toxicity of borate compounds has been extensively studied in both humans and laboratory animals, with most studies conducted using boric acid and borax. Boric acid and borax have similar toxicological properties across different species. In order to facilitate any comparisons between borax and boric acid, data are expressed in terms of the dose or concentration of borate compound (borax or boric acid) and in terms of boron equivalents (B).

At physiologic pH, borate salts convert almost entirely to unionized boric acid; thus, boric acid and borate salts have similar toxicologic properties. Inorganic borates are well absorbed following oral administration, with an oral absorption of greater than 90% of the administered dose. Borates are not readily absorbed through intact skin but is more quickly absorbed across abraded skin. Percutaneous absorption of borax from intact human skin was shown to be very low, with a dermal permeability coefficient of 1.8×10^{-7} cm/hr. Boron is also absorbed following inhalation exposure to borate dust, but absorption does not appear to be complete. Borates are distributed in body soft tissues and eliminated in the urine, primarily in the form of boric acid, with a half-life of approximately 12 hours. Due to the excessive energy required to break the boron-oxygen bond, borates are not metabolized by humans or animals.

Based on the results of acute exposure studies, borax is classified as moderately toxic, with an LD_{50} in male rats of 4.5 g borax/kg. Clinical signs of toxicity observed following acute exposures include depression, ataxia and convulsions. In dogs, acute exposure to borax produced a strong dose-dependent emetic response. As expected of a compound with low percutaneous absorption, the LD_{50} of borax following single dermal application is > 5 g borax/kg in rats and >2 g borax/kg in rabbits. Results of a single inhalation exposure study yield a 4-hour LC_{50} > 2.0 mg borax/kg.

Results of developmental, subchronic and chronic toxicity studies show that the primary targets for borate toxicity are the developing fetus and the male reproductive system. Regarding developmental effects, gestational exposure of rats, mice, and rabbits to boric acid resulted in increased fetal deaths, decreased in fetal weight, and increased fetal malformations. The types of fetal malformations observed include anomalies of the eyes, central nervous system, cardiovascular system, and axial skeleton in rats, short rib XIII and other skeletal anomalies pertaining to ribs in mice, and cardiovascular malformations in rabbits. The most sensitive effect observed following gestational exposure to boric acid is decreased body weight. No mechanisms has been identified for the developmental effects of borates. Results of subchronic and chronic toxicity studies show that the testis is the primary target organ for borate compounds in adult animals. Testicular toxicity is characterized by atrophy of the testes, degeneration of the seminiferous epithelium, and sterility. Results of reproductive studies show a dose-dependent decrease in fertility in male rats and dogs, with dogs being slightly more sensitive than rats. At lower exposure levels, testicular effects and infertility may be reversed, but adverse effects can persist for at least 8 months at higher exposure levels. Results of one study in rats indicate that borax exposure may also reduce ovulation in female rats. Although no mechanisms has been identified for borax-induced toxicity to the male reproductive system, data are consistent with the

Sertoli cell as the primary target. Borax and borate compounds do not appear to act as direct neurotoxins or cause effects on immune system function. Studies assessing carcinogenic and mutagenic potential show no carcinogenic or mutagenic activity for borax and other borate compounds. Borax is not irritating to skin (Toxicity Category 4). Borax can cause severe irritation to eyes (Toxicity Category 1). In standard mammalian studies to assay ocular irritation, the damage persisted for the duration of the study – i.e., 14 days.

Exposure Assessment – Sporax is applied directly to freshly cut tree stumps. Sporax is not applied as a liquid using backpack, broadcast or aerial spray methods and it is not applied directly to vegetation. Therefore, many of the standard exposure scenarios that are typically considered for Forest Service risk assessments, such as direct spray, oral exposure *via* ingestion of contaminated vegetation and direct exposure from contaminated vegetation, are not applicable for this risk assessment. The exposure scenarios used in this risk assessment are those expected to result in potentially significant exposures considering the application method for Sporax that is used in Forest Service programs – i.e., dry application to the stumps of trees.

As with typical Forest Service risk assessments, exposure scenarios are presented for both workers and members of the general public. For workers, accidental exposure *via* direct contact of the hands and lower legs with granular Sporax during application is the only exposure scenario considered in this risk assessment. For this scenario, exposure values range from approximately 0.000005 mg B/kg/event for the lower bound limit resulting from a 1-hour exposure to 0.0002 mg B/kg/event for the upper bound resulting from an 8-hour exposure. Other exposure scenarios are not considered to be reasonably plausible given the atypical application method for Sporax.

For the general public, the exposure scenarios considered quantitatively in this risk assessment are ingestion of Sporax from tree stumps by a small child and ingestion of contaminated pond water by a child or a young woman. For ingestion of Sporax from tree stumps by a child, exposure values range from 0.43 to 3.24 mg B/kg/event and are based on the average daily soil consumption by a child. For ingestion of contaminated pond water, contamination of water by both an accidental spill scenario and by runoff from the application site are considered. Acute exposures values for a small child from ingestion of water contaminated *via* an accidental spill of Sporax into a small pond range from 0.015 mg B/kg to 0.14 mg B/kg/event. To determine exposures to pond water contaminated by runoff of Sporax applied to tree stumps, exposure estimates are modeled by GLEAMS. For acute exposure of a child ingesting water from a pond contaminated by runoff, values range from approximately 0.0003 to 0.01 mg B/kg/event. For chronic exposure of adults ingesting surface waters contaminated by runoff, exposure values range from approximately 0.00004 to 0.002 mg B/kg/day.

Dose-Response Assessment – The U.S. EPA (2004) has recently derived a chronic RfD of 0.2 mg/kg/day for boron (from boric acid and borates), using the combined data of two developmental toxicity studies in rats using decreased fetal weight as the most sensitive endpoint. The RfD is based benchmark dose analyses identifying a 5% decrease in mean fetal body weight compared to control as the benchmark response (BMR) level. The 95% lower bound on the dose

corresponding to the BMR, i.e., the $BMDL_{05}$, of 10.3 mg B/kg/day is used as the *critical dose* value to calculate the RfD. The uncertainty factor of 66, which considers both the toxicokinetic and toxicodynamic aspects associated with interspecies and interindividual variability, was applied to the critical dose to derive the chronic RfD of 0.2 mg B/kg/day. The U.S. EPA has not derived an acute RfD for boron. Therefore, the chronic RfD of 0.2 mg B/kg/day will also be used to characterize risks associated with incidents or accidents that involve an exposure period of 1 day.

Risk Characterization **–** For exposures considered in this risk assessment, with the exception of the accidental exposure of a child *via* consumption of Sporax from tree stump, all hazard quotients are below the level of concern. For worker exposure from granular Sporax spilled on the lower legs and hands, hazard quotients are well below the level of concern. Thus, workers do not appear to be at risk from Sporax under typical application conditions. Because boron compounds may be more rapidly absorbed across damaged skin, individuals with large areas of damaged skin should avoid the application of Sporax or exercise extra caution if they do apply Sporax or other boron-containing compounds. Borax can cause eye irritation. Quantitative risk assessments for irritation are not derived; however, from a practical perspective, eye irritation is likely to be the only overt effect as a consequence of mishandling Sporax. This effect can be minimized or avoided by prudent industrial hygiene practices during the handling of the compound.

For the general public, hazard quotients for consumption of Sporax from a tree stump by a child range from 2 to 16 for ingestion of 50 to 400 mg of Sporax (5.67 to 45.36 mg B/day). These estimated levels of exposure are below levels of exposure associated with nonlethal effects such as diarrhea and vomiting by factors of about 4 to 32. Documented lethal doses are in the range 505 mg B/kg/day and 765 mg B/kg/day, factors of about 11 to 135 below the estimated levels of exposure. Thus, while this exposure scenario raises concern in that the RfD could be substantially exceeded in a child directly consuming Sporax from a treated stump, the most likely adverse effects would probably be vomiting and diarrhea.

For consumption of water from a pond contaminated by Sporax due to runoff, none of the hazard quotients exceed the level of concern, even for the highest application rate of 5 lbs Sporax/acre. The highest hazard quotient for consumption of water contaminated by an accidental spill is 0.7, associated with a child consuming water contaminated by the spill of 25 pounds of Sporax into a small pond. Thus, based on this risk assessment, the only exposure scenario that appears to present a significant potential risk is exposure by direct consumption under upper bound conditions.

ECOLOGICAL RISK ASSESSMENT

Hazard Identification **–** Borate salts are rapidly converted to boric acid under conditions typically found in the environment. At physiologic pH and in most surface waters, exposure of organisms is primarily to boric acid. Therefore, information on boric acid is reviewed as appropriate and used as surrogate data in this risk assessment for borax. In order to facilitate any

comparisons between borax and boric acid, data are expressed in terms of the dose or concentration of borate compound (borax or boric acid) and in terms of boron equivalents (B).

In terrestrial mammals, the primary target organ for chronic borax exposure is the testis, with exposure resulting in decreased male fertility. In birds, acute exposure to borax is practically non-toxic, with no significant clinical signs of toxicity at dietary concentrations up to 5000 ppm borax (567 ppm B equivalent to 567 mg B/kg diet). Although limited data are available in birds, it appears that longer-term dietary exposure to boron compounds results in adverse reproductive effects in avian species. Very little information is available on the effects of boron compounds on nontarget terrestrial invertebrates. Based on the results of a single acute topical exposure study of honey bees (LD_{50} >362.58 µg boric acid/bee or 41.1 µg B/bee), boric acid is considered essentially non-toxic. However, given that borax is used in the control of termites, ants and house flies, toxic effects may occur in other insects.

Boron is an essential trace element for terrestrial plants. The amount of boron required to produce optimal growth and development varies tremendously between species and even between strains of the same species. However, excess boron can lead to the development of phytotoxicity. In most species, there is a narrow range between the amount of boron required for optimal growth and the amount that is phytotoxic. Standard bioassays for toxicity of boron compounds to terrestrial plants (Tier I and Tier II seedling emergence or vegetative vigor studies) were not identified in the available literature. While there are many studies evaluating the phytotoxicity of boron compounds, few provide data that are useful in a quantitative assessment of the risk of boron toxicity. Data are available for a limited number of terrestrial plants – potatoes, winter wheat, sugarbeet, poppy, oats and turnip. Based on the lowest reported NOAEC, the most sensitive species appears to be the potato, with an NOAEC of 5 mg B/kg soil and the most tolerant species appears to the sugarbeet, with an NOAEC of 20 mg B/kg soil. However, it is likely that more sensitive and more tolerant species exist.

In fish and aquatic invertebrates, acute exposure to borax and boric acid appears to have a relatively low order of toxicity. In fish, 96-hour LC_{50} values range from >100 mg B/L in razorback suckers and squawfish to >1100 mg B/L in bluegill sunfish. The 48-hour LC_{50} values for *Daphnia magna* range from 126 to 141 mg B/L. Limited information is available on chronic exposure of fish to boric acid and borax. Chronic reproduction studies in daphnids yield an NOAEC for reproductive effects of 6 mg B/L.

Relative to the abundant literature on the essential role of boron in terrestrial plants, very little information is available on the effects of boron compounds on aquatic macrophytes. Short-term exposure studies were conducted with boric acid in watermilfoil, water buttercup, and waterweed, with similar LC_{50} values reported for all three plant species (watermilfoil and waterweed: 5 mg B/L; water buttercup 10 mg B/L). In algae, the 72-hour LC_{50} values reported for *Scenedesmus subpicatus* range from 34 mg B/L to 52 mg B/L and the 72-hour NOAEC values range from 10 mg B/L to 24 mg B/L, with similar NOAEC values reported for *Scenedesmus quadricauda* and *Microcystis aeruginosa*.

Exposure Assessment – Sporax is applied directly to the surfaces of freshly cut tree stumps. Sporax is not applied using backpack, broadcast or aerial spray methods and it is not applied directly to vegetation. Therefore, many of the standard exposure scenarios that are typically considered for Forest Service risk assessments, such as direct spray, oral exposure *via* ingestion of contaminated prey or vegetation, are not applicable for this risk assessment. The exposure scenarios used in this risk assessment are those expected to result in substantial exposure considering the atypical application method for Sporax. Since Sporax is not applied as a spray, wide-spread exposure of insects is not expected; thus, an exposure assessment for insects has not been conducted in this risk assessment. Due to a lack of toxicity data, no exposure assessment was conducted for nontarget soil microorganisms.

For terrestrial vertebrates, two exposure scenarios are considered for this risk assessment: acute exposure *via* consumption of Sporax applied to tree stumps, and acute as well as chronic exposure *via* exposure to contaminated pond water. Exposure values for acute exposure *via* consumption of Sporax applied to a tree stump range from 0.57 mg B/kg/event for a large mammal to 29 mg B/kg/event for a small bird.

For contamination of water by both an accidental spill scenario and by runoff from the application site are considered. As noted in the exposure assessment for human health, the use of Sporax in stump treatments is not likely to have a substantial affect on concentrations of boron in ambient water. For ingestion of contaminated water *via* accidental spill, acute exposure values for a small mammal range from 0.0001 to 0.0004 mg B/kg/event. For acute exposure of a small mammal *via* ingestion of water contaminated by runoff, acute exposure values range from approximately 0.0009 to 0.014 mg B/kg/event. For chronic exposure of a small mammal by water contaminated by runoff, exposure values range from about 0.0003 to 0.01 mg B/kg/day. Since Sporax is not applied to vegetation, the only exposure scenario considered for terrestrial macrophytes is exposure to boron that reaches soil *via* runoff. Based on the results of GLEAMS modeling, peak concentrations of boron in soil range from 0.0026 ppm for the lowest value associated with an application rate of 0.1 lb Sporax/acre to 2.29 ppm in soil for the highest value associated with an application rate of 5 lbs Sporax/acre.

Exposures to aquatic organisms are based on the same information used to assess the exposure to terrestrial species from contaminated water. For an accidental spill of Sporax into a small pond, the central peak estimated concentration of boron in ambient water is 0.64 mg B/L (0.32 - 1.28) mg B/L (ppm). For contamination of a small pond by runoff, the peak estimated concentration in ambient water is 30 (6 to 100) µg/L after a single application of 1 lb Sporax/acre (0.11 lb boron/acre). For longer-term exposures, the corresponding longer term concentrations in ambient water are estimated at about 14 (2 to 70) µg/L.

Dose-Response Assessment – Borate compounds are relatively non-toxic to mammals and birds. For mammals, the toxicity values used in the ecological risk assessment are identical to those used in the human health risk assessments: the 95% lower bound on the dose corresponding to the BMR, i.e., the $BMDL_{05}$, of 10.3 mg B/kg/day (the *critical dose*) for decreased fetal body

weight (Allen et al. 1996, U.S. EPA 2004) is used to assess both acute and chronic risk. For birds, the acute NOAEL for boron is taken as 136 mg B/kg based on lack of mortality or clinical signs of toxicity following 5-day dietary exposure of bobwhite quail to borax. For chronic exposure of birds, the limited data available suggest that longer-term exposure to boron compounds can cause testicular toxicity in avian species; however the available studies did not rigorously investigate the potential for boron compounds to produce testicular toxicity. Therefore, the mammalian *critical dose* of 10.3 mg B/kg/day will be used to characterize the risk of chronic exposure to boron compounds in birds. For terrestrial invertebrates, data used to characterize risk is from a single contact bioassay in the honey bee, with an NOAEL for mortality of 677 mg/kg.

Although there is an abundant literature regarding the role of boron as an essential element for terrestrial plants, standard bioassays on the effects of boron on seedling emergence and vegetative vigor are not available. Based on the relatively limited information available, the NOAEC of 5 mg B/kg soil for the potato will be used to characterize risk in the most sensitive and the NOAEC of 20 mg B/kg soil will be used to assess risk in the most tolerant nontarget plant species. However, it is likely that more sensitive and more tolerant species exist. Since borates are effective fungicides, some nontarget soil microorganisms could be affected by exposure to boron in soil. However, information to adequately assess risk in this class of organisms is not available.

Toxicity values for aquatic species indicate relatively little difference between fish and aquatic invertebrates based on acute toxicity. For fish, the acute 96-hour LC_{50} values are 233 mg B/L and >1100 mg B/L for sensitive and tolerant species, respectively. For aquatic invertebrates, a similar range in 48-hour LC_{50} values (133 mg B/L for sensitive species and 1376 mg B/L for tolerant species) was observed. For chronic exposures, fish appear more sensitive than aquatic invertebrates to boron exposure. In fish the range of NOAEC values is relatively narrow, with the NOAEC of 0.5 ppm boron in the most sensitive species and 1.0 ppm boron in the most tolerant species. In aquatic invertebrates, NOAEC values range from 6 mg B/L to the estimated value of 61.8 mg B/L. To characterize the risk of acute exposure to amphibians, the NOAEC of 1.0 ppm B obtained in a single study in leopard frog larvae will be used. No studies on the effects of chronic exposure of amphibians to boron compounds were identified in the available literature. Based on the available data, the most sensitive algal species is the green algae *Scenedesmus subpicatus*, with a 72-hour NOAEC of 10 mg B/L (Bringmann and Kuhn 1978, as cited in ECETOC 1997) and the most tolerant species is the blue-green alga *Microcystis aeruginosa*, with a 72-hour NOAEC of 20.3 mg B/L (Bringmann and Kuhn 1978, as cited in ECETOC 1997). Although these tests are conducted for a relatively short period of time (i.e. 72 hours), these NOAEC values are applied to both acute and longer-term concentrations because of the short life-cycle of individual algal cells. For aquatic macrophytes 21-day exposure studies yield a range of LC_{50} values of 5 to10 mg B/L; these values will be used to assess acute exposure risk to sensitive and tolerant aquatic macrophytes. For aquatic microorganisms, the NOAEC values of 0.3 mg B/L and 291 mg B/L are used to assess the consequences of both acute and

longer-term exposures for sensitive and tolerant species of aquatic microorganisms because of the short life-cycle of individual microorganisms.

Risk Characterization **–** For terrestrial species, risk associated with the application of Sporax to tree stumps appear to be very low. Most risk quotients are range from 0.000003 to 0.005 and are below the level of concern by factors of about 200 to over 330,000. As discussed in Section 3.2.3.4, this reflects the fact that the use of Sporax in Forest Service programs will not substantially contribute to or increase concentrations of boron in water or soil beyond those that are associated with the normal occurrence of boron in the environment. Even in the case of direct consumption of Sporax from a tree stump by a large mammal, the highest risk quotient is only 1.1. The hazard quotients for other organisms consuming Sporax – i.e., a small mammal, a small bird, and a large bird – range from 0.00004 to 0.08, below the level of concern by factors of about 12 to 25,000.

There also does not appear to be a risk to terrestrial plants exposed to boron through runoff of Sporax applied to tree stumps. Although risk to insects and soil microorganisms was not characterized, since borax is used effectively in the control of fungi and insects, adverse effects of environmental exposures to insects and nontarget microorganisms are possible. However, given the atypical application method for Sporax, widespread exposures are not likely.

The exposure scenarios considered for aquatic species are for water contaminated by accidental spill or by runoff of applied Sporax. Most aquatic animals do not appear to be at risk for any of the exposure scenarios considered. For amphibians, the level of concern is marginally exceeded for the accidental spill of 25 pounds of sporax into as small pond (HQ, 1.3). None of the acute or chronic HQs for exposure *via* water contaminated by runoff exceed the level of concern for any aquatic animal. These results indicate that aquatic animals are not at high risk for the exposure scenarios considered; however, accidental spill of large quantities of Sporax into a small pond may result in toxicity in amphibians.

For aquatic plants, the highest HQ for any exposure scenario is 0.3 associated with algae for the accidental spill of 25 pounds of Sporax into a small pond. All other HQs for the accidental spill scenario and for acute and longer-term exposures to water contaminated by runoff are well below the level of concern. Thus, based on this analysis, there is no basis for asserting that effects on aquatic macrophytes or algae are likely for either acute or longer-term exposures. Hazard quotients for sensitive species of aquatic microorganisms exceed the level of concern for all accidental spill scenarios, with HQs ranging from 1.1 to 4.3. For tolerant microorganisms, HQs are well below the level of concern for the worst-case accidental spill scenario. For acute exposure to water contaminated by runoff based on the maximum application rate of 5 lbs Sporax/acre, all HQs are below the level of concern for both sensitive and tolerant species. The results of this risk assessment indicate that more sensitive microorganisms may be at risk following accidental spill of large quantities of Sporax into a small pond, but that exposure *via* runoff does not present a risk to aquatic microorganisms.

1. INTRODUCTION

Boron-containing compounds, specifically boric acid and its sodium salts, have several agricultural uses based on their algaecidal, acaricidal, fungicidal, herbicidal and insecticidal properties. Currently the USDA uses Sporax®, a commercial formulation of sodium tetraborate decahydrate, also called borax, to limit the development of annosus root disease in conifer stands. Since Sporax is a formulation of 100% sodium tetraborate decahydrate, the terms borax and Sporax are used interchangeably throughout this document.

Borax (i.e., tetraborate decahydrate) will dissociate in the environment, particularly in aqueous solutions) and the species of boron containing compounds that will exist will be dependant on the pH of the aqueous solution. Consequently, the dose response assessments for both human health and ecological effects are based on boron equivalents rather than borax itself. In this risk assessment, application rates are always expressed in units of borax rather than boron. Both exposure values and toxicity values, however, are typically given in units of boron equivalents and are typically expressed in units such as *mg B/kg/day* (a dose in units of milligrams of boron per kilogram body weight) or *mg B/L* (a concentration in units of milligrams of boron per liter of water).

In 1993, the US EPA (US EPA 1993a) issued a Reregistration Eligibility Decision document (RED) addressing eligibility for pesticides containing boric acid and its sodium salts, specifically boric acid, sodium tetraborate decahydrate (borax decahydrate), sodium tetraborate pentahydrate (borax pentahydrate), sodium tetraborate (anhydrous), disodium octaborate tetrahydrate, disodium octaborate (anhydrous), and sodium metaborate. With the exception of sodium metaborate whose chemical properties differ from the other borate sodium salts, boric acid and its sodium salts exhibit similar chemical and toxicological properties and potency when the exposures are expressed in boron equivalent units (US EPA 1993a, WHO 1998). Thus, except for sodium metaborate, boric acid and it sodium salts are treated as a family of boron-containing compounds with similar toxicological and environmental fate and transport characteristics (US EPA 1993a). In this risk assessment, if data gaps exist for borax, information on boric acid is used as surrogate data. In order to facilitate any comparisons between borax and boric acid, data are expressed in terms of the dose or concentration of borate compound (borax or boric acid) and in terms of boron equivalents (B). The conversion factors for deriving boron equivalents are given in Table 2-1.

In water, boron compounds transform rapidly into borates, with borate speciation dependent upon pH (ATSDR 1992, WHO 1998). Since several different borate compounds can form once the borate salts are dissolved in water, information on the environmental fate and transport of specific borate sodium salts is not available. Therefore, the environmental fate and transport of borate sodium salts are best described in terms of the environmental fate and transport of boron. Due to the large body of literature, it is not practical to provide a comprehensive review of the primary literature on the environmental fate of boron within this risk assessment. However, comprehensive reviews on the environmental fate and transport of boron are available (ATSDR

1992, WHO 1998). For this risk assessment, much of the information on environmental boron is taken from these reviews, although relevant primary literature on boron has been reviewed and summarized as appropriate. Briefly, boron is a naturally occurring element that is widely distributed. It is found in oceans, sedimentary rocks, coal, shale, and some soils; boron is most commonly found in the environment in the form of borate salts (WHO 1998). Boron is released into the environment through weathering of rocks, volcanic activity and volatilization of seawater. Small amounts of boron are released from anthropogenic sources. Boron occurs naturally in fruits, vegetables, and forage crops, and is an essential nutrient for many organisms. Boron concentrations are approximately 10 mg/kg in the earth's crust and 4.5 mg/L in the ocean (WHO 1998). In fresh surface waters, boron concentrations are highly variable, but generally range from 1 to 200 ppb (Black et al. 1993, US EPA 1993a). In soil, boron-containing compounds dissolve in water and are transformed to borates (WHO 1998). Borate compounds may be transported by percolation, sediment, or runoff from soil to ambient water. Borate compounds are adsorbed to soils to varying degrees, depending on several factors, including soil type and water pH (ATSDR 1992).

The toxicity of borax (the sole component of Sproax) has been reviewed in the Reregistration Eligibility Decision document (RED) for boric acid and its sodium salts (US EPA 1993a). Comprehensive reviews on the toxicity and environmental fate of boron and boron compounds are also available (ATSDR 1992; Beyer et al. 1983; Coughlin 1996; Culver and Hubbard 1996; Dost et al. 1996; ECETOC 1995; 1997; Fail et al. 1998; Hovatter and Ross 1995; Hubbard 1998; Hubbard and Sullivan 1994, 1996; Moore 1997; Murray 1995; WHO 1998). In addition, risk assessments for human and ecological effects of boric acid and boric acid salts have been conducted by the U.S. EPA (U.S. EPA 1993b,c). These documents were obtained and reviewed for the purpose of conducting this Forest Service risk assessment. In addition, a complete search of the U.S. EPA files was conducted in the preparation of this risk assessment. Full text copies of the most relevant studies [n=52] were kindly provided by the U.S. EPA Office of Pesticide Programs. These studies, in addition to studies published in open literature, were reviewed, and synopses of the most relevant studies are included in the appendices to this document. Given the abundant literature on the toxicity of boron-containing compounds, a comprehensive review of the primary literature was impractical; thus, in preparation of this risk assessment, reviews were used to provide general information about boron-containing compounds as a class. However, when relevant information specific to borax was available, primary studies were reviewed.

The relationship between soil boron concentration and effects on terrestrial plants is complex. As discussed in Section 4.1.2.4, although boron is an essential nutrient for plants, the range between beneficial and phytotoxic soil boron concentrations is often very narrow. There is an extensive literature exploring boron requirements for plants, particularly in terrestrial crop species. Unfortunately, much of the literature investigating the phytotoxic effects of boron in soil does not provide the appropriate quantitative information for use in assessing risks to terrestrial plant species; thus, the information used to assess risk of boron in soil to terrestrial plants in this document is limited.

Sporax is applied in granular or liquid form directly to the surfaces of freshly cut tree stumps. Therefore, many of the standard exposure scenarios that are typically considered for Forest Service risk assessments involving broadcast applications (e.g., direct spray, oral exposure *via* ingestion of contaminated prey or vegetation) are not applicable for this risk assessment. The exposure scenarios used in this risk assessment are those reasonably expected to result in exposure considering the atypical application method for Sporax.

For the most part, the risk assessment methods used in this document are similar to those used in risk assessments previously conducted for the Forest Service as well as risk assessments conducted by other government agencies. Four chapters, including the introduction, program description, risk assessment for human health effects, and risk assessment for ecological effects or effects on wildlife species comprise the main body of this document. Each of the two risk assessment chapters has four major sections, including an identification of the hazards associated with Sporax, an assessment of potential exposure to the products, an assessment of the dose-response relationships, and a characterization of the risks associated with plausible levels of exposure. These sections incorporate the basic steps recommended by the National Research Council of the National Academy of Sciences (NRC 1983) for conducting and organizing risk assessments.

This is a technical support document, and it addresses some specialized technical areas. Nevertheless, an effort was made to ensure that the document can be understood by individuals who do not have specialized training in the chemical and biological sciences. Certain technical concepts, methods, and terms common to all parts of the risk assessment are described in plain language in a separate document (SERA 2001). The general technical terms used in this document are defined in an environmental glossary available at www.sera-inc.com. Some of the more complicated terms and concepts are defined, as necessary, in the text.

The information presented in the appendices and the discussions in chapters 2, 3, and 4 of the risk assessment are intended to be detailed enough to support a review of the risk analyses; however, they are not intended to be as detailed as the information generally presented in Chemical Background documents or other comprehensive reviews. Almost no risk estimates presented in this document are given as single numbers. Usually, risk is expressed as a central estimate and a range, which is sometimes very large. Because of the need to encompass many different types of exposure as well as the need to express the uncertainties in the assessment, this risk assessment involves numerous calculations. Most of the calculations are relatively simple, and the very simple calculations are included in the body of the document. Some of the calculations, however, are cumbersome. For those calculations, worksheets are included as an attachment to the risk assessment. The worksheets provide the detail for the estimates cited in the body of the document. The worksheets are divided into the following sections: general data and assumptions, chemical specific data and assumptions, exposure assessments for workers, exposure assessments for the general public, and exposure assessments for effects on nontarget organisms. The worksheets for Sporax are contained in an EXCEL workbook and are included as Supplement 1 to this risk assessment. SERA (2004a) contains documentation for the use of these worksheets.

2. PROGRAM DESCRIPTION

2.1. OVERVIEW

The primary focus of this risk assessment is sodium tetraborate decahydrate (Sporax®), also called borax decahydrate or borax. The Forest Service uses Sporax to limit the development of annosum root disease in conifer stands. Annosum root disease is caused by the fungus *Heterobasidion annosum*, which infects cut conifer stumps following thinning or cutting operations. Treatment of tree stumps with borax prevents annosus spores from establishing infections in tree stumps (Wilbur-Ellis Company, No Date). The commercial borate sodium salt formulation currently used by the Forest Service is Sporax, which contains 100% sodium tetraborate decahydrate.

Sporax is applied to tree stump surfaces by dry application of the solid material. For this risk assessment, the typical application rate for Sporax will be taken as 1 lb/acre, with a range of 0.1 lb/acre to 5 lbs/acre to reflect plausible ranges that the Forest Service may use. That is, for the typical application rate of 1 lb/acre, given the density of stumps to be treated in a 1 acre conifer stand, a total of 1 lb of Sporax will be applied to cut tree stumps in the 1 acre plot. For this risk assessment, exposures are based on the typical application rate of 1 lb/acre rather than the full range of application rates. The consequences of varying application rates within the range of 0.1 lb/acre to 5 lbs/acre are considered in the risk characterization for human health (Section 3.4) and ecological effects (Section 4.4). The Forest Service reported yearly application rates for borax ranging from 0.111 lb/acre to 1.869 lbs/acre for 2000 to 2002. Thus, the range of application rates calculated from actual use data encompasses the range of application rates used for this risk assessment (0.1 lb Sporax/acre to 5 lbs Sporax/acre).

2.2. CHEMICAL DESCRIPTION AND COMMERCIAL FORMULATIONS

Sporax is registered by the Wilbur-Ellis Company as a fungicide for use in the control of annosum root disease (Wilbur-Ellis Company, No Date,). Sporax contains 100 % sodium tetraborate decahydrate ($Na_2B_4O_7 \bullet 10H_20$) and has no other active or inert ingredients.

Selected chemical and physical properties of the active ingredient in the Sporax are summarized in Table 2-1, and the physical and chemical properties that are directly used in this risk assessment are presented in Worksheet A02. Since borax is applied directly to the stumps of trees and is not applied by broadcast spray, some of the environmental fate characteristics typically included in risk assessments, such as foliar half-time, are not applicable for this risk assessment. The environmental fate and transport of borate sodium salts is best described in terms of boron (ATSDR 1992, WHO 1998). Additional detailed information on environmental fate and transport of boron compounds are discussed in the exposure assessments for human health effects (Section 3.2) as well as ecological effects (Section 4.2). Briefly, in water, boron compounds transform rapidly into borates; no further transformation is possible.

Borates and boric acid are in pH-dependent equilibrium, with borate speciation dependent upon pH (ATSDR 1992, WHO 1998). Below pH 7, boric acid and its sodium salts are mainly in the

form of undissociated boric acid [$B(OH)_3$]. Above pH 6, highly water soluble polyborate ions such as $B_3O_3(OH)_4^-$, $B_4O_5(OH)_4^{2-}$, and $B_5O_6(OH)_4^-$, may be formed. Polyborates will occur, however, only at high concentrations (Bodek et al. 1988; WHO 1998). At environmental concentrations, monomeric anion species will be the most predominant form of boron compounds. Borate compounds may be transported by percolation, sediment, or runoff from soil to ambient water. Boron compounds dissolve in water and are transformed to borates (ATSDR 1992). Borate compounds are adsorbed to soils to varying degrees, depending on several factors, including soil type and water pH (ATSDR 1992). Since borax is converted primarily to boric acid in water, pertinent information on the environmental fate and transport of both boric acid and boron are also provided in Table 2-1.

2.3. APPLICATION METHODS

Sporax can be applied as a solid (dry application) or mixed with water for spray application. In Forest Service programs, Sporax is applied in a dry application to the surface of freshly cut stumps. Sufficient material is used to completely cover the surface of the stump (Wilbur-Ellis Company, No Date). The minimum target concentration in treated stumps for the control of *Heterobasidion annosum* is 300 ppm. Some applications of Sporax can lead to much higher concentrations, on the order of 1000 to 7000 ppm (Cram 2004). Moisture from the exposed stumps, dew or rain dissolves the product, allowing it to leach into the wood.

2.4. MIXING AND APPLICATION RATE

According to the Sporax product label, for both dry and wet applications, an application rate of 1 pound per 50 square feet of stump surface is recommended. Thus, for spray application methods, one pound of Sporax should be mixed with enough water to spray 50 square feet of stump surface.

For this risk assessment, the typical application rate for Sporax will be taken as 1 lb/acre, with a range of 0.1 lb/acre to 5 lbs/acre to reflect plausible ranges that the Forest Service may use (D. Bakke 2003, personal communication). For Forest Service applications, given the density of stumps to be treated in conifer stands, the assumption is that Sporax will be applied at a typical rate of 1 lb/acre. That is, given the density of stumps to be treated in a conifer stand, 1 lb of Sporax will be applied to tree stumps in a 1 acre plot. As discussed in Section 2.5, application rates of 0.1 lb/acre to 5 lbs/acre encompass the range of application rates used by the Forest Service during 2000 to 2002. For this risk assessment, exposure assessments are based on the typical application rate of 1 lb/acre rather than the full range of application rates. The consequences of varying application rates within the range of 0.1 lb/acre to 5 lbs/acre is considered in the risk characterization for human health (Section 3.4) and ecological effects (Section 4.4).

2.5. USE STATISTICS

Use of Sporax by the Forest Service from 2000 to 2002 is summarized in Table 2-2. Sporax use has been reported for Region 5 (Pacific Southwest) and Region 6 (Pacific Northwest). The average application rate in Region 5 for 2000 to 2002 was 1.1 lbs/acre, approximately 5-fold

higher than the application rate reported for Region 6 (0.195) for 2000 to 2002. With the exception of the application rate of 10 lbs/acre for Forest 14 in Region 5 in 2000, the application rates reported in Table 2-2 range from 0.111 lb/acre to 1.869 lbs/acre. The application rate of 10 lbs/acre appears to be a reporting error and this application rate will not be used in Forest Service programs.

3. HUMAN HEALTH RISK ASSESSMENT

3.1. HAZARD IDENTIFICATION

3.1.1. Overview

The toxicity of borate compounds has been extensively studied in both humans and laboratory animals, with most studies conducted using boric acid and borax. Boric acid and borax have similar toxicological properties across different species (ATSDR 1992, Fail 1998, Hubbard 1998, Hubbard and Sullivan 1996, WHO 1998). In the following sections, if data gaps exist for borax, information on boric acid is reviewed as appropriate and used as surrogate data in this risk assessment. In order to facilitate any comparisons between borax and boric acid, data are expressed in terms of the dose or concentration of borate compound (borax or boric acid) and in terms of boron equivalents (B).

At physiologic pH, borate salts convert almost entirely to unionized boric acid; thus, boric acid and borate salts have similar toxicologic properties. Inorganic borates are well absorbed following oral administration, with an oral absorption of greater than 90% of the administered dose. Borates are not readily absorbed through intact skin but is more quickly absorbed across abraded skin. Percutaneous absorption of borax from intact human skin was shown to be very low, with a dermal permeability coefficient of 1.8×10^{-7} cm/hr. Boron is also absorbed following inhalation exposure to borate dust, but absorption does not appear to be complete. Borates are distributed in body soft tissues and eliminated in the urine, primarily in the form of boric acid, with a half-life of approximately 12 hours. Due to the excessive energy required to break the boron-oxygen bond, borates are not metabolized by humans or animals.

Based on the results of acute exposure studies, borax is classified as moderately toxic, with an LD_{50} in male rats of 4.5 g borax/kg. Clinical signs of toxicity observed following acute exposures include depression, ataxia and convulsions. In dogs, acute exposure to borax produced a strong dose-dependent emetic response. As expected of a compound with low percutaneous absorption, the LD_{50} of borax following single dermal application is > 5 g borax/kg in rats and >2 g borax/kg in rabbits. Results of a single inhalation exposure study yield a 4-hour LC_{50} > 2.0 mg borax/kg.

Results of developmental, subchronic and chronic toxicity studies show that the primary targets for borate toxicity are the developing fetus and the male reproductive system. Regarding developmental effects, gestational exposure of rats, mice, and rabbits to boric acid resulted in increased fetal deaths, decreased in fetal weight, and increased fetal malformations. The types of fetal malformations observed include anomalies of the eyes, central nervous system, cardiovascular system, and axial skeleton in rats, short rib XIII and other skeletal anomalies pertaining to ribs in mice, and cardiovascular malformations in rabbits. The most sensitive effect observed following gestational exposure to boric acid is decreased body weight. No mechanisms has been identified for the developmental effects of borates. Results of subchronic and chronic toxicity studies show that the testis is the primary target organ for borate compounds in adult animals. Testicular toxicity is characterized by atrophy of the testes, degeneration of the

seminiferous epithelium, and sterility. Results of reproductive studies show a dose-dependent decrease in fertility in male rats and dogs, with dogs being slightly more sensitive than rats. At lower exposure levels, testicular effects and infertility may be reversed, but adverse effects can persist for at least 8 months at higher exposure levels. Results of one study in rats indicate that borax exposure may also reduce ovulation in female rats. Although no mechanisms has been identified for borax-induced toxicity to the male reproductive system, data are consistent with the Sertoli cell as the primary target. Borax and borate compounds do not appear to act as direct neurotoxins or cause effects on immune system function. Studies assessing carcinogenic and mutagenic potential show no carcinogenic or mutagenic activity for borax and other borate compounds. Borax is not irritating to skin (Toxicity Category 4). Borax can cause severe irritation to eyes (Toxicity Category 1). In standard mammalian studies to assay ocular irritation, the damage persisted for the duration of the study – i.e., 14 days.

3.1.2. Mechanism of Action

No mechanism of action for borax or other borate compounds has been identified. Regarding fungicidal activity against *Heterobasidion annosum*, borate compounds prevent the germination of fungal spores on newly cut stumps; however, the mechanism for this effect is unknown. Regarding toxicity in mammals, as discussed in Sections 3.1.5 and 3.1.9, the reproductive system is the primary target for boron toxicity, with testicular toxicity and developmental effects as the predominant findings. No mechanisms has been proposed or identified for the developmental effects of boron (decrease fetal weight and skeletal malformations). As discussed in Section 3.1.9 (Reproductive and Developmental Effects), borates appear to produce direct effects on Sertoli cells rather than through alteration of hypothalamic-pituitary-testes axis function (ECETOC 1995, Fail et al.1998). Although borates have been shown to affect the activity of several enzymes (Beyer et al. 1983), no association has been made between alterations in enzymatic activities and testicular toxicity. No mechanism for the phytotoxic action of borates or the toxicity of borates in aquatic organisms has been identified.

3.1.3. Kinetics and Metabolism

3.1.3.1. Pharmacokinetic Studies – The pharmacokinetics of borate compounds have been extensively studied in both humans and laboratory animals, with several reviews available in the published literature (ATSDR 1992, Beyer et al. 1983, ECETOC 1995, Fail et al. 1998, Hubbard 1998, Hubbard and Sullivan 1996, Moore 1997, Murray 1995, WHO 1998). The kinetics of borate compounds are similar in humans and animals (Hubbard 1998). Borates are readily absorbed following oral administration and it is generally accepted that oral absorption is greater than 90% of the administered dose (ATSDR 1992, Moore 1997, WHO 1998). Borates are not readily absorbed through intact skin. Percutaneous absorption from intact human skin was shown to be very low, with absorption of approximately 0.2% of the applied dose over a 24 hour period (Wester et al. 1998). Studies on the absorption of borates applied to the intact skin of rats and rabbits show that percutaneous absorption is negligible (Murray 1995, WHO 1998). Boron has been shown to be absorbed from abraded or damaged skin of animals (ATSDR 1992, Hubbard 1998, Murray 1995). However, percutaneous absorption of boron across abraded human skin was not increased compared to intact skin (Wester 1998). Boron is also absorbed

following inhalation exposures to borate dust, but absorption does not appear to be complete (ECETOC 1995, WHO 1998). Following administration of borate compounds, boron is distributed throughout the soft tissues of the body and does not appear to concentrate in any particular tissue type (Moore 1997, ECETOC 1995,). Due to the excessive energy (523 kJ/mol needed to break the boron-oxygen bond), borates are not metabolized by humans or animals (ECETOC 1995, Hubbard1998). However, at physiological pH borate salts convert to boric acid (ECETOC 1995, Hubbard1998, WHO 1998). Borates are excreted almost entirely in the urine, primarily in the form of boric acid, with a halftime of approximately 12 hours in rats and 13 hours in humans (ATSDR 1992, Hubbard 1998, Moore 1997, WHO 1998).

3.1.3.2. Dermal Absorption Rates – A permeability constant (Kp) for borax has been calculated from a dermal absorption study in human volunteers (Wester et al. 1998). In this study a radiolabeled ^{10}B-borax solution (5% solution) was applied over a 900 cm^2 area of intact human skin for a 24-hour period; absorption was measured based on recovery of ^{10}B in the urine over the14 day period following application. Results of this study show that approximately 0.2% of the applied dose was absorbed, with a Kp of 1.8×10^{-7} cm/hr and a flux of 0.009 $\mu g/cm^2/hr$. This Kp is considerably lower than the dermal permeability coefficient estimated by U.S. EPA, with the default assumption for inorganics of 1×10^{-3} cm/hr (U.S. EPA 1992). The value given by U.S. EPA (1992), however, is intended to be used as a plausible upper limit for the Kp in the absence of experimental data. The study by Wester et al. (1998) using human volunteers is clearly preferable to the use of the EPA default value. For this risk assessment, the Kp of 1.8×10^{-7} cm/hr from the study by Wester et al. (1998) will be used for all exposure assessments involving dermal exposures (Section 3.2.). Wester et al. (1998) due not provide information on the variability of the Kp values among individuals. Nonetheless, Wester et al. (1998) due report varying Kp values for boric acid, borax, and disodium octaborate tetrahydrate with and without sodium lauryl sulfate pretreatment. The reported Kp values range from 0.9×10^{-7} to 2×10^{-7} cm/h (Wester et al. 1998, Table 3, p. 47). In the absence of any other information, this range is used for the bounds of the Kp value in all exposure assessments in which the Kp is used.

Since Sporax is not applied in a broadcast spray, exposure scenarios involving immersion or prolonged contact with an aqueous solution are not considered for this risk assessment. The dermal exposure scenario considered in this risk assessment is associated with accidental contact of granular Sporax onto the surface of the skin. As detailed further in Section 3.2.2.2, estimates of dermal absorption are based on Fick's first law and the water solubility of borax.

3.1.4. Acute Toxicity

Information regarding the acute oral toxicity of borax in laboratory mammals is summarized in Appendix 1. As discussed in Section 3.1.1, if data gaps exist for borax, data obtained in studies using boric acid will be used as surrogate data. Thus, in order to facilitate comparison between borax and boric acid, study results are expressed in terms of both borax and boron equivalents (B).

Boric acid and borate compounds have a low-to-moderate order of acute oral toxicity (ATSDR 1992, ECETOC 1995, Hubbard 1998, WHO 1998). Although there is an abundance of data on the acute toxicity of borate compounds, particularly boric acid, only one study investigating the acute oral toxicity of borax in rats and dogs was identified in the available literature (Weir and Fisher 1972). Details of this study are provided in Appendix 1. Following administration of single doses of borax by gavage, the acute LD_{50} value in male rats was 4.5 g borax/kg (0.51 g B/kg) and in female rats was 4.98 g borax/kg (0.56 g B/kg). In this same study, the acute toxicity of boric acid was of a similar magnitude (males rats, 0.60 g B/kg; female rats 0.71 g B/kg). Similar signs of toxicity, including depression, ataxia and convulsion, were reported for both borax and boric acid; however, the dose ranges used in this study and the NOAEL and LOAEL values for these effects were not reported. Administration of single doses of borax (1.54-6.51 g borax/kg or 0.174-0.736 g B/kg) and boric acid (1.0-3.98 g boric acid /kg or 0.175-0.697 g B/kg) by capsule to dogs did not cause any deaths during the 14 day observation period following dosing. However, for both borax and boric acid, a strong emetic response occurred within one hour of administration of the test material. Therefore, since it is likely that some of the administered dose was eliminated prior to absorption, interpretation of these results is difficult. Based on the acute oral LD_{50} of 4.5 g borax/kg in rats, borax is classified as moderately toxic (Category III), with an oral LD_{50} value between 500 and 5,000 mg/kg (U.S. EPA 2003).

In addition to studies on the effects of acute exposure of laboratory mammals to borate compounds, accidental poisonings in humans provide information on the lethal dose of boric acid (ATSDR 1992; WHO 1998). As noted by WHO (1998) in a review of the information on poisonings in humans:

> *Overall, owing to the wide variability of data collected from poisoning centres, the average dose of boric acid required to produce clinical symptoms is still unclear but is presumably within the range of 100 mg to 55.5 g, observed by Litovitz et al. (1988).*

Note that this statement refers to *clinical symptoms* rather than serious adverse effects. This range is sufficiently broad to be of little use in the assessment of potential serious adverse effects. Assuming a 70 kg body weight, the above exposures would correspond to doses of about 1.6 mg/kg/day to 793 mg/kg/day in terms of boric acid. Using a conversion factor of 0.1748 for boron equivalents (Table 2-1), this would correspond to a range of doses from 0.28 mg B/kg to 139 mg B/kg. As summarized in Section 3.3.2, the lower end of this range is close to the chronic RfD of 0.2 mg B/kg/day recently derived by the U.S. EPA(2004). Thus, while the upper range of exposure – i.e., 55.5 g of boric acid – may be a useful estimate of a dose that would probably be associated with serious adverse effects, the lower range reported by WHO (1998) appears to be an artifact of uncertainties in the exposure assessment and this lower bound is not useful for estimating the plausibility of serious adverse effects.

The analysis presented by ATSDR (1992) provides a more useful review of a subset of information on human exposures to boron and boron containing compounds, particularly the

study by Wong et al. (1964). This publication involves an incident in which 11 infants were inadvertently given formula prepared with a 2.5% solution of boric acid. Five of the infants subsequently died. Relatively good estimates of doses are available for two of the fatally exposed infants: 505 mg boron/kg/day and 765 mg boron/kg/day. Estimates of exposure for the other infants range from a total dose of 4,510 mg to 14,000 mg of boric acid, equivalent to 788 mg B to 2447 mg B. Sublethal effects in infants, including vomiting and diarrhea, were noted at doses of 184 mg B/kg/day (Wong et al. 1964). Sublethal but serious signs of toxicity, including vomiting, have also been noted in adults at doses of 241 mg/kg/day to 895 mg B/kg/day after unsuccessful suicide attempts (Linden et al. 1986).

3.1.5. Subchronic or Chronic Systemic Toxic Effects

Several studies have been conducted on the subchronic and chronic toxicity of boric acid and borate compounds, with most of the available data on boric acid and borax (ATSDR 1992, Hubbard 1998, WHO 1998). The effects of short-term gestational exposure to boric acid have been investigated in rats, mice, and rabbits (Heindel et al. 1992, 1994, Price et al. 1996a,b). Longer-term toxicity studies (60-90 days) have assessed the subchronic and chronic toxicity of borax in rats and dogs (Weir and Fisher 1972, Dixon et al. 1976, 1979, Lee et al. 1978). Details for all studies are provided in Appendix 1. Results of developmental, subchronic and chronic toxicity studies show that the developing fetus and the male reproductive system are the primary targets for borate-induced toxicity.

Gestational exposure of rats (Heindel et al. 1992, 1994, Price et al. 1996a), mice (Heindel et al. 1992, 1994), and rabbits (Heindel et al. 1994, Price et al. 1996b) to boric acid resulted in increased fetal deaths, decreased in fetal weight, and increased fetal malformations. The types of fetal malformations observed include anomalies of the eyes, central nervous system, cardiovascular system, and axial skeleton in rats, short rib XIII and other skeletal anomalies pertaining to ribs in mice, and cardiovascular malformations in rabbits. The most sensitive effect observed from gestational exposure to boric acid is decreased body weight, with the lowest NOAEL of 9.6 mg B/kg/day in rats (Price et al. 1996a). Based on comparison of NOAELs for decreased fetal weight in rats (9.6 mg B/kg/day, Price et al. 1996a) and mice (43.3 mg B/kg/day, (Heindel et al. 1992, 1994), fetal rats appears to be more sensitive than fetal mice to boric acid exposure. In addition to effects on the developing fetus, maternal toxicity was observed, with decreased maternal weight or weight gain and increased kidney weight as the most commonly observed effects (Heindel et al. 1992, 1994, Price et al. 1996a,b). In all developmental toxicity studies, maternal toxicity was observed at higher exposure levels than fetal toxicity.

Subchronic exposure of rats and dogs to borax in food and drinking water resulted in testicular toxicity characterized by atrophy of the testes, degeneration of the spermatogenic epithelium and spermatogenic arrest (Dixon et al. 1976, 1979, Lee et al. 1978, Paynter 1963, Seal and Weeth 1980, Weir and Fisher 1972). Dietary exposure of rats for 90 days to borax resulted in a dose-dependent atrophy of the testes and spermatogenic arrest, with an NOAEC of 175 ppm B equivalents and an LOAEC of 525 ppm B equivalents (Weir and Fisher 1972). Complete testicular atrophy was observed in rats exposed to 1750 ppm B. At higher dietary concentrations

of 1750 and 5250 ppm B, decreased body weight and decreased weight of several organs, including liver, spleen, kidneys and brain, were observed. In the 5250 ppm group, all animals died within 6 weeks of exposure. In this same study, similar results were observed for dietary exposure to boric acid. Testicular toxicity was also observed in rats exposed to borax in drinking water at concentrations of 150 and 300 mg B/L (Seal and Weeth 1980). Subchronic exposure of dogs to dietary borax resulted in testicular atrophy, including degeneration of the spermatogenic epithelium, with an NOAEC of 175 ppm B and an LOAEC of 1750 ppm B (Weir and Fisher 1972). A decrease in thyroid size was also observed in the 1750 ppm B treatment group. Borax-induced testicular toxicity was also observed following 90-day dietary exposure of dogs equivalent to doses of about 270 mg/kg/day (Paynter 1963). As was observed in rats, similar results were observed for dietary exposure of dogs to boric acid (Weir and Fisher 1972). As discussed in Section 3.1.9, in studies designed to assess the effects of borax exposure on reproduction in rats, exposure to dietary borax for up to 90 days resulted in toxicity to the testes (Dixon et al. 1976, 1979, Lee et al. 1978).

In rats exposed to borax in the diet for 2 years, the NOAEC for toxicity to the testes, including decreased testicular weight, atrophied seminiferous epithelium and decreased tubular size, was 350 ppm B (equivalent to 17.5 mg B/kg/day, according to U.S. EPA 1989), with an LOAEC of 1170 ppm B (equivalent to 58.5 mg B/kg/day, according to U.S. EPA 1989) (Weir and Fisher 1972). Other signs of toxicity noted in the 1170 ppm B treatment group included scaly tails, hunched posture, swelling and desquamation of paws and inflamed eyes. In a similar 2-year feeding study of borax in dogs, the NOAEC for toxicity to the testes was 350 ppm B (equivalent to 8.8 mg B/kg/day, according to U.S. EPA 1989), with an LOAEC of 1170 ppm B (equivalent to 28 mg B/kg/day, according to U.S. EPA 1989 (Weir and Fisher 1972). Thus, based on comparison of NOAEC and LOAEC values (expressed on a mg B/kg/day basis), dogs appear slightly more sensitive than rats to boron-induced testicular toxicity. In the 1170 treatment group, severe testicular atrophy and spermatogenic arrest were observed. Similar results were observed for dogs treated with boric acid in the diet for 2-years (Weir and Fisher 1972). In boric acid treated dogs, adverse effects on the testes were nearly completely reversed within 25 days when dogs were removed from the boric acid diet and placed on a control diet. For both borax and boric acid, no other adverse effects were observed at any dose level.

3.1.6. Effects on Nervous System

As discussed in Durkin and Diamond (2002), a neurotoxicant is a chemical that disrupts the function of nerves, either by interacting with nerves directly or by interacting with supporting cells in the nervous system. This definition of neurotoxicant distinguishes agents that act directly on the nervous system (direct neurotoxicants) from those agents that might produce neurologic effects that are secondary to other forms of toxicity (indirect neurotoxicants). Virtually any chemical will cause signs of neurotoxicity in severely poisoned animals and, thus, can be classified as an indirect neurotoxicant.

By this definition, borax may be classified as an indirect neurotoxicant. As reviewed in Section 3.1.4, acute exposure of rats to lethal doses of borax causes depression, ataxia and convulsion

(Weir and Fisher 1972). These findings, however, do not implicate borax as a direct neurotoxicant. No studies designed specifically to detect impairments in motor, sensory, or cognitive functions in animals or humans exposed borax were identified. No evidence for borax producing direct effects on the nervous system was found.

3.1.7. Effects on Immune System

Immunotoxicants are chemical agents that disrupt the function of the immune system. Two general types of effects, suppression and enhancement, may be seen and both of these are generally regarded as adverse. Agents that impair immune responses (*immune suppression*) enhance susceptibility to infectious diseases or cancer. Enhancement or *hyperreactivity* can give rise to *allergy* or hypersensitivity, in which the immune system of genetically predisposed individuals inappropriately responds to chemical or biological agents (e.g., plant pollen, cat dander, flour gluten) that pose no threat to other individuals; or the agent may give rise to *autoimmunity*, in which the immune system produces antibodies to endogenous components leading to destruction of the organ or tissue involved.

There is very little direct information on which to assess the immunotoxic potential of borax or other borate compounds. Nonetheless, the toxicity of borax has been examined in several acute, subchronic, and chronic bioassays. Although many of these studies did not focus on the immune system, evidence of changes in immune function (e.g., increased susceptibility to infection compared to controls) were not observed in any of the available long-term animal studies (Appendix 1). Typical subchronic or chronic animal bioassays conduct morphological assessments of the major lymphoid tissues, including bone marrow, major lymph nodes, spleen and thymus (thymus weight is usually measured as well), and blood leukocyte counts. These assessments can detect signs of inflammation or injury indicative of a direct toxic effect of the chemical on the lymphoid tissue. Changes in cellularity of lymphoid tissue and blood, indicative of a possible immune system stimulation or suppression, can also be detected (Durkin and Diamond 2002). None of these effects have been noted in any of the longer term toxicity studies on borax (Appendix 1). Results of a dermal challenge study show that exposure to borax did not cause a sensitization effect (Wnorowski 1994b, Appendix 1).

3.1.8. Effects on Endocrine System

The *endocrine system* participates in the control of metabolism and body composition, growth and development, reproduction, and many of the numerous physiological adjustments needed to maintain constancy of the internal environment (*homeostasis*). The *endocrine system* consists of *endocrine glands*, *hormones*, and *hormone receptors*. *Endocrine glands* are specialized tissues that produce and export (*secrete*) *hormones* to the bloodstream and other tissues. The major endocrine glands in the body include the adrenal, hypothalamus, pancreas, parathyroid, pituitary, thyroid, ovary, and testis. Hormones are also produced in the gastrointestinal tract, kidney, liver, and placenta. *Hormones* are chemicals produced in endocrine glands that bind to *hormone receptors* in target tissues. Binding of a hormone to its receptor results in a process known as *postreceptor activation* which gives rise to a *hormone response* in the target tissue, usually an adjustment in metabolism or growth of the target tissue. Examples include the release of the

hormone *testosterone* from the male testis, or *estrogen* from the female ovary, which act on receptors in various tissues to stimulate growth of sexual organs and development of male and female sexual characteristics. The target of a hormone can also be an endocrine gland, in which case, receptor binding may stimulate or inhibit hormone production and secretion. Adverse effects on the endocrine system can result in abnormalities in growth and development, reproduction, body composition, homeostasis (the ability to tolerate various types of stress), and behavior.

As discussed in Sections 3.1.5 and 3.1.9, subchronic exposure to borax results in spermatogenic arrest and sterility in male rats and decreased ovulation in female rats (Weir and Fisher 1972). It is most likely that the adverse effects of borax on reproductive function is due to a direct testicular effect, rather than an effect on the hypothalamic-pituitary axis (ECETOC 1995, Fail et al. 1998). Although time- and dose-dependent decreases in plasma luteinizing hormone (LH) and follicle stimulating hormone (FSH) levels were reported in rats exposed to borax in the diet (daily doses of 35 and 50 mg B/kg/day) (Lee et al. 1978), it is generally accepted that borate compounds are not endocrine disrupters and that the reduction in plasma FSH and LH levels are secondary to testicular toxicity (Fail et al. 1998).

In dogs exposed to dietary borax (1750 ppm B) for 90 days, a significant decrease in thyroid weight was observed (Weir and Fisher 1972). Based on these results, borax and other boron-containing salts may be toxic to the thyroid. However, no studies specifically designed to investigate the effects of borax on thyroid gland function were identified in the available literature.

3.1.9. Reproductive and Teratogenic Effects

As discussed in Section 3.1.5, effects on the male reproductive system and the developing fetus appear to be the most sensitive endpoints in borate toxicity (i.e., the effects occurring at the lowest doses), with the developing fetus more sensitive than the male reproductive system. Although no studies investigating the developmental effects of borax were identified in the available literature, given the similar toxicological profiles for borate compounds, it is likely that gestational exposure to borax would produce similar effects to those produced by boric in the developing fetus. As summarized in Appendix 1, gestational exposure of rats (Heindel et al. 1992, 1994, Price et al. 1996a), mice (Heindel et al. 1994), and rabbits (Heindel et al. 1992, 1994, Price et al. 1996b) to boric acid resulted in increased fetal deaths, decreased in fetal weight, and increased fetal malformations. The types of fetal malformations observed include anomalies of the eyes, central nervous system, cardiovascular system, and axial skeleton in rats, short rib XIII and other skeletal anomalies pertaining to ribs in mice, and cardiovascular malformations in rabbits. The most sensitive effect observed from gestational exposure to boric acid is decreased body weight, with a NOAEL of 43.3 mg B/kg/day in mice and NOAELs ranging from 9.6 (Price et al. 1996a) to <13.6 mg B/kg/day (Heindel et al. 1992, 1994) in rats. As discussed in Section 3.3.2, the chronic RfD for boron and boron compounds was derived by the U.S. EPA (2004) from combined data from Price et al. (1996) and Heindel et al. (1992), using decreased fetal body weight in rats as the most sensitive effect.

Regarding the effects of borate compounds on the reproductive system of adult animals, since the testes is a primary target organ for boron-induced toxicity, adverse effects on male fertility are expected outcomes of borax exposure. Several studies have been conducted to evaluate the effects of borax exposure in rats (Dixon et al. 1976, 1979, Lee et al. 1978, Weir and Fisher 1972). Study details are provided in Appendix 1. Exposure of male rats to single doses of borax up to 450 mg B/kg did not result in decreased fertility, as measured by the number of spermatozoa, spermatids, spermatocytes and spermatogonia (Dixon et al. 1976). However, dietary exposure to rats to 50 and 100 mg B/kg/day for 60 to 90 days, resulted in testicular toxicity (as described in Section 3.1.5) and decreased fertility in male rats (Dixon et al. 1979, Lee 1978, Weir and Fisher 1972); no signs of systemic toxicity were observed at these exposure levels. From these studies, the NOAEC for decreased reproductive function, as measured by the number of litters produced, is approximately 25 mg B/kg/day and the LOAEC is approximately 50 mg B/kg/day. At the highest dose level assessed (approximately 100 mg B/kg/day), male rats were completely sterile, with no litters produced (Lee et al. 1978, Weir and Fisher 1972). At the lower dose level (approximately 50 mg B/kg/day), sterility was reversed within 5 weeks of discontinuing borax treatment (Dixon et al. 1979). However, at the higher dose level (100 mg B/kg/day), rats remained sterile up to 8 months after borax treatment was discontinued (Lee et al. 1978).

The reproductive effects of borax do not appear restricted to males. Results of a single study show that dietary exposure to borax decreased ovulation in female rats (Weir and Fisher 1972). In female rats exposed to dietary borax at a concentration of 1170 ppm B (58.5 mg B/kg/day) for14 weeks, no litters were produced when females were mated with unexposed males. Decreased ovarian weight was also observed. No effects on female reproduction were observed at exposure levels of 5.9 and 17.5 mg B/kg/day. Additional information on the effects of borax on the female reproduction system was not identified in the available literature.

The specific mechanism of borax-induced toxicity to the reproductive system has not been identified. The induction of spermatogenic arrest in the absence of other systemic toxicity suggests that borax produces direct effects on the testes, rather than effects on the hypothalamic-pituitary-testicular axis (Fail et al. 1998). Based on histological findings showing degeneration of the spermatogenic epithelium,(Weir and Fisher 1972), it has been proposed that the Sertoli cell is the most likely target for borate compounds (ECETOC 1995, Fail et al. 1998, WHO 1998).

3.1.10. Carcinogenicity and Mutagenicity

The potential carcinogenicity of borax was assessed in a 2-year feeding study in rats and dogs, as summarized in Appendix 1 (Weir and Fisher 1972). In both species, borax was negative for carcinogenic activity. Furthermore, no borate compound has been shown to have produced cancer in any long-term exposure study in any species (ATSDR 1992, Beyer et al. 1983, Dieter et al. 1991, Fail et al. 1998, Hubbard 1998, WHO 1998). Based on the available data, boron (and borate compounds) is classified by U.S. EPA as Group E chemical – i.e., evidence of non-carcinogenicity in humans (U.S. EPA 1993a, p. 27).

The mutagenic potential of borax has been tested in *Salmonella typhimurium* and several cultured mammalian cell lines with and without metabolic activation; no mutagenic activity of borax was observed (Benson et al. 1984, Landolph 1985). It is generally accepted that boron and borate compounds are not mutagenic (ATSDR 1992, Beyer et al. 1983, ECETOC 1995, Fail et al. 1998, Hubbard 1998, WHO 1998).

3.1.11. Irritation and Sensitization (Effects on the Skin and Eyes)

Borax was tested for irritant effects on the skin of rabbits and guinea pigs (Reagan 1985b, Wnorowski 1994b) and the eyes of rabbits (Reagan 1985c); study details are provided in Appendix 1. Application of 0.5 g borax to shaved skin of rabbits did not results in any dermal irritation (Reagan 1985b). Boric acid is rated as Category III skin irritant (moderate irritant) and anhydrous borax is rated as a Category IV skin irritant (mild irritant) (U.S. EPA 1993a, pp. 23-24). Dermal challenge studies in guinea pigs show that borax does not cause skin sensitization effects, with no skin irritation noted either pre- or post-challenge (Wnorowski 1994b). Ocular application of 0.1 g borax in rabbits resulted in severe irritation, including irritation of the iris and corneal opacity (Reagan 1985c). Borax is rated as a Category I (severe) eye irritant (U.S. EPA 1993a, p. 24).

3.1.12. Systemic Toxic Effects from Dermal Exposure

Single dermal applications of borax to rats at doses up to 5 g/kg (Wnorowski 1996) and to rabbits at doses up to 2 g/kg (Reagan 1985a) did not result in any mortality or in the development of significant toxicity (studies detailed in Appendix 1). Thus, in rats the dermal LD_{50} is greater than 5 g borax/kg and in rabbits is greater than 2 g borax/kg. Based on the LD_{50} greater than 2 g/kg in rabbits, borax is rated as a Category 3 compound for systemic effects resulting from dermal exposure. These findings are consistent with the data indicating that borax has a low order of oral toxicity.

3.1.13. Inhalation Exposure

Inhalation exposure of rats for 4 hours to 2.0 mg borax/L did not results in any mortality, placing the 4-hour LC_{50} value at greater than 2.0 mg borax/L (Wnorowski 1994a). Clinical signs of toxicity noted during the exposure period included ocular and nasal discharge, hunched posture and hypoactivity. All symptoms resolved within 7 days of exposure.

These extremely limited data suggest that borax can induce irritant effects and perhaps systemic toxic effects in laboratory mammals following inhalation exposure. In addition, several studies of occupational exposure in workers show that inhalation of dust containing boron causes irritation to the nasal mucosa and respiratory tract (Garabrant et al. 1985, Heederik et al. 1994, Woskie et al, 1994, 1998, Hu et al. 1992). As discussed in Section 3.2.2, this finding is not directly relevant to this risk assessment because of the implausibility of inhalation exposure to the high concentrations of boron reported for these confined industrial facilities.

3.1.14. Inerts and Adjuvants

As discussed in Section 2.2, the borax formulation Sporax contains 100 % sodium tetraborate decahydrate (borax) and has no other active or inert ingredients.

3.1.15. Impurities and Metabolites

3.1.15.1. Impurities – No information on the impurities of borax was identified in the available literature. The toxicity studies reviewed in this report were conducted with technical grade borax. Thus, if toxic impurities are present, they are likely to be encompassed by the available toxicity studies using technical grade borax.

3.1.15.2. Metabolites – As discussed in Section 3.1.3.1, due to the excessive energy (523 kJ/mol) required to break the boron-oxygen bond, borates are not metabolized by humans or animals (ECETOC 1995, Hubbard1998). However, at physiological pH borate salts convert to boric acid (ECETOC 1995, Hubbard1998, WHO 1998). Therefore, it is likely that most of the administered dose of borax is converted to boric acid following absorption. Thus, the toxicity of boric acid is encompassed in the available toxicity studies on borax.

3.1.16. Toxicologic Interactions

As discussed in Section 2, borax is used as a sole agent for the control of annosum root disease in conifer stands. Thus, it is not expected that application of borax will be combined with other agents. No information has been encountered on the toxicologic interactions of borax with other agents.

3.2. EXPOSURE ASSESSMENT

3.2.1. Overview.

Unlike most other risk assessments on pesticides used by the Forest Service, the agent of toxicologic concern in Sporax – i.e., boron – occurs naturally and exposures to boron are unavoidable. Except for the most extreme exposure scenario considered in this risk assessment – i.e., the direct consumption of Sporax from a tree stump by a child – the use of Sporax in Forest Service programs will not substantially contribute to boron exposures in humans. In addition, the use of Sporax in Forest Service programs will not typically or substantially contribute to concentrations of boron in water or soil.

As discussed in Section 2.3, Sporax is applied directly to freshly cut tree stumps. Sporax is not applied as a liquid using backpack, broadcast or aerial spray methods and it is not applied directly to vegetation. Therefore, many of the standard exposure scenarios that are typically considered for Forest Service risk assessments, such as direct spray, oral exposure *via* ingestion of contaminated vegetation and direct exposure from contaminated vegetation, are not applicable for this risk assessment. The exposure scenarios used in this risk assessment are those expected to result in potentially significant exposures considering the application method for Sporax that is used in Forest Service programs – i.e., dry application to the stumps of trees.

As with typical Forest Service risk assessments, exposure scenarios are presented for both workers and members of the general public. For workers, accidental exposure *via* direct contact of the hands and lower legs with granular Sporax during application is the only exposure scenario considered in this risk assessment. For this scenario, exposure values range from approximately 0.000005 mg B/kg/event for the lower bound limit resulting from a 1-hour exposure to 0.0002 mg B/kg/event for the upper bound resulting from an 8-hour exposure. Other exposure scenarios are not considered to be reasonably plausible given the atypical application method for Sporax.

For the general public, the exposure scenarios considered quantitatively in this risk assessment are ingestion of Sporax from tree stumps by a small child and ingestion of contaminated pond water by a child or a young woman. For ingestion of Sporax from tree stumps by a child, exposure values range from 0.43 to 3.24 mg B/kg/event and are based on the average daily soil consumption by a child. For ingestion of contaminated pond water, contamination of water by both an accidental spill scenario and by runoff from the application site are considered. Acute exposures values for a small child from ingestion of water contaminated *via* an accidental spill of Sporax into a small pond range from 0.015 mg B/kg to 0.14 mg B/kg/event. To determine exposures to pond water contaminated by runoff of Sporax applied to tree stumps, exposure estimates are modeled by GLEAMS. For acute exposure of a child ingesting water from a pond contaminated by runoff, values range from approximately 0.0003 to 0.01 mg B/kg/event. For chronic exposure of adults ingesting surface waters contaminated by runoff, exposure values range from approximately 0.00004 to 0.002 mg B/kg/day.

3.2.2. Workers.

Sporax is applied in granular form to the surfaces of cut tree stumps using a "salt-shaker" style. Although the Forest Service uses a standard set of exposure assessments in most risk assessment documents, the typical general exposures considered for directed foliar (backpack), boom (hydraulic ground spray), and aerial spray as well as typical accidental exposures to a liquid are not applicable for this risk assessment, since Sporax is not applied as a liquid. Additionally, although there are several reports detailing local irritant effects resulting from occupational exposures to borate dust, inhalation exposures are not considered in this risk assessment due to the implausibility of inhalation exposures in the field reaching the high concentrations of boron reported in confined industrial facilities (Garabrant et al. 1985; Heederik et al. 1994; Woskie et al, 1994, 1998; Hu et al. 1992). Thus, the only exposure scenario that is considered plausible for workers is accidental dermal exposure to the hands and lower legs of granular Sporax during application.

For accidental exposure of workers to Sporax, dermal exposure is characterized by contamination of the lower legs and hands. In these scenarios, it is assumed that granular Sporax powder contaminates a given surface area of skin and that a certain amount of the powdered or granular chemical adheres to the skin. The absorbed dose is then calculated based on Fick's first law (U.S. EPA 1992). In most Forest Service risk assessments, this type of exposure assessment is modeled using the concentrations of the chemical in the solution used by the worker. This exposure assessment is somewhat atypical because borax is not in solution – i.e., it is applied as a powder. Consistent with the approach recommended by EPA (1992) for neat applications of a compound to the skin, the concentration of borax on the surface of the skin is assumed to be equal to the water solubility of borax (47,000 mg borax /L). In other words, the concentration of borax in the pore water of the skin will be limited by the chemicals solubility in water. To estimate the absorbed dose in units of mg chemical/kg body weight, the amount of absorbed chemical is divided by body weight (kg). For this scenario, it is assumed that the contaminated skin is effectively cleaned after 1 and 8 hours. Details of the assumptions and calculations involved in these exposure assessments are given in Worksheet C01a for a 1-hour exposure and Worksheet C01b for an 8-hour exposure. A summary of worker exposure assessments is provided in Worksheet E01. Plausible levels of exposure are extremely low, ranging from 0.000013 mg B/kg/event (the lower range for a 1-hour exposure) to 0.00023 mg B/kg bw/event (the upper bound for an 8-hour exposure). As noted in Section 3.1.3.1, higher exposures could be anticipated in workers with serious skin damage – i.e., substantial areas of abraded skin. This factor is considered further in Section 3.4.

Borax is classified as a Category I eye irritant and may cause severe irritation upon ocular exposure (Section 3.1.11). The available literature does not include quantitative methods for characterizing exposure or responses associated with accidental ocular exposure; furthermore, there appear to be no reasonable approaches to modeling this type of exposure scenario quantitatively. Consequently, accidental exposure scenarios of this type are considered qualitatively in the risk characterization (section 3.4).

3.2.3. General Public.

3.2.3.1. General Considerations – Under normal conditions of application, members of the general public should not be exposed to substantial levels of Sporax as a result of Forest Service activities. Nonetheless, any number of exposure scenarios can be constructed for the general public. As discussed in the exposure assessment for workers (Section 3.2.2), the atypical application method for Sporax limits the number of exposure scenarios for the general public that can be reasonably expected to occur. Therefore, typical exposures involving spray of a chemical to vegetation, such as dermal contact with contaminated vegetation and the consumption of contaminated fruit, are not applicable to this risk assessment. Exposure scenarios based on oral exposures from consumption of contaminated fish are not considered since borate compounds do not bioaccumulate in fish (Ohlendorf et al.1986; Klasing and Pilch 1988).

Two types of exposure scenarios, ingestion of Sporax from a tree stump by a child and ingestion of contaminated water, are considered the most likely exposure for the general public. For ingestion of Sporax from a tree stump, only acute exposure is considered. Exposure scenarios developed for the general public for contaminated water include acute exposure and longer-term or chronic exposure. The scenarios developed for this risk assessment should tend to over-estimate exposures in general. The exposure scenarios developed for the general public are summarized in Worksheet E03. As with the worker exposure scenarios, details of the assumptions and calculations involved in these exposure assessments are given in the worksheets that accompany this risk assessment (Worksheets D01–D04). The remainder of this section focuses on a qualitative description of the rationale for and quality of the data supporting each of the assessments.

Boron is a naturally occurring element and a normal constituent in environmental media (e.g., water, soil, and air) as well as plants and animals, including humans. While exposures to Sporax used in Forest Service programs may be limited, this risk assessment also considers background levels of exposure to boron and the relative contribution of Sporax to other sources of exposure to boron compounds (Section 3.2.3.4) as well as the potential cumulative effects of these exposures (Section 3.4.6).

3.2.3.2. Oral Exposure of Sporax Applied to Tree Stumps – Although Sporax is not applied in residential areas, it is applied in campgrounds used by members of the general public. For this risk assessment, an acute exposure scenario is used in which a child ingests Sporax applied to tree stumps. There is no information in the available literature to estimate the amount of Sporax that a child could be predicted to consume in one day. The estimated amount of Sporax that a child may consume in one day is based on the amount of soil that an average child may ingest per day. According to the EPA Exposure Factors Handbook (U.S. EPA 1996), the mean amount of soil that a child consumes per day is estimated to be 100 mg soil/day, with an upper bound estimate of 400 mg soil/day.

For this risk assessment, the amount of Sporax consumed from tree stumps in a single day is taken as the range of 50 (an estimated lower bound) to 400 mg Sporax/day (5.67 to 45.36 mg

B/day). A central estimate for Sporax consumption is taken as 100 mg Sporax/day (11.34 mg B/day). To yield an estimated dose in units of mg chemical/kg body weight, these exposure numbers are divided by body weight (kg). Details for the calculations involved in this exposure scenario are given in the worksheets that accompany this risk assessment (Worksheet D01). The estimated doses range from about 0.4 mg B/kg bw/event to 3.2 mg B/kg bw/event. It should be emphasized that this exposure estimate is highly uncertain and not based on empirical data for consumption of any borate compound; thus exposures *via* this scenario may be under- or overestimated.

3.2.3.3. Contaminated Water – The borax application method considered in this risk assessment – application to tree stumps – has a limited potential to contaminate water. Nonetheless, after application of tree stumps, rainfall and consequent runoff could lead to contamination of standing water or streams. In addition, accidental spills of the Sporax formulation into a small body of water are possible. Exposure assessments for both of these scenarios are presented in the following subsections.

3.2.3.3.1. Accidental Spill – The accidental spill scenario assumes that a young child consumes contaminated water shortly after an accidental spill into a small pond. The specifics of this scenario, which are given in Worksheet D02, are based on the spill of Sporax into a small pond. The amount of Sporax spilled ranges from 6.25 to 25 lbs (0.7 to 2.8 pounds of boron equivalents), with a central estimate of 12.5 lbs (1.42 pounds of boron equivalents). Because this scenario is based on the assumption that exposure occurs shortly after the spill, no dissipation of Sporax is considered. This scenario is dominated by variability and uncertainty and the specific assumptions used may overestimate or underestimate exposure. The actual concentrations in the water would depend on the actual amount of compound spilled, the size of the water body into which it is spilled, the time at which water consumption occurs relative to the time of the spill, and the amount of contaminated water that is consumed.

Based on the spill scenario used in this risk assessment, the concentration of boron in a small pond is estimated to range from about 0.3 to 1.3 mg B/L with a central estimate of approximately 0.6 mg B/L. As discussed in Section 3.2.3.4., these are within the range of naturally occurring concentrations of boron in water. Based on plausible ranges of water consumption (U.S. EPA/ORD 1996), the estimated doses for the child are estimated at about 0.015 to 0.14 mg B/kg/event, with a central estimate of approximately 0.05 mg B/kg/event (Worksheet D02). This is intended to be an extreme accidental exposure scenario. The purpose of this scenario is simply to suggest the intensity of measures that would be appropriate in response to a relatively large spill of Sporax into a relatively small body of water.

3.2.3.3.2. Gleams Modeling – Modeling of concentrations in stream water conducted for this risk assessment are based on GLEAMS (Groundwater Loading Effects of Agricultural Management Systems) modeling. GLEAMS is a root zone model that can be used to examine the fate of chemicals in various types of soils under different meteorological and hydrogeological conditions (Knisel and Davis 2000). As with many environmental fate and transport models, the

input and output files for GLEAMS can be complex. The general application of the GLEAMS model and the use of the output from this model to estimate concentrations in ambient water are detailed in SERA (2004b).

GLEAMS is typically applied to and validated with organic compounds for which adsorption and desorption to soil are the predominant factors affecting transport in soil. Borax and related compounds are inorganics and the modeling of such compounds using GLEAMS may be viewed as tenuous. Nonetheless, boron interactions with soil will be governed by adsorption/desorption processes analogous to those of many organic weak acids rather than precipitation and dissolution processes (Bodek et al. 1990; Tanji 1998).

Environmental transport models for inorganics, however, are not available. In addition, as reviewed by U.S. EPA (1993b), borax will rapidly convert to boric acid, which has a pKa of 9.14. Thus, at neutral pH, the proportion of boric acid that will be non-ionized (protonated) is greater than 0.99 and the behavior of boric acid in soil may approximate that of a neutral organic compound. Another complication in modeling the movement of boron involves interactions with minerals in soils which can substantially impact transport (Tanji 1990).

For the current risk assessment, the application site was assumed to consist of a 10 hectare area that drained directly into a small pond or stream. The chemical-specific values as well as the details of the pond and stream scenarios used in the GLEAMS modeling are summarized in Table 3-1. All simulations were conducted at an application rate of 1 lb borax/acre. Because borax rapidly converts to boric acid (U.S. EPA 1993a,b), the Kow of boric acid was used as an input parameter for GLEAMS. As discussed below, the concentrations of borax were converted to boron equivalents because boron equivalents are the basis for the dose-response assessments of both human health effects (Section 3.3) and ecological effects (Section 4.3).

The GLEAMS modeling yielded estimates of loss of the compound in runoff, sediment and percolation that were used to calculate concentrations in a stream and pond adjacent to a treated plot, as detailed in Section 6.4 of SERA (2004b). Over annual rainfall rates of 5 to 250 inches per year, the concentrations modeled in a small stream were less than 0.00001 ppb (µg/L). These very low modeled concentrations were the result of the amount of runoff water required to transport boric acid to the stream as well as the base flow rate of the stream (i.e., 710,000 L/day as specified in Table 3-1 and discussed in Section 6.4. of SERA 2004b). This runoff water and base flow diluted the concentration of boric acid to very low and essentially negligible values.

Higher concentrations were modeled in a small pond (Table 3-2). This is in some respects an artifact of the pond model. As detailed in SERA 2004b (Section 6.4), a variable volume pond model is used but no overflow or drainage from the pond is considered. Thus, boron is transported to the pond and is diluted only by the volume of water in the pond as well as rainfall and runoff. The upper portion of Table 3-2 gives the concentration as borax at an application rate of 1 lb/acre. The bottom portion of Table 3-2 gives the concentration in water as boron equivalents – i.e., µg of boron per liter of water.

For regions with annual rainfall rates of 15 inches or more, the modeled peak concentrations in ponds expressed as boron equivalents range from about 6 µg/L (clay at 250 inches of rainfall per year) to about 100 µg/L (sand or loam at an annual rainfall rate of 15 inches per year). Because degradation is assumed to be negligible – i.e., elemental boron will not be transmuted – the longer term concentrations are only somewhat less than the peak concentrations. It will be noted in Table 3-2 that the concentrations of boron in water are inversely related to rainfall rate. This occurs because borax may be transported off site once the amount of rainfall reaches the minimum necessary for runoff. Because of the high water solubility of borax (as boric acid), relatively small amounts of water can transport a large amount of borax. As the amount of water increases, the primary effect is dilution of borax rather than an increase in the amount of borax in runoff. Thus, the expected concentrations of borax in a small pond increase as the rainfall rate decreases.

3.2.3.3.3. Other Modeling Efforts and Monitoring Data – Detailed modeling efforts for borax or related compounds have not been encountered. As summarized in Table 3-3, the U.S. EPA (1993b) conducted a very simple modeling exercise for boric acid assuming that a proportion of 0.05 of the applied boric acid contaminates a six foot deep pond, similar to the pond used in the GLEAMS analysis (see Table 3-1). Based on this assumption, the U.S. EPA (1993b) estimated a concentration of boric acid in water of 30.5 ppb as boric acid, equivalent to 5.2 ppb as boron (Table 3-3). While the U.S. EPA (1993b) does not provide a detailed rationale for the runoff assumption, this is a standard value used by U.S. EPA in screening level assessments. The concentration of 5.2 ppb as boron is at the lower range of the peak values estimated from GLEAMS.

Very little monitoring data on boron have been encountered in the literature and no monitoring studies associated with the type of applications used by the Forest Service are available. Available monitoring data on boron concentrations in U.S. surface waters are summarized in Table 3-3. Normal ambient concentrations of boron in water are highly variable, ranging from 1 ppb (U.S. EPA 1993b) to 750 ppb (Black et al. 1993). As discussed further in Section 3.2.3.4, some areas may have much higher concentrations of boron in water – i.e., up to 5 ppm. The upper range of typical concentrations, 750 ppb, exceeds the upper range of concentrations (100 ppb) that are modeled using GLEAMS by a factor of 7.5 Thus, in areas that have naturally low levels of boron in water (i.e, about 1 ppb), the use of boron in Forest Service programs could have a substantial impact on local concentrations of boron in standing bodies of water such as small ponds. Likewise, in areas with a naturally high level of boron in water (i.e., about 750 ppb), the use of boron in Forest Service programs would have little impact on boron concentrations in surface waters.

Monitoring data in soils after applications of Sporax to tree stumps have been compiled by Dost et al. (1996). These data are relevant to the assessment of exposures in ambient water because they offer another means of comparing the concentrations of boron in soil modeled using GLEAMS to actual concentrations found in the field after applications that are comparable to those used in Forest Service programs. As summarized in Dost et al. (1996, Appendix A, Tables

1 to 4), concentrations of boron in soil after stump treatments ranged from about 0.1 to 2 mg B/kg soil (0.1 to 2 ppm boron). As discussed further in Section 4.2.3 and detailed in Table 4-1, peak concentrations of boron in soil modeled by GLEAMS are about 0.3 ppm to 0.5 ppm, very near the geometric mean (0.44 ppm) of the range reported by Dost et al. (1996).

3.2.3.3.4. Concentrations of Boron in Water Used for Risk Assessment – The peak and longer term average concentrations of boron in ponds, summarized in Table 3-3, are used in this risk assessment as water contamination rates – i.e., concentrations in water in units of mg/L or ppm that are expected at an application rate of 1 lb borax/acre. By comparison to the lower concentrations used by U.S. EPA (1993b), these values appear to be conservative – i.e., they may somewhat overestimate likely concentrations. As noted in Section 3.2.3.4.2, however, there are substantial uncertainties in the application of GLEAMS to an inorganic compound. This as well as the lack of monitoring data for applications of borax similar to those conducted by the Forest Service adds uncertainty to this risk assessment.

3.2.3.4. Background Levels of Exposure – Boron is a naturally occurring element and is relatively abundant in water, foods, and soil. In general, the exposure of humans to boron is attributable primarily to the consumption of food and, to a lesser extent, the consumption of water containing boron compounds (ATSDR 1992; WHO 1998). The normal background exposure to boron has a substantial impact on the current risk assessment in terms of determining whether the use of Sporax in Forest Service programs will have a significant effect on normal levels of exposure to boron and whether exposures associated with the use of Sporax could combine with background exposures to cause otherwise unanticipated effects. A summary of typical background exposures to boron and a comparison to levels of exposure to boron from Forest Service uses is given in Table 3-4 and discussed in this section. As discussion of the potential toxicologic significance of these increased exposures is given in Section 3.4.6.

In terms of consumption by humans, food is the predominant source of exposure to boron (ATSDR 1992; WHO 1998). Levels of boron in food items vary substantially. The review by WHO (1998) provides an extensive summary of boron levels in various environmental media: aquatic animals (3-11 ppm), aquatic vegetation (26-382 ppm), and most terrestrial vegetation (2.3-94.7 ppm). Much higher concentrations of boron may occur in fruit as well as some forms of vegetation – i.e., boron levels in different consumables may range from 1 ppm in lemons to over 300 ppm in red cabbage (U.S. EPA (1993a, pp. 27-28). Because of the high concentrations of naturally occurring boron in foods and the relatively low toxicity of boron compounds, the U.S. EPA (1993a) has determined that boric acid and the salts of boric acid are exempted from tolerances on raw agricultural commodities.

Based on an assessment of all sources of exposure (i.e., food, water, air, consumer products), ATSDR (1992, p. 55) has estimated that humans typically consume boron at levels of about 10 to 25 mg/day. Assuming a standard 70 kg body weight, this corresponds to daily doses of about 0.14 to 0.36 mg/kg/day. WHO (1998) does not provide a single estimate of total daily boron intake but the figures provided by WHO (1998) for various sources of exposure suggest a total

average intake of about 5.5 mg/day, somewhat below the lower range of the estimate given by ATSDR (1992).

An alternative approach to estimating normal daily exposures to boron can be based on a consideration of the pharmacokinetics of boron and typical body burdens of boron. The typical body burden of boron in humans is estimated at less than 0.02 grams or 20 mg (ICRP 1975, p. 294). Assuming a 70 kg body weight, this is equivalent to about 0.286 mg/kg bw. Using the *plateau principle* (e.g., Goldstein et al. 1974), the body burden can be related to daily dose as:

$$X_{Inf} = X_0 / (1- e^{-ke\ t^*)})$$

where X_{Inf} is the body burden after an infinite exposure/steady state, X_0 is the body burden after an initial dose, k_e is the first-order elimination rate, t* is the fixed interval between dosing. As summarized in Section 3.1.3.1, the halftime in humans is about 13 hours or 0.54 days. This corresponds to a first-order elimination rate of about 1.3 $days^{-1}$ [ln(2)/0.54 days]. Taking t* as one day and using 0.286 mg/kg bw as an upper bound on body burden, X_0 can be calculated by rearrangement of the above equation as a surrogate for daily intake of about 0.21 mg/kg/day [X_0 = 0.286 mg/kg bw × $(1-e^{-1.3})$] or about 14.7 mg/day for a 70 kg man. This is within the range of intake estimated by ATSDR (1992) – i.e., 0.14 to 0.36 mg/kg/day.

Based on the exposure scenarios derived for this risk assessment, the use of Sporax in Forest Service programs would not typically contribute to background levels of exposure. As summarized in Table 3-4, the plausible non-accidental routes of exposure are associated with the consumption of contaminated water. The estimated doses are 0.002 (0.0003-0.011) mg/kg bw/day based on peak exposures and 0.0004 (0.00004-0.0024) mg/kg bw/day based on longer-term exposures. These are below typical levels of exposure by factors of about 13 [the lower range of background exposure {0.14 mg/kg/day} divided by the peak acute exposure {0.011 mg/kg bw} for a one day period] to a factor of 9000 [the upper range of background exposure {0.36 mg/kg/day} divided by the lower range of longer-term exposure {0.00004 mg/kg bw}]. Taking 0.25 mg/kg/day as the central estimate of normal background exposures (i.e., the mean of the range given by ATSDR 1992) and using the central estimates associated with the application of Sporax – i.e., an acute dose of 0.002 mg/kg and a longer term does of 0.0004 mg/kg/day, the typical exposure is above those associated with normal background exposures by a factor of 125 for acute exposure and 625 for chronic exposure.

These exposure factors simply reflect the differences in normal concentrations of boron in water and concentrations of boron in water that could be added by the use of Sporax in Forest Service programs. Actual levels of exposure to background concentrations of boron will be variable due in large part to different distributions of boron in different regions and in different materials. The average concentration of boron in the earth's crust is about 10 ppm. Boron is occurs primarily in sedimentary rock and sediment and is released to soil and water by weathering (WHO 1998). Because of differences in the distribution of boron in the earths crust, there are substantial

differences in the concentrations of boron in soil and water in different regions. The average concentration of boron in drinking water is in the range of 0.1 and 0.3 mg boron/L (WHO 1998). In the United States, the average concentration of boron in water is about 0.1 mg/L but the range of concentrations is vary large: about 0.001 mg/L to 5 mg/L (ATSDR 1992, p. 54). As noted in Table 3-4, these concentrations are less than the concentrations that would be expected in water after applications of Sporax.

Concentrations in soil are similarly variable, with a mean concentration in the U.S. of about 26 ppm with an upper bound of about 300 ppm (ATSDR 1992, p. 54). These concentrations, however, are far in excess of the concentrations that would be added to soil as a result of Sporax applications based either on GLEAMS modeling or the monitoring data presented by Dost et al. (1996).

3.3. DOSE-RESPONSE ASSESSMENT

3.3.1. Overview

The U.S. EPA (2004) has recently derived a chronic RfD of 0.2 mg/kg/day for boron (from boric acid and borates), using the combined data of two developmental toxicity studies in rats using decreased fetal weight as the most sensitive endpoint (Price et al. 1996a, Heindel et al. 1992). The RfD is based on a benchmark dose analyses identifying a 5% decrease in mean fetal body weight compared to control as the benchmark response (BMR) level (Allen et al. 1996). The 95% lower bound on the dose corresponding to the BMR, i.e., the $BMDL_{05}$, of 10.3 mg B/kg/day is used as the *critical dose* value to calculate the RfD. The uncertainty factor of 66, which considers both the toxicokinetic and toxicodynamic aspects associated with interspecies and interindividual variability, was applied to the critical dose to derive the chronic RfD of 0.2 mg B/kg/day. The U.S. EPA has not derived an acute RfD for boron. Therefore, the chronic RfD of 0.2 mg B/kg/day will also be used to characterize risks associated with incidents or accidents that involve an exposure period of 1 day.

3.3.2. Chronic RfD

The U.S. EPA recently derived an agency-wide chronic RfD for boron (from boric acid and borates) of 0.2 mg B/kg/day (U.S. EPA 2004), as currently listed at the U.S. EPA web site for RfDs http://www.epa.gov/ngispgm3/iris/. For this risk assessment, the chronic RfD value of 0.2 mg/kg/day is used directly for consistency with the U.S. EPA. As discussed in Section 3.1.9, results of several studies demonstrate developmental effects following gestational exposure to boron compounds (decreased fetal weight, increased fetal death, and increase in fetal malformations). Specific developmental effects observed include a dose-dependent decreases in fetal body weight and fetal malformations (primarily skeletal and central nervous system). Based on an analysis of the data from developmental studies, the Institute for Evaluating Health Risks (Moore 1997) concluded that decreased fetal body weight occurred at the same or lower boron doses than skeletal malformations; thus, U.S. EPA (2004) has used decreased fetal weight as the most sensitive effect of boron exposure. Although the previous RfD for boron and borates of 0.08 mg B/kg/day was based on the slightly lower NOAEL or *critical dose* of 8.8 mg B/kg/day for testicular toxicity in dogs (Weir and Fisher 1972, U.S. EPA 1989), due to limitations of the dogs studies (small number of animals per treatment group, NOAEL and LOAEL values obtained at different time points), the U.S. EPA (2004) considers results of the developmental studies in rats (Price et al. 1996a, Heindel et al. 1992) to be a more appropriate basis for the oral RfD.

The chronic RfD for boron and boron compounds was derived by the U.S. EPA (2004) from combined data of two developmental toxicity studies in rats using decreased fetal weight as the most sensitive endpoint (Price et al. 1996a, Heindel et al. 1992). In the Heindel et al. (1992) study, time-mated rats were fed diets containing 1, 0.1, 0.2, or 0.4% boric acid (equivalent to approximately 0, 13.6, 28.5, or 57.7 mg B/kg/day) on gestational days 0-20, or 0.8% boric acid (equivalent to approximately 94.2 mg B/kg/day) on gestational days 6-20. A dose-dependent decrease in fetal weight was observed, with mean fetal weights significantly decreased compared to control in all boron-treatment groups. The LOAEL for decreased fetal weight was defined as

0.1% dietary boric acid (13.6 mg B/kg/day), the lowest dietary concentration tested; a NOAEL was not established. In the Price et al. (1996a) study, time-mated rats were exposed to dietary boric acid at concentrations of 0, 0.025, 0.050, 0.075, 0.10, or 0.20% (equivalent to approximately 19, 36, 76, and 143 mg B/kg/day) on gestational days 0-20. Decreases in fetal body weights were observed in the 0.10 and 0.20% boric acid treatment groups, with a NOAEL of 0.075% dietary boric acid (equivalent to approximately 9.6 mg B/kgday) and a LOAEL of 0.10% dietary boric acid (equivalent to approximately 13.3 mg B/kg/day).

The RfD for boron is based on results of benchmark dose analyses conducted by Allen et al. (1996) using the combined Heindel et al. (1992) and Price et al. (1996a) data. Allen et al. identified a 5% decrease in mean fetal body weight compared to control as the benchmark response (BMR) level. The 95% lower bound on the dose corresponding to the BMR, i.e., the $BMDL_{05}$, is used as the *critical dose* value to calculate the RfD. Allen et al. (1996) defined the $BMDL_{05}$ as 10.3 mg B/kg/day, a value very close to the NOAEL of 9.6 mg B/kg/day reported by Price et al. (1996). The *critical dose* (the $BMDL_{05}$ of 10.3 mg B/kg/day) is then divided by an uncertainty factor of 66 to derive the chronic RfD of 0.2 mg B/kg/day. The uncertainty factor consists of animal-to-human (UF_A) and sensitive-human (UF_H) uncertainty factors, both of which are divided into toxicokinetic and toxicodynamic *adjustment factors.* The total uncertainty factor is the product of four adjustment factors, which were assigned the following values for boron: AF_{AK} – interspecies toxicokinetic adjustment factor (value 3.3, based on differences in kinetic parameters between pregnant rats and pregnant women); AK_{AD} – interspecies toxicodynamic adjustment factor (default value 3.16); AF_{HK} – interindividual toxicokinetic adjustment factor (value 2, based on interindividual differences in kinetic parameters among pregnant women); AF_{HD} – interindividual toxicodynamic adjustment factor (default value 3.16). Thus, the total uncertainty factor is calculated as 66 [$3.3 \times 3.16 \times 2 \times 3.16$].

3.3.3. Acute RfD

The U.S. EPA has not derived an acute/single dose RfD for boron compounds. As discussed in Section 3.3.2, decreased fetal weight is considered the most sensitive endpoint resulting from gestational exposure to dietary boron (Heindel et al. 1992, Price et al. 1996a). Although the exposure duration in these studies was actually quite short (20 days), results were used to derive the oral (chronic) RfD, based on a *critical dose* of 10.3 mg B/kg/day. As summarized in Section 3.1.5 and 3.1.9, results of reproductive toxicity studies identify testicular toxicity as the most sensitive endpoint for longer-term exposures, with an NOAEL of 8.8 mg/kg/day in dogs (Weir and Fisher 1972). However, given the concerns raised by U.S. EPA (2004) regarding the dog study, coupled with the shorter exposure duration used in the developmental studies in rats, assessing acute risk based on the results of the gestational studies in rats appears more appropriate than using results of the longer-term toxicity studies in dogs. Thus, the RfD of 0.2 mg B/kg/day derived by EPA (2004) for chronic exposure will also be used to characterize risks associated to incidents or accidents that involve an exposure period of 1 day.

As detailed in Section 3.4 (Risk Characterization), some of the accidental exposures to boron that are considered in this risk assessment exceed the RfD of 0.2 mg B/kg/day by a very large margin.

In order to better assess the potential consequences of such exposures, the approximate lethal doses to infants of 505 mg boron/kg/day and 765 mg boron/kg/day as well as the non-lethal dose in infants of 184 mg B/kg/day (Wong et al. 1964) and the non-lethal doses of 241 mg/kg/day to 895 mg B/kg/day in adults (Linden et al. 1986) are used. These estimates are discussed in Section 3.1.4.

3.4. RISK CHARACTERIZATION

3.4.1. Overview

For exposures considered in this risk assessment, with the exception of the accidental exposure of a child *via* consumption of Sporax from tree stump, all hazard quotients are below the level of concern. For worker exposure from granular Sporax spilled on the lower legs and hands, hazard quotients are well below the level of concern. Thus, workers do not appear to be at risk from Sporax under typical application conditions. Because boron compounds may be more rapidly absorbed across damaged skin, individuals with large areas of damaged skin should avoid the application of Sporax or exercise extra caution if they do apply Sporax or other boron-containing compounds. Borax can cause eye irritation. Quantitative risk assessments for irritation are not derived; however, from a practical perspective, eye irritation is likely to be the only overt effect as a consequence of mishandling Sporax. This effect can be minimized or avoided by prudent industrial hygiene practices during the handling of the compound.

For the general public, hazard quotients for consumption of Sporax from a tree stump by a child range from 2 to 16 for ingestion of 50 to 400 mg of Sporax (5.67 to 45.36 mg B/day). These estimated levels of exposure are below levels of exposure associated with nonlethal effects such as diarrhea and vomiting by factors of about 4 [184÷ 45.36] to 32 [184 ÷ 5.67]. Documented lethal doses are in the range 505 mg B/kg/day and 765 mg B/kg/day, factors of about 11 to 135 below the estimated levels of exposure. Thus, while this exposure scenario raises concern in that the RfD could be substantially exceeded in a child directly consuming Sporax from a treated stump, the most likely adverse effects would probably be vomiting and diarrhea.

For consumption of water from a pond contaminated by Sporax due to runoff, none of the hazard quotients exceed the level of concern, even for the highest application rate of 5 lbs Sporax/acre. The highest hazard quotient for consumption of water contaminated by an accidental spill is 0.7, associated with a child consuming water contaminated by the spill of 25 pounds of Sporax into a small pond. Thus, based on this risk assessment, the only exposure scenario that appears to present a significant potential risk is exposure by direct consumption under upper bound conditions.

3.4.2. Workers

A quantitative summary of the risk characterization for workers is presented in Worksheets E02a, E02b and E02c (Supplement 1). Risk is characterized as the estimated dose divided by the RfD. This ratio is referred to as the hazard quotient (HQ). An HQ of one or less indicates that the estimated exposure is less than the toxicity value; when this is the case, there is no basis for asserting that adverse effects are plausible. Estimated exposures are summarized in Worksheet E01. For acute accidental/incidental exposures, the acute RfD of 0.2 mg B/kg/day is used. As noted in Section 3.3.3, the U.S. EPA (2004) has not derived an acute RfD for boron and the chronic RfD derived by U.S. EPA (2004) is used in this risk assessment as a surrogate acute RfD. As discussed in Section 3.2.2, the only exposure scenario considered in this risk assessment is accidental spill of granular Sporax to the skin of the lower legs and hands during application.

Since the exposure scenarios is not dependant on application rate – i.e., it is an incident that could occur while applying Sporax at any application rate – the hazard quotients given in Worksheets E02a, E02b and E02c are the same and range from 0.00003 to 0.001. These hazard quotients are below a level of concern by factors of 1000 to about 33,300. The highest hazard quotient is 0.001, associated with an 8-hour dermal exposure of granular Sporax spilled on the lower legs and hands. Thus, based on the available information and under the foreseeable conditions of application, there is no route of exposure or scenario suggesting that workers will be at any substantial risk from acute exposures to Sporax.

As noted in Section 3.1.3.1, rates of dermal absorption could be much higher in individuals with large areas of abraded or otherwise damage skin. This is not considered quantitatively because the impact of damaged skin would be highly dependent on the surface area of skin that was damaged. In addition, it does not seem likely that individuals with large areas of seriously damaged skin would be involved in the types of physical activities associated with the application of Sporax. Nonetheless, the increased dermal absorption of boron compounds in individuals with damaged skin suggests that workers will seriously damaged skin should either not be involved in the application of Sporax or that these individuals should employ extra measures to ensure that Sporax does not come into contact with damaged skin.

As also discussed in Section 3.1.3.1, borates are rapidly excreted in humans, with a halftime of about 13 hours. Using the *plateau principle* (Section 3.2.3.4), the increase in body burden after an infinite period of time (X_{Inf}) relative to the body burden after a single dose (X_0) can be calculated as:

$$X_{Inf}/X_0 = 1 / (1- e^{-ke\ t^*)})$$

where t* is the interval between exposures and ke is the first-order rate of elimination. Using a halftime of 13 hours (0.54 days, ke=1.27 $days^{-1}$) and a one day exposure interval, the increase in body burden would be a factor of about 1.4. Based on this factor, the highest hazard quotient of 0.001 for a single event would correspond to a chronic hazard quotient of no greater than 0.0014 for any longer term exposure. Thus, even if workers were to repeatedly spill granular Sporax on the lower legs and hands every day, the hazard quotient associated with longer term exposures would be far below the level of concern.

Borax can cause eye irritation (section 3.1.11). Quantitative risk assessments for irritation are not derived; however, from a practical perspective, eye irritation is likely to be the only overt effect as a consequence of mishandling Sporax. This effect can be minimized or avoided by prudent industrial hygiene practices during the handling of the compound. The Sporax label requires eye protection during application.

3.4.3. General Public

A quantitative summary of the risk characterization for members of the general public is presented in Worksheets E04a, E04b, E04c for the range of application rates considered in this risk assessment. As with the risk characterization for workers, risk is expressed quantitatively as the hazard quotient using the oral RfD of 0.2 mg B/kg for acute and chronic exposures (Section 3.3) . With the exception of the direct consumption of Sporax applied to a tree stump by a small child, none of the hazard quotients exceed the level of concern.

For a child ingesting Sporax from a tree stump, hazard quotients range from 2 to 16, with a central estimate of 4. As discussed in Section 3.2.3.2, the estimated amount of Sporax that a child may consume in one day is based on the range for the amount of soil that may be consumed by children – i.e., 50 to 400 mg/day (5.67 to 45.36 mg B/day) (U.S. EPA 1996) and this may not reflect the amount of Sporax that a child might consume in a single event. Since the exposure estimate is highly uncertain and not based on empirical data for borate consumption, risk for this exposure scenario may be underestimated or overestimated. As discussed in Section 3.1.4, relatively good estimates of lethal and sublethal doses in children are available (ATSDR 1992;Wong et al. 1964). Documented lethal doses are in the range 505 mg B/kg/day and 765 mg B/kg/day, factors of about 11 [505÷ 45.36] to 135 [765 ÷ 5.67] below the estimated levels of exposure from ingesting borax from a treated stump. A nonlethal dose in children is about 184 mg B/kg/day and this dose is associated with gastrointestinal effects such as vomiting and diarrhea. The estimated levels of exposure for a child ingesting borax from a treated stump are below this nonlethal level by factors of about 4 [184÷ 45.36] to 32 [184 ÷ 5.67]. Thus, while this exposure scenario raises concern in that the RfD is substantially exceeded, the most likely adverse effects would probably be vomiting and diarrhea.

Hazard quotients for a small child consuming water contaminated by an accidental spill of borax into a small pond range from 0.07 to 0.7. For this worst-case scenario, the spill of a 25 pounds of Sporax, the hazard quotient is below the level of concern. The exposures for the accidental spill scenario are based on amounts of borax ranging from 6.25 to 25 pounds. Since risk is linearly related to the amount of the chemical that is spilled into a pond, for spills of larger amounts, hazard quotients could exceed the level of concern.

For exposure *via* consumption of water contaminated by runoff, the range of application rates considered is 0.1 lb Sporax/acre to 5 lbs Sporax/acre (0.01 to 0.57 lb B/acre), with a typical rate of 1 lb Sporax/acre (0.11 lb B/acre). Hazard quotients for acute exposure of a child and chronic exposure of an adult male to water contaminated by runoff are below the level of concern for all application rates considered. The highest hazard quotient of 0.3 is associated with the upper bound for acute exposure of a child. Thus, even at the highest application rate, there does not appear to be a risk associated with acute or chronic exposure to water contaminated by runoff.

The number of other exposure scenarios could be considered. For example, deer may consume Sporax from a tree trunk. A hunter consuming meat from a deer that previously consumed Sporax might then be exposed to a greater than normal amount of boron. This type of exposure

scenario for a deer is considered in Section 4.2. As detailed in Worksheet F01, the maximum dose for a deer is estimated at 11.5 mg B/kg bw. As detailed in Section 3.2.3.4, however, this concentration (equivalent to 11.5 ppm boron) is in the range of normal concentrations of boron in most terrestrial vegetation (2.3-94.7 ppm) and near the lower end of range of boron in many food commodities (1 to 300 ppm). Thus, the consumption of deer is not considered quantitatively. Like most other exposure scenarios covered in this risk assessment, all but the most extreme exposure scenarios associated with the use of Sporax in Forest Service programs simply do not lead to a substantial increase in normal exposures to boron (e.g., Table 3-4).

3.4.4. Sensitive Subgroups

As discussed in Section 3.1.5, the primary targets for boron toxicity are the developing fetus and the testes. Thus, exposure of pregnant women to borate compounds places the developing fetus at risk. Since the oral (chronic) RfD for boron and borates is based on effects (decreased fetal weight) in the developing fetus, risk to this subgroup is assessed throughout this document. Regarding other sensitive subgroups, males with underlying testicular dysfunction could be at increased risk for boron-induced testicular toxicity. However, no data are available to quantify this risk.

3.4.5. Connected Actions

Sporax is not applied in combination with other products or additives. In addition, no data are available regarding the effects of boron compounds applied in conjunction with other chemicals. Thus, an assessment of toxicological effects of borax mixed with other chemicals cannot be made.

3.4.6. Cumulative Effects

As noted above, chronic exposure to borax is considered for the exposure scenario of an adult consuming surface water contaminated by runoff. Based on the limited analysis in this risk assessment, as discussed above and summarized in Worksheet E04c, there is no indication that repeated exposures will exceed the threshold for toxicity.

As detailed in Section 3.2.3.4, Sporax is unusual for a pesticide in that the toxicologic agent of concern – i.e., boron – is a naturally occurring compound. Boron is a normal consistent of the earths crust, all environmental media, as well as all forms of life including humans. Based on estimates of normal background exposures supported by pharmacokinetic analysis, typical exposures to boron are about 0.14 to 0.36 mg/kg/day. Based on central estimates of exposures to boron associated with the application of Sporax in Forest Service programs, non-accidental exposures are below normal background concentrations by factors of about the typical exposure is above those associated with normal background exposures by a factor of 125 for acute exposure and 625 for chronic exposure. Considering the variability of the estimates of both normal background exposures and estimates of exposure associated with the application of Sporax, Sporax applications lead to exposures that are below those associated with normal background exposures by factors of 13 to 9000 (Section 3.2.3.4). Thus, under foreseeable and typical conditions, applications of Sporax in Forest Service programs will not lead to any

substantial increase in exposure. This is not the case for accidental exposures. For these scenarios, the application of Sporax could approach normal background exposures in the case of an accidental spill and could substantially exceed normal background exposures in the case of a child consuming borax from a treated stump.

In considering the added exposure to boron associated with the application of Sporax, consideration of the design of the toxicity studies in important. The toxicity studies used to characterize risk quantitatively were all conducted based on the addition of boric acid to the diet (e.g., Heindel et al. 1992, 1994, Price et al. 1996a,b). The total exposure of the animals to boron, the agent of concern, involved both the added boric acid as well as background concentrations of boron. Similarly , the reports of human exposures to borax that are used qualitatively modify the risk characterization (i.e., Linden et al. 1986; Wong et al. 1964) also involved exposures to boric acid and background concentrations of borax.

The significance of this is evident in a simple comparison of the chronic RfD of 0.2 mg B/kg/day (Section 3.3) to normal background levels of exposure – i.e., 0.14 to 0.36 mg/kg/day (Section 3.2.3.4). Mathematically, these numbers could be used to derive risk quotients of 0.7 to 1.8. Interpreting these risk quotients in a manner to suggest that humans are typically exposed to hazardous or nearly hazardous levels of boron would be a misinterpretation. Many naturally occurring substances such as oxygen and carbon dioxide can be toxic and some of the mechanisms of action – e.g., oxidative damage to tissue and binding of carbon dioxide to hemoglobin – are normal processes in living organisms that cannot be avoided. A more appropriate interpretation of the RfD would be that increase exposure to boron by the amount of the RfD would reach a level of concern. This is the interpretation given in the current risk assessment and is consistent with approach taken by U.S. EPA (1993a) in waiving tolerances for boric acid and the salts of boric acid in agricultural commodities.

4. ECOLOGICAL RISK ASSESSMENT

4.1. HAZARD IDENTIFICATION

4.1.1. Overview.

As discussed in Section 2, borate salts are rapidly converted to boric acid under conditions typically found in the environment. At physiologic pH and in most surface waters, exposure of organisms is primarily to boric acid. Therefore, information on boric acid is reviewed as appropriate and used as surrogate data in this risk assessment for borax. In order to facilitate any comparisons between borax and boric acid, data are expressed in terms of the dose or concentration of borate compound (borax or boric acid) and in terms of boron equivalents (B).

As discussed in Section 3.1, in terrestrial mammals, the primary target organ for chronic borax exposure is the testis, with exposure resulting in decreased male fertility. In birds, acute exposure to borax is practically non-toxic, with no significant clinical signs of toxicity at dietary concentrations up to 5000 ppm borax (567 ppm B equivalent to 567 mg B/kg diet). Although limited data are available in birds, it appears that longer-term dietary exposure to boron compounds results in adverse reproductive effects in avian species. Very little information is available on the effects of boron compounds on nontarget terrestrial invertebrates. Based on the results of a single acute topical exposure study of honey bees (LD_{50} >362.58 µg boric acid/bee or 41.1 µg B/bee), boric acid is considered essentially non-toxic. However, given that borax is used in the control of termites, ants and house flies, toxic effects may occur in other insects.

Boron is an essential trace element for terrestrial plants. The amount of boron required to produce optimal growth and development varies tremendously between species and even between strains of the same species. However, excess boron can lead to the development of phytotoxicity. In most species, there is a narrow range between the amount of boron required for optimal growth and the amount that is phytotoxic. Standard bioassays for toxicity of boron compounds to terrestrial plants (Tier I and Tier II seedling emergence or vegetative vigor studies) were not identified in the available literature. While there are many studies evaluating the phytotoxicity of boron compounds, few provide data that are useful in a quantitative assessment of the risk of boron toxicity. Data are available for a limited number of terrestrial plants – potatoes, winter wheat, sugarbeet, poppy, oats and turnip. Based on the lowest reported NOAEC, the most sensitive species appears to be the potato, with an NOAEC of 5 mg B/kg soil and the most tolerant species appears to the sugarbeet, with an NOAEC of 20 mg B/kg soil. However, it is likely that more sensitive and more tolerant species exist.

In fish and aquatic invertebrates, acute exposure to borax and boric acid appears to have a relatively low order of toxicity. In fish, 96-hour LC_{50} values range from >100 mg B/L in razorback suckers and squawfish to >1100 mg B/L in bluegill sunfish. The 48-hour LC_{50} values for *Daphnia magna* range from 126 to 141 mg B/L. Limited information is available on chronic exposure of fish to boric acid and borax. Chronic reproduction studies in daphnids yield an NOAEC for reproductive effects of 6 mg B/L.

Relative to the abundant literature on the essential role of boron in terrestrial plants, very little information is available on the effects of boron compounds on aquatic macrophytes. Short-term exposure studies were conducted with boric acid in watermilfoil, water buttercup, and waterweed, with similar LC_{50} values reported for all three plant species (watermilfoil and waterweed: 5 mg B/L; water buttercup 10 mg B/L). In algae, the 72-hour LC_{50} values reported for *Scenedesmus subpicatus* range from 34 mg B/L to 52 mg B/L and the 72-hour NOAEC values range from 10 mg B/L to 24 mg B/L, with similar NOAEC values reported for *Scenedesmus quadricauda* and *Microcystis aeruginosa*.

4.1.2. Toxicity to Terrestrial Organisms.

4.1.2.1. Mammals– As summarized in the human health risk assessment (see Section 3.1), the mode of action of borax and other borate salts in mammals is not well understood. There are several standard toxicity studies in experimental mammals that were conducted as part of the registration process. Results of studies in laboratory mammals are summarized in Section 3.1, with additional information provided in Appendix 1. Based on the results of acute exposure studies, borax is classified as moderately toxic, with an LD_{50} in male rats of 4.5 g borax/kg (Weir and Fisher 1972). Clinical signs of toxicity observed following acute exposures include depression, ataxia and convulsions. In dogs, acute exposure to borax produced a strong dose-dependent emetic response (Weir and Fisher 1972). As expected of a compound with a low dermal absorption rate, the LD_{50} of borax following single dermal application is > 5 g/kg in rats (Wnorowski 1996a) and > 2 g/kg in rabbits (Reagan 1985a). Results of a single inhalation exposure study yielded a 4-hour LC_{50} > 2.0 mg/L (Wnorowski 1994a).

Results of developmental, subchronic and chronic toxicity studies show that the developing fetus and the male reproductive system are the primary targets for borate-induced toxicity (Sections 3.1.5 and 3.1.9). Gestational exposure of rats, mice, and rabbits to boric acid resulted in increased fetal deaths, decreased in fetal weight, and increased fetal malformations. The types of fetal malformations observed include anomalies of the eyes, central nervous system, cardiovascular system, and axial skeleton in rats, short rib XIII and other skeletal anomalies pertaining to ribs in mice, and cardiovascular malformations in rabbits. The most sensitive effect observed from gestational exposure to boric acid is decreased body weight. Regarding testicular toxicity, results of subchronic and chronic dietary exposure studies in adult rats and dogs show that testicular toxicity is characterized by dose-dependent atrophy of the testes, degeneration of the seminiferous epithelium, and sterility (Weir and Fisher 1972, Dixon et al. 1976, 1979, Lee et al. 1978). At lower exposure levels, testicular effects and infertility may be reversed (Dixon et al. 1979), but adverse effects can persist for at least 8 months at higher exposure levels (Lee et al. 1978).

As discussed in Section 3.3.3, the U.S. EPA (2004) has recently derived an oral (chronic) RfD of 0.2 mg/kg/day for boron (boron and borates only), using the combined data of two developmental toxicity studies in rats using decreased fetal weight as the most sensitive endpoint (Price et al. 1996a, Heindel et al. 1992). The RfD is based on a benchmark dose analyses identifying a 5% decrease in mean fetal body weight compared to control as the benchmark response (BMR) level

(Allen et al. 1996). The 95% lower bound on the dose corresponding to the BMR, i.e., the $BMDL_{05}$, of 10.3 mg B/kg/day is used as the *critical dose* value to calculate the RfD. The uncertainty factor of 66, which considers both the toxicokinetic and toxicodynamic aspects associated with interspecies and interindividual variability, was applied to the critical dose to derive the chronic RfD of 0.2 mg B/kg/day. Based on a review of the studies considered by the U.S. EPA, the selection of this study seems reasonable and appropriate. The U.S. EPA has not derived an acute RfD for boron. Therefore, the chronic RfD of 0.2 mg B/kg/day will also be used to characterize risks associated to incidents or accidents that involve an exposure period of 1 day. Additional details on these developmental studies are provided in Sections 3.1.5, 3.1.9, and 3.3.2 and in Appendix 1.

Two internal Forest Service documents provide information on the effects of borax in field settings - one study on the attractant effects of borax applied to tree stumps and a veterinarian's report on the death of a cow in a borax-treated area. In a field study conducted by the Forest Service, the attractant effects of borax applied to freshly cut Douglas fir stumps were evaluated (Campbell et al., no date). Deer were introduced to a 2.5 acre pen with freshly cut tree stumps that were either untreated or had been treated with 1 oz (28.4 g borax) of borax. Deer appeared equally attracted to both control stumps and borax-treated stumps, exhibiting sniffing and licking behavior. There was no apparent attractant effect of borax-treated stumps and there were no obvious signs of toxicity to deer that did eat borax from the stumps. The amount of borax that deer licked from the stumps was not quantified. Dost (1994) summarizes an incident involving the death of a cow in an area that had been treated with borax. Although Dost (1994) concluded that it was unlikely that the cow had died due to the ingestion of borax, this opinion appears to be formulated largely on the basis of the literature reviewed by Dost (1994) on the toxicity of borax and on the environmental circumstances encountered. As the cow was found at least 10 days after death, Dost (1994) also noted that pathological or chemical examinations of the carcass were not possible.

4.1.2.2. Birds– Limited information is available on the acute and chronic effects of borax and other boron-containing salts in avian species. In standard test species, acute single and acute dietary exposure studies have been conducted on borax and boric acid (Fink et al. 1982a, Reinart and Fletcher 1977, U.S. EPA 1993b); results are summarized in Appendix 2. Based on the LD_{50} of >2510 mg borax/kg (equivalent to >284 mg B/kg) in bobwhite quail, exposure to a single oral dose of borax is considered to be practically non-toxic to avian species (Fink et al. 1982a). A similar low level of toxicity was also observed following 5-day dietary exposures of bobwhite quail to borax, with an LC_{50} value >5000 ppm dietary borax (>567 ppm B) (Reinhart and Fletcher 1977). In these two studies, no clinical signs of toxicity were observed. Similarly, 5-day dietary exposures of bobwhite quail and mallard ducks to boric acid yielded LC_{50} values >5000 ppm boric acid (equivalent to 874 ppm B), indicating that boric acid is also practically non-toxic to avian species (U.S. EPA 1993b). Since LD_{50} and LC_{50} values obtained in these studies were greater than the highest dose tested, it is difficult to draw conclusions regarding the toxicity of borax relative to boric acid. However, based on the limited results available, birds appear to exhibit similar sensitivity to borax and boric acid in acute exposures.

No chronic exposure studies (21-week exposure studies) on borax or boric acid using standard test avian species were identified. The only avian reproduction study on borax identified in the available literature is a 28-day dietary exposure study in broiler chickens (Rossi et al. 1993). Results of this study show decreased hatchability in offspring of chickens exposed to 250 ppm B. In male chickens exposed to borax (250 ppm B), an increase in the number of damaged spermatozoa was observed ($p = 0.051$) (Rossi et al. 1993). Only one concentration of borax was tested in this study; thus, the NOAEL is <250 ppm B and the LOAEL is 250 ppm B. A single avian reproduction study in mallard ducks exposed to dietary boric acid for 6 weeks reported decreased hatching, post-hatching growth and survival in the 1000 ppm B treatment group (NOAEL = 300 ppm B; LOAEL = 1000 ppm B) (Smith and Anders 1989). There was no effect of treatment on adult survival or egg fertility and no evidence of male reproductive toxicity was observed (NOAEL >1000 ppm B). Details of these studies are provided in Appendix 2.

4.1.2.3. Terrestrial Invertebrates – Very little information is available on the effects of borate compounds in nontarget terrestrial invertebrates. No studies on the acute or chronic effects of borax in nontarget terrestrial invertebrates were identified in the available literature. Results of a single study on the effects of acute topical exposure of honey bees to boric acid show that boric acid is essentially non-toxic to honey bees (Atkins 1987, U.S. EPA 1993b). No mortality was observed in honey bees exposed to 363 µg boric acid/bee (equivalent to about 63 µg B/bee).

Results of efficacy studies show that borax is effective for the control of various insect pests, including termites (Grace and Abdallay 1990, Grace and Yamamoto 1994, Toyoshima et al. 1997), ants (Klotz et al. 2000) and the house fly (Hogsette and Koehlet 1992). Based on its effective use as an insecticide, it is likely that borax may have adverse effects on other insects. However, data on the effects of boric acid and boric acid salts on nontarget insects are not available in the literature.

4.1.2.4. Terrestrial Plants (Macrophytes)– Boron is an essential trace element for terrestrial plants. The amount of boron required to produce optimal growth and development varies tremendously between species and even between strains of the same species (ECETOC 1997, Jamjod and Rerkasem 1999, Moore 1997, Tanji 1990, WHO 1998). Symptoms of boron deficiency include cessation of root and leaf growth, leaf, stem and root tip necrosis, reduced germination, and death (WHO 1998). Use of fertilizers containing boron can improve plant vigor and increase crop yield for plants grown in boron-deficient soils (ECETOC 1997). However, excess boron can lead to adverse effects in plants including chlorosis of leaves, leaf necrosis and decreased germination (ECETOC 1997, WHO 1998). In most plant species, there is a narrow range between the amount of boron required for optimal growth and the amount that is phytotoxic (ECETOC 1997, Moore 1997, WHO 1998). According to the product label for Sporax (Wilbur-Ellis Company, no date), borax spilled or applied to crops may retard plant growth or kill plants. The label does not specify which plants species are at greatest risk for borax-induced phytotoxicity.

Standard bioassays for toxicity of boron compounds to terrestrial plants (Tier I and Tier II seedling emergence or vegetative vigor studies) were not identified in the CBI literature. While there are many studies evaluating the phytotoxicity of boron compounds, few provide data that are useful in a quantitative assessment of the risk of boron toxicity; much of the available data is from studies focused primarily on the correlation between boron toxicity and boron accumulation in plant leaves. The studies providing adequate data to allow for a quantitative assessment of risk are summarized in Appendix 4. Data are available for a limited number of terrestrial plants – potatoes, winter wheat, sugarbeet (Kluge 1990, as cited in ECETOC 1997), poppy (Sopova et al. 1981),oats and turnip (Stanley and Tapp 1982, as cited in Windeatt et al. 1991). All studies summarized in Appendix 4 follow similar protocols: seeds are planted in boron-containing soil (added as borax or boric acid). Phytotoxicity and plant development are assessed at a later time point in the study. However, it is difficult to compare results of these studies since toxicity endpoints vary between studies (in some studies the toxicity endpoints are reported as the EC_{50} and in others as the NOAEC) and standard toxicity bioassay protocols were not followed. Based on the lowest reported NOAEC, the most sensitive species appears to be the potato, with an NOAEC of 5 mg B/kg soil (Kluge 1990, as cited in ECETOC 1997) and the most tolerant species appears to be the sugarbeet with an NOAEC of 20 mg B/kg soil (Kluge 1990, as cited in ECETOC 1997). However, it is likely that more sensitive and more tolerant species exist.

4.1.2.5. Terrestrial Microorganisms – Very little information is available on the effects of boric acid or borax on nontarget terrestrial microorganisms. There is no evidence to suggest that boron is an essential nutrient for soil microorganisms (WHO 1998). An *in vitro* study of soil treated with borax (concentrations not specified) showed that borax treatment had no effect on total soil counts of actinomyces, fungi, protozoa and bacteria involved in nitrification (Smith et al. 1946). Borax is effective in the control of various wood-rotting fungi, including *Heterobasidion annosum* (Findlay 1953, 1960, Graham 1970). Although inadequate data are available to provide an assessment of the effects of borax in nontarget microorganisms, given the effectiveness of borax in the control of annosum root disease, it is likely that borax will have effects on nontarget microorganisms.

4.1.3. Aquatic Organisms.

4.1.3.1. Fish – Information on the toxicity of boron to fish is summarized in Appendix 5. Standard bioassays on the acute toxicity of borax in fish were not identified in the CBI literature. As discussed in Section 2, since borax is converted to boric acid in water, studies on boric acid can be used to supplement the limited information available on the effects of acute borax exposure in fish. Acute exposure studies on borax have been conducted in rainbow trout (Alabaster 1969, as cited in Hovatter and Ross 1995) and western mosquito fish (Wallen et al. 1957, as cited in Hovatter and Ross 1995). Based on the 48-hour LC_{50} values obtained in these studies, rainbow trout (LC_{50} = 387 mg B/L) appear more sensitive than mosquito fish (LC_{50} = 930 mg B/L) to acute exposure to borax. More information is available on acute exposure of fish to boric acid, with data available in bluegill sunfish, rainbow trout (LaLievre 1988, as cited in U.S. EPA 1993b), Colorado squawfish, razorback sucker, bonytail (Hamilton 1995) and young salmon fry (Hamilton and Buhl 1990). Based on the available acute LC_{50} values for borax and boric

acid, razorback suckers in the fry stage appear to be the most sensitive species to acute boron exposure (96-hour LC_{50} of 233 mg B/L from Hamilton 1995) and rainbow trout appear to be the most tolerant species (96-hour LC_{50} >1100 mg B/L from U.S. EPA 1993b). Based on these values and the classification scheme typically used by the U.S. EPA (U.S. EPA/EFED 2001), these compounds are classified as practically nontoxic to fish.

Longer-term toxicity studies on borax were conducted using rainbow trout, channel catfish, and goldfish. Data from these studies were reported in a single publication from the open literature (Birge and Black 1977) and are summarized in Appendix 5. No standard chronic exposure studies on borax or boric acid were identified in the CBI literature. Results of the Birge and Black (1977) study show a similar degree of sensitivity for the three species tested. The lowest estimated NOAEC (for mortality) of 0.5 ppm B was reported for goldfish and the highest estimated NOAEC (for mortality) of 1.0 ppm B was reported for rainbow trout and channel catfish. Since different exposure times were used for each of the three species tested (up to 28 days for trout, 9 days for catfish, and 7 days for goldfish), it is difficult to identify a most sensitive and most tolerant species for longer-term exposure.

***4.1.3.2. Amphibians*–**Very little information is available on the effects of borax to amphibians. A single study in larval leopard frogs exposed to borax for 7.5 days reports an LC_{50} of 47 ppm B, with an estimated NOAEC (for mortality) of 1.0 ppm B and an estimated LOAEC (for mortality) of 5.0 ppm B (Birge and Black 1977). Thus, toxicity of borax to leopard frogs appears to be relatively low. Results of a study in wood frog, Jefferson salamander, spotted salamander, and American toad show that boron concentrations of 50 and 100 mg B/L caused a dose-related decrease in proportion of eggs hatching in American toad, while hatching was unaffected in the other three species (Laposata and Dunson 1998). In this same study, a dose-dependent increase in proportion of deformed larvae was observed in wood frog, Jefferson salamander, and spotted salamander (not assessed in American toad). Details of these studies are provided in Appendix 5.

***4.1.3.3. Aquatic Invertebrates* –**No standard bioassays of the acute and chronic toxicity of borax or boric acid to aquatic invertebrates were identified in the CBI literature. Acute toxicity studies on borax and boric acid have been conducted in *Daphnia magna*, with results reported in the published literature (Appendix 6). Results of 48-hour exposure studies show similar LC_{50} values for borax (48-hour LC_{50} = 141 mg B/L, Maier and Knight 1991) and boric acid (48-hour LC_{50} = 133 mg B/L, Gersich 1984; 48-hour LC_{50} = 126 mg B/L, Lewis and Valentine 1981). The larval freshwater midge *Chironomus decorus* (a benthic organism) appears to be more tolerant than daphnids to acute boron exposure, with a 48-hour LC_{50} value of 1376 mg B/L (Maier and Knight 1991).

Two 21-day exposure studies in daphnids were conducted with boric acid, with results reported in the published literature; similar results were reported for both studies (Appendix 6). The lowest 21-day LC_{50} value reported for exposure of daphnids to boric acid is 52.2 mg B/L

(Gersich 1984). The lowest NOAEC value reported for reproductive parameters is 6 mg B/L with a LOAEC for reproductive parameters of 13 mg B/L (Lewis and Valentine 1981).

4.1.3.4. Aquatic Plants – No studies on the effects of borax in aquatic macrophytes were identified in the available literature. Short-term exposure studies were conducted with boric acid in watermilfoil, water buttercup, and waterweed (Nobel 1981, as cited in WHO 1998). Similar LC_{50} values were reported for all three plant species (watermilfoil and waterweed: 5 mg B/L; water buttercup 10 mg B/L). A chronic exposure study of boric acid in common reed *(Phragmites australis*) reports a 2-3 month NOAEC of 8 mg B/L and a 2-year NOAEC of 4 mg B/L (Bergmann et al. 1995, as cited in ECETOC 1997 and WHO 1998).

The effects of boron exposure in algae have been reviewed by ECETOC (1997) and WHO (1998). The 72-hour LC_{50} values reported for *Scenedesmus subpicatus* range from 34 mg B/L to 53 mg B/L and the 72-hour NOAEC values range from 10 mg B/L to 24 mg B/L. Similar NOAEC values were reported for *Scenedesmus quadricauda* and *Microcystis aeruginosa*. Based on the information presented in the ECETOC 1997 and WHO 1998 reviews, the algal species tested show a similar degree of sensitivity to the toxic effects of boron. Based on the information presented in these reviews, it is not possible to determine the chemical species of boron used in these studies because exposures were reported in terms of boron equivalents.

4.1.3.5. Aquatic Microorganisms (Other than algae) –
The effects of boron exposure to aquatic microorganisms (other than algae) was recently reviewed by WHO (1998). Data are reported in several species, with 72-hour NOAEC values ranging from 0.3 mg B/L in *Entosiphon sulfacum*, a flagellate (Bringmann and Kuhn 1980, as cited in WHO 1998), to 291 mg B/L in *Pseudomonas putida* (Schoberl and Huber 1988, as cited in WHO 1998).

4.2. EXPOSURE ASSESSMENT

4.2.1. Overview

As discussed in Section 3.2, Sporax is applied directly to the surfaces of freshly cut tree stumps. Sporax is not applied using backpack, broadcast or aerial spray methods and it is not applied directly to vegetation. Therefore, many of the standard exposure scenarios that are typically considered for Forest Service risk assessments, such as direct spray, oral exposure *via* ingestion of contaminated prey or vegetation, are not applicable for this risk assessment. The exposure scenarios used in this risk assessment are those expected to result in substantial exposure considering the atypical application method for Sporax. Since Sporax is not applied as a spray, wide-spread exposure of insects is not expected; thus, an exposure assessment for insects has not been conducted in this risk assessment. Due to a lack of toxicity data, no exposure assessment was conducted for nontarget soil microorganisms.

For terrestrial vertebrates, two exposure scenarios are considered for this risk assessment: acute exposure *via* consumption of Sporax applied to tree stumps, and acute as well as chronic exposure *via* exposure to contaminated pond water. Exposure values for acute exposure *via* consumption of Sporax applied to a tree stump range from 0.57 mg B/kg/event for a large mammal to 29 mg B/kg/event for a small bird.

For contamination of water by both an accidental spill scenario and by runoff from the application site are considered. As noted in the exposure assessment for human health, the use of Sporax in stump treatments is not likely to have a substantial affect on concentrations of boron in ambient water. For ingestion of contaminated water *via* accidental spill, acute exposure values for a small mammal range from 0.0001 to 0.0004 mg B/kg/event. For acute exposure of a small mammal *via* ingestion of water contaminated by runoff, acute exposure values range from approximately 0.0009 to 0.014 mg B/kg/event. For chronic exposure of a small mammal by water contaminated by runoff, exposure values range from about 0.0003 to 0.01 mg B/kg/day. Since Sporax is not applied to vegetation, the only exposure scenario considered for terrestrial macrophytes is exposure to boron that reaches soil *via* runoff. Based on the results of GLEAMS modeling, peak concentrations of boron in soil range from 0.0026 ppm for the lowest value associated with an application rate of 0.1 lb Sporax/acre to 2.29 ppm in soil for the highest value associated with an application rate of 5 lbs Sporax/acre.

Exposures to aquatic organisms are based on the same information used to assess the exposure to terrestrial species from contaminated water. For an accidental spill of Sporax into a small pond, the central peak estimated concentration of boron in ambient water is 0.64 mg B/L (0.32 - 1.28) mg B/L (ppm). For contamination of a small pond by runoff, the peak estimated concentration in ambient water is 30 (6 to 100) µg/L after a single application of 1 lb Sporax/acre (0.11 lb boron/acre). For longer-term exposures, the corresponding longer term concentrations in ambient water are estimated at about 14 (2 to 70) µg/L.

4.2.2. Terrestrial Vertebrates

4.2.2.1. Oral Exposure to Sporax Applied to Tree Stumps – Very little information is available to estimate the amount of Sporax that deer, other mammals, or birds are likely to consume. Thus, exposures developed for this scenario are highly uncertain.

A field study conducted by the Forest Service on the attractant effects of Sporax applied to tree stumps (Campbell et al., no date) reports that deer will lick borax applied to the surface of tree stumps. Because deer also licked the surface of untreated control stumps, it is not clear that Sporax is an attractant for deer. Nonetheless, the study by Campbell et al. (no date) suggests that the consumption of Sporax from treated stumps is a plausible exposure scenario for deer and may be plausible for other species as well.

For large mammals such as a deer, exposure is based on the underlying assumption that a deer might consume all of the Sporax applied to a tree stump that is 1 foot in diameter. Based on the application rate for Sporax of 1 lb/50 ft^2 of stump area and the application area of a 1 foot diameter stump of 0.7854 ft^2 [$\pi r^2 = (3.1416)\ (0.5\ ft)^2 = 0.7854\ ft^2$], the amount of Sporax applied to a 1 foot diameter stump is 0.0157 pounds [1 lb/50 $ft^2 \times 0.7854\ ft^2 = 0.0157$ lb] or 7.12 grams of Sporax or 807 mg boron equivalents [7.12 g × 1000 mg/g × 0.1134]. As with the exposure assessments for small mammals and birds, the central estimate of the proportion of the Sporax that is consumed from the stump will be taken as 0.3 with a range of 0.05 to 1.0. Thus, the consumption in units of boron equivalents is 242 mg [807 mg × 0.3] with a range of 40 mg [807 mg × 0.05] to 807 mg. This exposure scenario is detailed in Worksheet F01.

While the direct consumption of Sporax by a large mammal such as a deer seems plausible, direct consumption by a large bird (such as a goose or heron) seems implausible. Large birds such as heron or geese will typically consume either vegetation or fish (U.S. EPA/ORD 1993). Nonetheless, a similar scenario is developed for a Canada goose with a body weight of 4 kg. The amount of boron that might be consumed is reduced in proportion to the body weight of the goose relative to the deer – i.e., 4/70 or about 0.057. Thus, the consumption in units of boron equivalents is estimated at 13.7 mg [242 mg × 0.057] with a range of 2.3 mg [40 mg × 0.057] to 46 mg [807 mg × 0.057]. This exposure scenario is detailed in Worksheet F02.

For smaller species, it seems less plausible that the animal would consume all of the Sporax on a treated stump. The body weights that are used in most Forest Service risk assessments are adopted from U.S. EPA/ORD (1993) and range from 10 grams for a small bird and 20 grams for a small mammal (SERA 2001). As noted above, the amount of Sporax on a stump with a 1 foot diameter would be approximately 7 grams. Based on allometric relationships given in U.S. EPA/ORD (1993), the daily food consumption for small mammals and birds will typically be equivalent to about 10% to 20% of their body, depending on the caloric value of the food source. Consuming 7 grams of Sporax would be equivalent to 35% to 70% of the body weight of a small mammal and bird, respectively.

As an alternative to assuming complete consumption for small mammals and birds, the assumption is made that the amount of Sporax that might be consumed from the surface of a treated stump will range from 0.05 to 0.2 of the body weight of the animal, with a central estimate of 0.1. These values for Sporax are adjusted downward by a factor of 0.1134 to convert the consumption of Sporax to boron equivalents (Table 2-1). Thus, rounding to 2 significant figures, the proportion of the body weights used to estimate boron consumption is 0.011 with a range of 0.0056 to 0.023. The scenarios for a small mammal and small bird are given in worksheets F03 and F04, respectively.

4.2.2.2. Ingestion of Contaminated Water – As discussed in the human health exposure assessment (Section 3.2.3.3), the borax application considered in this risk assessment – application of granular product to tree stumps – has a limited potential to contaminate water. Nonetheless, after application to tree stumps, rainfall and consequent runoff could lead to contamination of standing water or streams. In addition, accidental spills of the Sporax formulation into a small body of water are possible.

The accidental spill scenario parallels that used in the human health risk assessment (3.2.3.4.1). The amount of Sporax spilled ranges from 6.25 to 25 lbs (0.7 to 2.8 pounds of boron equivalents), with a central estimate of 12.5 lbs (1.42 pounds of boron equivalents). This exposure scenario is detailed in Worksheet F05 for a small mammal.

For non-accidental exposures, estimated concentrations of boron in water are identical to those used in the human health risk assessment (Worksheet B06). The only major differences involve the weight of the animal and the amount of water consumed. There are well-established relationships between body weight and water consumption across a wide range of mammalian species (e.g., U.S. EPA 1989). Unlike the human health risk assessment, estimates of the variability of water consumption are not available. Thus, the only factor affecting the variability of the ingested dose estimates is the concentration of the boron in water. The acute and chronic scenarios for non-accidental exposures are given in Worksheets F06 and F07, respectively.

4.2.3. Terrestrial Plants

Since Sporax is not applied to vegetation and is not applied as a liquid, exposure scenarios that are typically included in Forest Service risk assessment documents for terrestrial macrophytes, such as exposure by direct spray or spray drift, are not applicable to this risk assessment. The only exposure scenario considered for plants is exposure to boron in soil.

The available toxicity data on boron in terrestrial plants are expressed in units of soil concentration – i.e., mg boron/kg soil which is equivalent to parts per million (ppm) concentrations in soil. The GLEAMS modeling discussed in Section 3.2.3.4.2 provides estimates of concentration in soil as well as estimates of off-site movement (runoff, sediment, and percolation). Based on the GLEAMS modeling, concentrations in clay, loam, and sand over a wide range of rainfall rates are summarized in Table 4-1. As indicated in this table, peak soil concentrations in the range of about 0.46 ppm boron are likely in arid loam at an application rate

of 1 lb Sporax/acre (0.11 lb boron/acre). As rainfall rate increases, maximum soil concentrations are substantially reduced for each soil type because of losses from soil through percolation. The potential consequences of such exposures are discussed in Section 4.4 (Risk Characterization). Based on monitoring data, which show that normal boron concentrations range from 10 to 30 ppm, it is not expected that runoff from application of Sporax to tree stumps will contribute significantly to boron soil concentrations.

4.2.4 Other Terrestrial Organisms

Borax is a fungicide and it is anticipated that at least some soil microorganisms will be exposed to borax and could be adversely affected. However, due to a lack of quantitative toxicity data applicable to soil exposures, the risks cannot be quantitatively characterized. Thus, no exposure assessment is conducted for soil microorganisms in this risk assessment. Acute toxicity data are available for honey bees. However, since Sporax is applied only to cut tree stumps and is not applied by broadcast spray, it is unlikely that there will be wide-spread exposure to insects. Thus, an exposure assessment for insects is not conducted as part of this risk assessment. Exposure of individual insects that are on the treated stump surface at the time of treatment may result in toxicity to a susceptible insect species.

4.2.5. Aquatic Organisms

The potential for effects on aquatic species is based on estimated concentrations of borax (as boron equivalent) in water that are identical to those used in the human health risk assessment. For this risk assessment, contamination of water is considered for two scenarios – accidental spill of a bag of Sporax (containing an amount ranging from 6.25 to 25 pounds Sporax) into a small pond and contamination of pond water and contamination of a small pond by runoff. For an accidental spill of Sporax into a small pond, the peak estimated concentration of boron in ambient water is 0.64 mg B/L (0.32 - 1.28) mg B/L (ppm). Details of this calculation are provided in Worksheet F05. As summarized in Table 3-3, for contamination of a small pond by runoff, the peak estimated concentration of boron in ambient water is 30 (6 to 100) µg boron/L after a single application of 1 lb Sporax/acre (0.11 lb boron/acre). For longer-term exposures, the corresponding longer term concentrations in ambient water are estimated at about 14 (2 to 70) µg boron/L.

4.3. DOSE-RESPONSE ASSESSMENT

4.3.1. Overview

The specific toxicity values used in this risk assessment are summarized in Table 4-2, and the derivation of each of these values is discussed in the various subsections of this dose-response assessment. The first column in Table 4-2 specifies the organism to which the toxicity value applies. The available toxicity data support separate dose-response assessments in ten classes of organisms: terrestrial mammals, birds, nontarget terrestrial invertebrates, terrestrial macrophytes, fish, aquatic invertebrates, amphibians, aquatic macrophytes, algae, and aquatic microorganisms. Different units of exposure are used for different groups of organisms depending on how exposures are likely to occur and how the available toxicity data are expressed.

Borate compounds are relatively non-toxic to mammals and birds. For mammals, the toxicity values used in the ecological risk assessment are identical to those used in the human health risk assessments: the 95% lower bound on the dose corresponding to the BMR, i.e., the $BMDL_{05}$, of 10.3 mg B/kg/day (the *critical dose*) for decreased fetal body weight (Allen et al. 1996, U.S. EPA 2004) is used to assess both acute and chronic risk. For birds, the acute NOAEL for boron is taken as 136 mg B/kg based on lack of mortality or clinical signs of toxicity following 5-day dietary exposure of bobwhite quail to borax. For chronic exposure of birds, the limited data available suggest that longer-term exposure to boron compounds can cause testicular toxicity in avian species; however the available studies did not rigorously investigate the potential for boron compounds to produce testicular toxicity. Therefore, the mammalian *critical dose* of 10.3 mg B/kg/day will be used to characterize the risk of chronic exposure to boron compounds in birds. For terrestrial invertebrates, data used to characterize risk is from a single contact bioassay in the honey bee, with an NOAEL for mortality of 677 mg/kg.

Although there is an abundant literature regarding the role of boron as an essential element for terrestrial plants, standard bioassays on the effects of boron on seedling emergence and vegetative vigor are not available. Based on the relatively limited information available, the NOAEC of 5 mg B/kg soil for the potato will be used to characterize risk in the most sensitive and the NOAEC of 20 mg B/kg soil will be used to assess risk in the most tolerant nontarget plant species. However, it is likely that more sensitive and more tolerant species exist. Since borates are effective fungicides, some nontarget soil microorganisms could be affected by exposure to boron in soil. However, information to adequately assess risk in this class of organisms is not available.

Toxicity values for aquatic species indicate relatively little difference between fish and aquatic invertebrates based on acute toxicity. For fish, the acute 96-hour LC_{50} values are 233 mg B/L and >1100 mg B/L for sensitive and tolerant species, respectively. For aquatic invertebrates, a similar range in 48-hour LC_{50} values (133 mg B/L for sensitive species and 1376 mg B/L for tolerant species) was observed. For chronic exposures, fish appear more sensitive than aquatic invertebrates to boron exposure. In fish the range of NOAEC values is relatively narrow, with the NOAEC of 0.5 ppm boron in the most sensitive species and 1.0 ppm boron in the most tolerant species. In aquatic invertebrates, NOAEC values range from 6 mg B/L to the estimated

value of 61.8 mg B/L. To characterize the risk of acute exposure to amphibians, the NOAEC of 1.0 ppm B obtained in a single study in leopard frog larvae will be used. No studies on the effects of chronic exposure of amphibians to boron compounds were identified in the available literature. Based on the available data, the most sensitive algal species is the green algae *Scenedesmus subpicatus*, with a 72-hour NOAEC of 10 mg B/L (Bringmann and Kuhn 1978, as cited in ECETOC 1997) and the most tolerant species is the blue-green alga *Microcystis aeruginosa*, with a 72-hour NOAEC of 20.3 mg B/L (Bringmann and Kuhn 1978, as cited in ECETOC 1997). Although these tests are conducted for a relatively short period of time (i.e. 72 hours), these NOAEC values are applied to both acute and longer-term concentrations because of the short life-cycle of individual algal cells. For aquatic macrophytes 21-day exposure studies yield a range of LC_{50} values of 5 to10 mg B/L; these values will be used to assess acute exposure risk to sensitive and tolerant aquatic macrophytes. For aquatic microorganisms, the NOAEC values of 0.3 mg B/L and 291 mg B/L are used to assess the consequences of both acute and longer-term exposures for sensitive and tolerant species of aquatic microorganisms because of the short life-cycle of individual microorganisms.

4.3.2. Toxicity to Terrestrial Organisms

4.3.2.1. Mammals – As summarized in the dose-response assessment for the human health risk assessment (Section 3.3), the most sensitive effect in experimental animals is decreased body weight in the developing fetus. The *critical dose* used to derive the oral (chronic) RfD for boron and borates is the 95% lower bound on the dose corresponding to the BMR, i.e., the $BMDL_{05}$, of 10.3 mg B/kg/day (the *critical dose*) for decreased fetal body weight (Allen et al. 1996, U.S. EPA 2004). The NOEC of 10.3 mg B/kg/day will be use in the ecological risk assessment to characterize risks associated with longer-term exposures of mammalian wildlife species to borax.

As discussed in Section 3.3.3, the U.S. EPA has not derived an acute/single dose RfD for boron compounds. Decreased fetal weight is considered the most sensitive endpoint resulting from gestational exposure to dietary boron (Heindel et al. 1992, Price et al. 1996a). Although the exposure duration in these studies was actually quite short (20 days), results were used to derive the oral (chronic) RfD, based on a *critical dose* of 10.3 mg B/kg/day. As summarized in Section 3.1.5 and 3.1.9, results of reproductive toxicity studies identify testicular toxicity as the most sensitive endpoint for longer-term exposures, with an NOAEL of 8.8 mg/kg/day in dogs (Weir and Fisher 1972). However, given the concerns raised by U.S. EPA (2004) regarding the dog study (Section 3.3.2), coupled with the shorter exposure duration used in the developmental studies in rats, assessing acute risk based on the results of the gestational studies in rats appears more appropriate than using results of the longer-term toxicity studies in dogs. Thus, the *critical dose* of 10.3 mg B/kg/day used for longer-term exposures will also be used to characterize risks to mammals associated to incidents or accidents that involve an exposure period of 1 day.

4.3.2.2. Birds – Compared to the many studies conducted in laboratory mammals, there is very little information available on the effects of acute and chronic exposure of avian species to boron compounds. As detailed in Appendix 2, results of an acute (5-day) dietary exposure of bobwhite quail yield an LC_{50} value >5000 ppm borax (equivalent to >567 ppm B), indicating that acute

exposure to borax has a low order of toxicity in avian species (Reinart and Fletcher 1977). No clinical signs of toxicity were observed in birds exposed to dietary concentrations up to 5000 ppm borax. Thus, the NOAEL for acute exposure of birds is taken as 567 ppm B in the diet (136 mg B/kg/day). Conversion of dietary concentrations of boron to a daily dose of boron was made by multiplying the average fractional weight of food consumption per bird (0.24) by the concentration of boron in food (567 ppm B). The average fractional weight of food consumption of 0.24 was determined by dividing the average food consumption/bird/day (10.4 g/bird/day) by the average body weight (43 g). Both the average food consumption/bird/day and the average body weight were reported by the authors. Thus, acute (1-day) exposures to avian species will be based on the acute NOAEL of 136 mg B/kg/day from the 5-day dietary borax exposure study in young bobwhite quail (Reinart and Fletcher 1977).

Standard bioassays of the reproductive effects of boron compounds in birds were not identified in the available literature. A 6-week exposure study of boric acid in mallard ducks yielded an NOAEL of 300 ppm B (60 mg B/kg/day) and an LOAEL of 1000 ppm boron (200 mg B/kg/day) for decreased hatching and post-hatching growth and survival (Smith and Anders 1989). Conversion of dietary concentrations of boron to a daily dose of boron was made by multiplying the average fractional weight of food consumption per bird (0.20) by the concentration of boron in food (300 and 1000 ppm B). The average fractional weight of food consumption of 0.20 was determined by dividing the average food consumption/bird/day (209 g/bird/day) by the average body weight (1,056 g). Both the food consumption/bird/day and the average body weight were reported by the authors. A 28-day dietary exposure study of borax in broiler chickens reports a LOAEL of 250 ppm B (6.5 mg B/kg/day) for decreased hatchability and damage to spermatozoal cells, indicating that exposure to boron can cause developmental and testicular toxicity in birds (Rossi et al. 1993); however, only one exposure level was tested in this study. Conversion of dietary concentrations of boron to a daily dose of boron was made by multiplying the average fractional weight of food consumption per bird (0.026) by the concentration of boron in food (250 ppm B). The average fractional weight of food consumption of 0.026 was determined by dividing the average food consumption/bird/day (146 g/bird/day) by the average body weight (5,667 g). Both the food consumption/bird/day and the average body weight were reported by the authors. In this study, only one dietary concentration (250 ppm B) was evaluated; no other boron concentrations were tested.

Based on the limited data available, it appears that birds are susceptible to boron-induced developmental and testicular toxicity. Data from the Rossi et al. (1993) study are of limited usefulness since only one exposure level was assessed. In the Smith and Anders (1989) study, decreased hatchability was observed at the 200 mg B/kg/day dose, with the NOAEL of 60 mg B/kg/day. The results of these studies indicate that exposure to boron compounds can adversely affect reproductive function in birds. However, since neither of these studies rigorously assessed the potential of boron to produce developmental or testicular effects in birds or followed standard bird reproduction bioassay protocols, the *critical dose* of 10.3 mg B/kg/day for developmental effects in rats used to derive the oral (chronic) RfD will be used to assess risk of chronic exposure to boron in birds.

4.3.2.3. Terrestrial Invertebrates – As detailed in Appendix 3, a single study on the acute topical exposure of boric acid in honey bees reports an LD_{50} >362.58 µg boric acid/bee (63.38 µg B/bee) (Atkins 1987). Since no mortality occurred at this exposure level, 63.38 µg B/bee is taken as the NOAEL for mortality in this study. Using a body weight of 0.093 g for the honey bee (USDA/APHIS 1993), this value corresponds to a dose of 677 mg B/kg [0.063 mg/0.000093 kg]. This type of toxicity value, however, is used to assess the consequences of broadcast applications. Because Sporax is not applied by this method, no quantitative risk characterization for insects is developed.

4.3.2.4. Terrestrial Plants and Microorganisms – As reviewed in Section 4.1.2.4, boron is an essential trace element for terrestrial plants. The amount of boron required to produce optimal growth and development varies tremendously between species and even between strains of the same species. However, excess boron can lead to phytotoxicity. In most species, there is a narrow range between the amount of boron required for optimal growth and the amount that is phytotoxic. Standard bioassays for toxicity of boron compounds to terrestrial plants (Tier I and Tier II seedling emergence or vegetative vigor studies) were not identified in the literature. Due to the limited data available, coupled with the narrow dose range between beneficial and phytotoxic effects, it is difficult to identify a most sensitive and a most tolerant plant species. Based on results of studies published in the open literature (detailed in Appendix 4), the most sensitive species appears to be the potato, with an NOAEC of 5 mg B/kg soil (Kluge 1990, as cited in ECETOC 1997) and the most tolerant species appears to be the sugarbeet with an NOAEC of 20 mg B/kg soil (Kluge 1990, as cited in ECETOC 1997). These values will be used to characterize risk to nontarget terrestrial plants. However, it is likely that more sensitive and more tolerant species exist.

Based on the effective use of borax in the control of various wood-rotting fungi, including *Heterobasidion annosum*, it is likely that borax could adversely affect nontarget microorganisms. However, no standard toxicity studies have been encountered that could be used to quantify risk to soil microorganisms. Consequently, no dose-response assessment can be conducted for this group of organisms.

4.3.3. Aquatic Organisms.

4.3.3.1. Fish – The acute bioassays on fish summarized in Appendix 5 provide estimates of exposure which might be associated with acute effects in fish. Acute 96-hour LC_{50} values for boric acid range from >100 mg B/L in large juvenile razorback sucker fish (Hamilton 1995) and 233 mg B/L in swimup razorback sucker fish (Hamilton 1995) to >1100 mg B/L in rainbow trout (LaLievre 1988, as cited in U.S. EPA 1993b). Based on the available acute exposure data on borax and boric acid, razorback sucker fry (96-hour LC_{50} 233 mg B/L) appear to be the most sensitive aquatic organisms and rainbow trout (96-hour LC_{50} >1100 mg B/L) appear to be the most tolerant aquatic species. The LC_{50} of >100 mg B/L in juvenile razorback sucker fish is not considered as a endpoint to assess risk, since no mortality occurred at the highest exposure level; thus an LC_{50} could not be estimated from the available data. For this risk assessment the 96-hour LC_{50} of 233 mg B/L will be used to assess the risk of acute exposure to boron in the most

sensitive species and the 96-hour LC_{50} >1100 mg B/L will be used to assess acute exposure of the most tolerant species.

Standard chronic exposure studies on the effects of borax or boric acid in fish were not identified in the literature; all of the available data are from a single study on the effects of borax on rainbow trout, channel catfish, and goldfish (Birge and Black 1977). Results of this study show a similar degree of sensitivity for the three species tested. The lowest estimated NOAEC (for mortality) of 0.5 mg B/L was reported for goldfish and the highest estimated NOAEC (for mortality) of 1.0 mg B/L was reported for rainbow trout and channel catfish. NOAEC values were estimated based on tabular results reported in the study. Since different exposure times were used for each of the three species tested (up to 28 days for trout, 9 days for catfish, and 7 days for goldfish), it is difficult to identify a most sensitive and a most tolerant species for longer-term exposure. To assess the risk of longer-term exposures of fish to boron, the NOAEC of 0.5 mg B/L in goldfish will be used to represent the most sensitive species and the NOAEC of 1.0 mg B/L in rainbow trout and channel catfish will be used to represent the most tolerant species.

4.3.3.2. Aquatic Invertebrates – As detailed in Appendix 6, acute toxicity studies on boron using borax and boric acid have been conducted in aquatic invertebrates. Based on the 48-hour LC_{50} value, *Daphnia magna* appears to be the most sensitive species (48-hour LC_{50} 133 mg B/L) (Gersich 1984), and *Chironomas decorus*, a midge, is the most tolerant species (48-hour LC_{50} 1376 mg B/L) (Maier and Knight 1991). These values will be used to assess risk of acute boron exposure in sensitive and tolerant aquatic invertebrates.

For chronic exposure studies on boron, data are only available in daphnids. The lowest NOAEC reported for daphnids is 6 mg B/L for decreased brood size in organisms exposed to boric acid (Lewis and Valentine 1981). Although no chronic exposure data are available in a more tolerant species, a NOAEC for tolerant species can be derived based on the relative acute toxicity of daphnids and midges. Based on comparisons of the 48-hour LC_{50} values for daphnids (133 mg B/L) and midges (1376 mg B/L), midges are more tolerant to boron toxicity by a factor of 10.3 [1376 ÷ 133 = 10.3]. Thus, to calculate a surrogate NOAEC in midges, the daphnid NOAEC of 6 mg B/L is multiplied by 10.3, yielding a value of 61.8 mg B/L. To characterize the risk of chronic exposure to boron compounds, the NOAEC of 6 mg B/L will be used for the most sensitive species and the surrogate NOAEC of 61.8 mg B/L will be used for the most tolerant species.

4.3.3.3 Amphibians – Exposure of leopard frog larvae to borax for 7.5 days yielded an LC_{50} value of 47 ppm boron and estimated NOAEC and LOAEC for mortality of 1.0 and 5.0 ppm B, respectively (Birge and Black 1977). To assess the risk of acute exposure to amphibians, the NOAEC of 1.0 ppm B will be used. No studies on the effects of chronic exposure of amphibians to boron compounds were identified in the available literature.

4.3.3.4 Aquatic Plants – The relevant data on the toxicity of boron compounds to aquatic plants are summarized in Appendix 7. Based on the available data, the most sensitive algal species is the green alga *Scenedesmus subpicatus*, with a 72-hour NOAEC of 10 mg B/L (Bringmann and Kuhn 1978, as cited in ECETOC 1997) and the most tolerant species is the blue-green alga *Microcystis aeruginosa*, with a 72-hour NOAEC of 20.3 mg B/L (Bringmann and Kuhn 1978, as cited in ECETOC 1997). Although these tests are conducted for a relatively short period of time (i.e. 72 hours), these NOAEC values are applied to both acute and longer-term concentrations because of the short life-cycle of individual algal cells.

For aquatic macrophytes, results of a 21-day exposure study on the effect of boric acid in watermilfoil, water buttercup and waterweed show that these three species have a similar level of sensitivity to boron in terms of decreases in photosynthesis (Nobel 1981, as cited in WHO 1998). However, the 21-day EC_{50} of water buttercup (10 mg B/L) is 2-fold higher than the 21-day EC_{50} value reported for watermilfoil and waterweed. Thus, to assess acute exposure risk of boron exposure to aquatic macrophytes, the value of 5 mg B/L will be used to represent sensitive species and the value of 10 mg B/L will be used to represent tolerant species. Results of a 2-year study on the common reed yielded an NOAEC of 4 mg B/L (Bergmann et al. 1995, as cited in ECETOC 1997). Due to the lack of long-term exposure data in other plant species, a sensitive and tolerant species cannot be identified to characterize the chronic risks in aquatic macrophytes exposed to boron. Thus, the value of 4 mg B/L will be used to assess risk for both sensitive and tolerant aquatic plant species.

4.3.3.5. Aquatic Microorganisms – As reviewed in Section 4.1.3.5, for aquatic microorganisms, the 72-hour NOAEC values range from 0.3 mg B/L in *Entosiphon sulfacum*, a flagellate (Bringmann and Kuhn 1980, as cited in WHO 1998), to 291 mg B/L in *Pseudomonas putida* (Schoberl and Huber 1988, as cited in WHO 1998). For this risk assessment, these NOAEC values of 0.3 mg B/L and 291 mg B/L are used to assess the consequences of both acute and longer-term exposures for sensitive and tolerant species of aquatic microorganisms.

4.4 Risk Characterization

4.4.1 Overview

For terrestrial species, risk associated with the application of Sporax to tree stumps appear to be very low. Most risk quotients are range from 0.000003 to 0.005 and are below the level of concern by factors of about 200 to over 330,000. As discussed in Section 3.2.3.4, this reflects the fact that the use of Sporax in Forest Service programs will not substantially contribute to or increase concentrations of boron in water or soil beyond those that are associated with the normal occurrence of boron in the environment. Even in the case of direct consumption of Sporax from a tree stump by a large mammal, the highest risk quotient is only 1.1. The hazard quotients for other organisms consuming Sporax – i.e., a small mammal, a small bird, and a large bird – range from 0.00004 to 0.08, below the level of concern by factors of about 12 to 25,000.

There also does not appear to be a risk to terrestrial plants exposed to boron through runoff of Sporax applied to tree stumps. Although risk to insects and soil microorganisms was not characterized, since borax is used effectively in the control of fungi and insects, adverse effects of environmental exposures to insects and nontarget microorganisms are possible. However, given the atypical application method for Sporax, widespread exposures are not likely.

The exposure scenarios considered for aquatic species are for water contaminated by accidental spill or by runoff of applied Sporax. Most aquatic animals do not appear to be at risk for any of the exposure scenarios considered. For amphibians, the level of concern is marginally exceeded for the accidental spill of 25 pounds of sporax into as small pond (HQ, 1.3). None of the acute or chronic HQs for exposure *via* water contaminated by runoff exceed the level of concern for any aquatic animal. These results indicate that aquatic animals are not at high risk for the exposure scenarios considered; however, accidental spill of large quantities of Sporax into a small pond may result in toxicity in amphibians.

For aquatic plants, the highest HQ for any exposure scenario is 0.3 associated with algae for the accidental spill of 25 pounds of Sporax into a small pond. All other HQs for the accidental spill scenario and for acute and longer-term exposures to water contaminated by runoff are well below the level of concern. Thus, based on this analysis, there is no basis for asserting that effects on aquatic macrophytes or algae are likely for either acute or longer-term exposures. Hazard quotients for sensitive species of aquatic microorganisms exceed the level of concern for all accidental spill scenarios, with HQs ranging from 1.1 to 4.3. For tolerant microorganisms, HQs are well below the level of concern for the worst-case accidental spill scenario. For acute exposure to water contaminated by runoff based on the maximum application rate of 5 lbs Sporax/acre, all HQs are below the level of concern for both sensitive and tolerant species. The results of this risk assessment indicate that more sensitive microorganisms may be at risk following accidental spill of large quantities of Sporax into a small pond, but that exposure *via* runoff does not present a risk to aquatic microorganisms.

4.4.2 Terrestrial Organisms

4.4.2.1. Terrestrial Vertebrates – The quantitative risk characterization for mammals and birds is summarized in Worksheets G02a – G02c. As with the human health risk assessment, risk is characterized as the estimated dose divided by the toxicity value. This ratio is referred to as the hazard quotient (HQ). A HQ of one or less indicates that the estimated exposure is less than the toxicity value; when this is the case, there is no basis for asserting that adverse effects are plausible. Exposure values are summarized in Worksheet G01. For exposure *via* consumption of water contaminated by runoff, the application rate range used is 0.1 lb Sporax/acre to 5 lbs Sporax/acre, with the typical application rate taken as 1 lb Sporax/acre. Toxicity values are displayed in the last column of Worksheets G02a – G02c and are also summarized in Table 4-2.

As discussed in Section 4.2.2 for terrestrial vertebrates, the exposure scenarios considered in this risk assessment are the direct consumption of Sporax applied to tree stumps (acute exposure), consumption of water contaminated by an accidental spill (acute exposure), and acute and chronic exposure by consumption of water contaminated by runoff. With the exception of direct consumption of Sporax applied to tree stumps, none of the exposure scenarios are associated with hazard quotients that exceed the level of concern.

For the direct consumption scenario, there appears to be very little risk to either mammals or birds. The only HQ to exceed a level of concern is the upper bound of the HQ for the direct consumption of Sporax from a treated stump by a large mammal such as deer. The exceedence, however, is minor with an HQ of 1.1. As noted in Worksheet G01, this HQ is associated with a dose of about 11.5 mg/kg bw, which is only marginally above the NOAEL of 10.3 mg/kg bw. As discussed in Section 4.1.2.1, Sporax applied to tree stumps does not appear to have attractant effects for deer and no clinical signs of toxicity were observed in deer allowed free access to Sporax-treated stumps (Campbell et al., no date). The hazard quotients for other organisms – i.e., a small mammal, a small bird, and a large bird – range from 0.00004 to 0.08, below the level of concern by factors of about 12 to 25,000.

Risk associated with other exposure scenarios are very low. As shown in worksheets G02a – G02c, risk of exposure *via* the longer term consumption of contaminated water is characterized for a small mammal. These risk quotients are very low, ranging from 0.000003 to 0.005 and are below the level of concern by factors of about 200 to over 330,000. As discussed in Section 3.2.3.4, this reflects the fact that the use of Sporax in Forest Service programs will not substantially contribute to or increase concentrations of boron in water or soil beyond those that are associated with the normal occurrence of boron in the environment.

4.4.2.2. Terrestrial Plants – A quantitative summary of the risk characterization for exposure of terrestrial plants to boron in soil *via* runoff is presented in Table 4-3. Exposure estimates for terrestrial plants are taken from GLEAMS modeling (Table 4-1) and are summarized in Table 4-3. Toxicity values, summarized in Table 4-3, are based on NOAEC values for the most sensitive and most tolerant species (Section 4.3.2.4).

None of the HQ values derived for terrestrial plants exceeds the level of concern. The highest HQ is 0.46 associated with exposure of the most sensitive species for the application rate of 5 lbs Sporax/acre and the peak soil concentration in clay with 5 inches of rainfall per year. For these same conditions, the HQ for the most tolerant species (sugarbeet) is 0.11. All other HQ values associated with lower application rates do not approach the level of concern. Based on this analysis, nontarget terrestrial plants do not appear to be at risk from exposure to borax at the maximum application rate used by the Forest Service. However, this risk assessment is based on data from relatively few terrestrial plant species. It is possible that more sensitive species exist and may be at risk for boron-induced toxicity.

4.4.2.3 Other Terrestrial Organisms – As discussed in Section 4.2.1, exposure assessments were not conducted for insects and soil microorganisms. Thus, risk of exposure of these organisms cannot be characterized quantitatively. Since borax is used effectively in the control of fungi and insects, adverse effects of environmental exposures to insects and nontarget microorganisms is possible. However, given the atypical application method for Sporax, widespread exposures are not likely.

4.4.3. Aquatic Organisms.

4.4.3.1. Aquatic Animals – The quantitative risk characterization for aquatic animals is summarized in Worksheets G03a – G03c. Exposure values are the same as those to assess risk of exposure to contaminated water in the human health risk assessment (Worksheet E04). As with the human health risk characterization, risk is characterized as the estimated dose divided by the toxicity value. For exposure *via* consumption of water contaminated by runoff, the application rate range used is 0.1 lb Sporax/acre to 5 lbs Sporax/acre, with the typical application rate taken as 1 lb Sporax/acre. Exposures values for an accidental spill are based on spill of 6.25 to 25 lbs Sporax, with a central value of 12.5 lbs Sporax, into a small pond. Acute and chronic toxicity values are displayed in the last column of Worksheets G02a – G02c and are also summarized in Table 4-2.

With the exception of amphibians, all HQs associated with exposure of aquatic animals to water contaminated by an accidental spill are well below the level of concern. For worst-case scenario of the spill of 25 pounds of Sporax into a small pond, the HQ for amphibians of 1.3 only marginally exceeds the level of concern; HQs for spill of 6.25 and 12.5 pounds of Sporax are below the level of concern. Based on the results of this analysis, if large amounts of borax accidentally contaminate surface waters, amphibians may be at risk. However, for all other aquatic animals, there is no indication that adverse effects will occur.

Hazard quotients for acute and chronic exposure of aquatic animals to water contaminated by runoff are all below the level of concern, even at the maximum application rate of 5 lbs Sporax/acre. The HQs for acute exposure range from 0.0000004 in aquatic invertebrates for the lower bound estimate associated with an application rate of 0.1 lb Sporax/acre to 0.5 in amphibians for the upper bound estimate associated with an application rate of 5 lbs Sporax/acre. For longer-term exposure, HQs range from 0.000003 in aquatic invertebrates for the lower bound

estimate associated with an application rate of 0.1 lb Sporax/acre to 0.7 in fish for the upper bound estimate associate with an application rate of 5 lbs Sporax/acre. Thus, there is no basis for asserting that effects on nontarget aquatic species are likely for either acute or longer-term exposures.

4.4.3.2. Aquatic Plants – Exposure scenarios for aquatic plants are the same as those conducted for aquatic animals. The quantitative risk characterization for aquatic plant species includes assessments for macrophytes and algae (Worksheets G03a – G03c). Exposure values are the same as those used to assess risk of exposure to contaminated water in the human health risk assessment (Worksheet E04). Acute and chronic toxicity values are displayed in the last column of Worksheets G02a – G02c and are also summarized in Table 4-2.

The highest HQ for any exposure scenario is 0.3 associated with algae for the accidental spill of 25 pounds of Sporax into a small pond. All other HQs for the accidental spill scenario and for acute and longer-term exposures to water contaminated by runoff are well below the level of concern. Thus, based on this analysis, there is no basis for asserting that effects on aquatic macrophytes or algae are likely for either acute or longer-term exposures.

4.4.3.2. Aquatic Microorganisms – Exposure scenarios for aquatic microorganisms are the same as those conducted for aquatic animals. The quantitative risk characterization for aquatic microorganisms is summarized in Table 4-4. Exposure values are the same as those used to assess risk of exposure to contaminated water for aquatic animals (Worksheet G03a for accidental exposure and Worksheet G03c for exposure *via* runoff using the maximum application rate). Toxicity values are displayed in the last column of Table 4-4.

Hazard quotients for the most sensitive species of microorganisms exceed the level of concern for all accidental spill scenarios, with HQs ranging from 1.1 to 4.3. For tolerant microorganisms, HQs are well below the level of concern, ranging from approximately 0.001 to 0.004. For acute exposure to water contaminated by runoff based on the maximum application rate of 5 lbs Sporax/acre, all HQs are below the level of concern for both sensitive and tolerant species. The results of this risk assessment indicate that more sensitive microorganisms may be at risk following accidental spill of large quantities of Sporax into a small pond, but that exposure *via* runoff does not present a risk to aquatic microorganisms.

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Table 2-1. Selected physical and chemical properties of boron compounds

	Boron	Boric Acid	Sodium Tetraborate Decahydrate
Appearance, ambient	black or brown solid	white crystalline powder[1]	white crystalline solid [2]
Bioconcentration factor	NA	NA	NA
% Boron	100	17.48 [3]	11.34 [3]
CAS number	7440-42-8 [4]	10043-35-3 [1]	1303-96-4 [2]
Commercial formulations	NA	NA	Sporax
Empirical Formula	B	H_3BO_3 [1]	$Na_2B_4O_7 \bullet 10H_20$ [1]
EPA Registration Number	NA	NA	2935-501 [2]
$K_{o/w}$	no data [3]	Kow = 0.175 [1]	NA
Molecular weight	10.81[3]	61.83 [1]	381.37 [1,4]
pH	NA	5.1 (1% solution) at 20 ˚C [1]	9.24 (1% solution) at 20 ˚C [1]
Soil half-time (days)	NA	NA	NA
Soil sorption, $K_{o/c}$	NA	NA	NA
Specific Gravity	NA	1.5128 at 20 ˚C [1]	NA
Synonyms	none	boracid; orthoboric acid [1]	borax; sodium borate decahydrate; borax decahydrate [1]
Vapor pressure	1.56×10-4 atm at 20 ˚C [4]	$<10^{-4}$ torr at 20 ˚C [1]	$<10^{-6}$ torr [1]
Volatility	NA	NA	NA
Water half-time (days)	NA	NA	NA
Water solubility (mg/L)	insoluble [3,4]	4.72% at 20 ˚C [1]; 63.5 g/L at 25 ˚C [3]; 64.5 g/L at 30 ˚C [4]	4.70 g/100mL at20˚C [1]; 20.1 g/L at 0˚C [4]; 5.92g/100 g at20˚C [1,4]

[1] US EPA 1993a (RED)
[2] Wilbur Ellis 2002 (MSDS).
[3] WHO 1998
[4] ATSDR 1993
NA = not available

Table 2-2. Summary of the Use of Sporax by the Forest Service from 2000 to 2002 (Source: http://www.fs.fed.us/foresthealth/pesticide/reports.shtml)

Year	Region	Forest	Lbs Applied	Acres Treated	Lbs/Acre
20002000	5 5	5 4	5965 246	5480 549	0.46
2000	5	7	15	20	0.750
2000	5	11	585	2234	0.262
2000	5	12	125	460	0.272
2000	5	13	200.5	417	0.481
2000	5	13	27	58	0.466
2000	5	14	8380	838	10.000
2000	5	15	10	40	0.250
2000	5	17	8573.5	4675	1.834
2000	5	6	5125.5	4469	1.147
2000	5	9	830	2353	0.353
	Region 5 Total/Average:		30091.5	21603	1.393
2000	6	14	217	1074	0.202
	Region 6 Total/Average:		217	1074	0.202
2001	5	1	5	10	0.500
2001	5	4	563	1870	0.301
2001	5	5	43	370	0.116
2001	5	6	2515	4472	0.562
2001	5	9	4815	4938	0.975
2001	5	11	663	2168	0.306
2001	5	12	125	380	0.329
2001	5	15	10	10	1.000
2001	5	17	3417	2185	1.564
2001	5	19	30	111	0.270
	Region 5 Total/Average:		12186	16514	0.738
2001	6	1	80	259	0.309
2001	6	14	125	258	0.485
	Region 6 Total/Average:		205	517	0.397
2002	5	1	10	20	0.500
2002	5	11	698	2333	0.299
2002	5	17	5274	2822	1.869
2002	5	19	58	210	0.276
2002	5	4	555	1700	0.326
2002	5	5	1012	2441	0.415
2002	5	6	9327.5	5837	1.598
2002	5	9	190	483	0.393
	Region 5 Total/Average:		17124.5	15846	1.081
2002	6	14	145	1302	0.111
	Region 6 Total/Average:		145	1302	0.111
Summary for Region 5 All Years			59402	53963	1.100
Summary for Region 6 All Years			567	2893	0.195
Summary for Both Regions All			59969	56856	1.054

Table 3-1: Chemical and site parameters used in GLEAMS modeling for modeling Borax as boric acid.

Chemical Specific Parameters

Parameter	Clay	Loam	Sand	Comment/ Reference
Halftimes (days)				
Aquatic Sediment		∞		Note 1
Foliar		10000		Note 1
Soil		10000		Note 1
Water		∞		Note 1
Kow		0.175		Note 2
Ko/c, mL/g		0.11		Note 3
K_d, mL/g	0.0033	0.0165	0.00033	Note 4
Water Solubility, mg/L		47,200		Note 5
Foliar wash-off fraction		1		Note 6
Fraction applied to foliage		0		Note 6

Note 1 Borax is modeled using chemical and physical properties of boric acid. The results of the modeling is given as boron equivalents. The assumption is made that no degradation occurs in terms of boron. GLEAMS requires a finite halftime for vegetation and soil. A value of 10,000 days (about 27 year) is used to set the degradation rate to a negligible value over the 4-year course of the model run.

Note 2 This the Kow cited by US EPA (1993a, p.19) for boric acid. Borax is modeled using the chemical and physical properties of boric acid and the results are converted to boron equivalents. See text for discussion.

Note 3 The Koc is estimated from the relationship given by Winegardner (1996):

log Koc = log Kow - 0.21
log Koc = log 0.175 - 0.21 = -0.97
Koc = $10^{-0.97}$ = 0.11

Note 4 Based on the general relationship: Kd = Koc × OC using OC values of 0.003 for sand, 0.015 for loam, and 0.030 for clay (SERA 2004b).

Note 5 This the water solubility given for boric acid by US EPA (1993a, p.19) as 47.2 g/L at 20°C.

Note 6 Borax is not applied to leaf surfaces. Thus, foliar washoff for modeling is set to 1.0 and fraction applied to foliage is set to 0. These are necessary for the adaptation of GLEAMS to borax. See text for discussion.

Site Parameters

(see SERA 2004, TD 2004-02.04a dated February 8, 2004 for details)

Pond 1 hectare pond, 2 meters deep, with a 0.01 sediment fraction. 10 hectare square field (1093' by 1093') with a root zone of 12 inches.

Stream Base flow rate of 710,000 L/day with a flow velocity of 0.08 m/second or 6912 meters/day. Stream width of 2 meters (about 6.6 feet'). 10 hectare square field (1093' by 1093') with a root zone of 12 inches.

Table 3-2: Summary of modeled concentrations of borax and boron equivalents in ponds (all units are µg/L or ppb) at an application rate of 1 lb/acre.

Annual Rainfall (inches)	Rainfall per Event (inches)[1]	Clay		Loam		Sand	
		Average	Maximum	Average	Maximum	Average	Maximum
		Concentration per lb/acre applied (from GLEAMS)					
5	0.14	0.00	0.00	0.00	0.00	0.00	0.00
10	0.28	0.00	0.00	0.00	0.00	0.00	0.00
15	0.42	415.29	718.04	556.07	882.67	613.40	909.47
20	0.56	292.51	395.81	356.14	447.00	376.44	454.87
25	0.69	224.32	272.70	265.08	300.25	276.60	333.17
50	1.39	107.37	149.67	124.05	258.80	127.15	303.64
100	2.78	53.68	105.99	62.71	229.98	63.98	272.22
150	4.17	35.83	80.25	42.62	206.02	43.54	245.19
200	5.56	26.90	64.19	32.47	185.87	33.21	233.04
250	6.94	21.56	53.64	26.30	166.78	26.93	223.98
Conversion factor[2]:		**0.1134**	lbs/acre as boron equivalents				
		Concentration at above application rate					
5	0.14	0	0	0	0	0	0
10	0.28	0	0	0	0	0	0
15	0.42	47.09	81.43	63.06	100.09	69.56	103.13
20	0.56	33.17	44.88	40.39	50.69	42.69	51.58
25	0.69	25.44	30.92	30.06	34.05	31.37	37.78
50	1.39	12.18	16.97	14.07	29.35	14.42	34.43
100	2.78	6.09	12.02	7.11	26.08	7.26	30.87
150	4.17	4.06	9.10	4.83	23.36	4.94	27.80
200	5.56	3.05	7.28	3.68	21.08	3.77	26.43
250	6.94	2.44	6.08	2.98	18.91	3.05	25.40

[1] Rain is assumed to occur at the same rate every 10th day – i.e., 36 rainfall events per year.
[2] The molecular weight of Borax is 381.37 g/mole and borax contains 4 atoms of boron (atomic weight of 10.81). Thus, the conversion factor is approximately 0.1134 (4×10.81/381.37).

Table 3-3: Estimated Environmental Concentrations (µg/L or ppb) of boron equivalents in surface water at an application rate of 1 lb/acre of Borax.

Scenario	Peak	Long-Term Average
GLEAMS, Stream	<0.00001	<0.00001
GLEAMS, Pond [1]	30 (6 to 100)	14 (2 to 70)
OTHER MODELING		
U.S. EPA/OPP 1993b, Appendix 1	30.5 ppb as boric acid at 1 lb boric acid/acre [equivalent to 5.2 ppb boron [2]]	N/A
MONITORING STUDIES		
Water		
U.S. EPA/OPP 1993b	Normal ambient concentrations of boron in fresh water are in the range of 1 to 100 ppb.	
Moore 1997	Average ambient concentrations in U.S. surface waters typically range from 100 to 200 ppb	
Black et al. 1993	Ambient boron concentration in natural Lake waters ranged from 0.023 ppm to 0.75 ppm. Waters were collected from Tennessee (0.023 ppm), Wyoming (0.75 ppm) and Indiana (0.19 ppm).	
Other	No monitoring data on concentration of boron in water associated with stump treatment applications has been encountered.	
Soil		
WHO 1998, Moore 1997	Boron generally occurs in soils at concentrations ranging from 10 to 30 mg/kg, depending on such factors as soil type, amount of rainfall, and irrigation type	

[1] Water contamination rates – concentrations in units of mg boron/L expected at an application rate of 1 lb borax/acre. These values are converted to units of mg/L (ppm) and are entered into Worksheet A04 for borax. This rate is adjusted to the program application rate in all worksheets involving exposure to contaminated water.

[2] MW of boric acid = 61.84. Atomic weight of boron = 10.81. Conversion factor = 0.17 [10.81 ÷ 61.84 = 0.17480]

Table 3-4: Estimated background concentrations of boron in environmental media and normal intakes of boron relative to exposure scenarios in this risk assessment.

Media/ Exposure	Normal Background [1]	Sporax Scenarios in this risk assessment	Comment
Total intake	0.14-0.36 mg B/kg bw/day	0.85 (0.4-3.2) mg/kg bw	Direct consumption from tree stump [WS D01]
		0.05 (0.015-0.14) mg/kg bw/ day	Water, accidental spill [WS D02]
		0.002 (0.0003-0.011) mg/kg bw/day	Water, acute ambient [WS D03]
		0.0004 (0.00004-0.0024) mg/kg bw/day	Water, chronic ambient [WS D03]
Water	0.1 (0.001 - 5) mg/L	0.03 (0.006-0.1) mg/L	Expected concentration based on GLEAM modeling [WS D03]
		0.6 (0.3-1.3) mg/L	Accidental spill [WS D02]
Soil	26-300 mg/kg soil	0.3 ppm - 0.5 mg/kg soil	Peak based on GLEAMS modeling (Table 4-1)
		0.1 to 2 mg/kg soil	Monitored levels after stump treatment (Dost et al. 1996)

[1] See Section 3.2.3.1.

Table 4-1: Summary of modeled concentrations of boric acid in soil (all units are mg/kg or ppm)

Annual Rainfall (inches)	Rainfall per Event (inches)[1]	Clay		Loam		Sand	
		Average	Maximum	Average	Maximum	Average	Maximum
		Concentration per lb/acre applied (from GLEAMS)					
5	0.14	1.11265	2.39208	2.05470	4.03529	1.13548	2.49736
10	0.28	1.00287	2.30443	0.94758	2.25804	0.87079	2.05700
15	0.42	0.30745	0.94675	0.15204	0.66760	0.09484	0.48669
20	0.56	0.18238	0.76443	0.07705	0.52685	0.04786	0.39754
25	0.69	0.13582	0.68811	0.05145	0.45302	0.03185	0.34213
50	1.39	0.07530	0.57113	0.01972	0.28814	0.01238	0.23125
100	2.78	0.05323	0.52866	0.00961	0.23125	0.00587	0.23125
150	4.17	0.04852	0.52249	0.00708	0.23125	0.00402	0.23125
200	5.56	0.04692	0.51431	0.00594	0.23125	0.00315	0.23125
250	6.94	0.04594	0.50891	0.00529	0.23125	0.00264	0.23125
Application rate:		**0.1134**	lbs/acre as boron equivalents				
		Concentration as boron equivalents at above application rate					
5	0.14	0.12617	0.27126	0.233	0.4576	0.12876	0.2832
10	0.28	0.11373	0.26132	0.10746	0.25606	0.0987	0.23326
15	0.42	0.0349	0.10736	0.0172	0.0757	0.0108	0.0552
20	0.56	0.0207	0.0867	0.009	0.0597	0.005	0.0451
25	0.69	0.0154	0.078	0.006	0.0514	0.004	0.0388
50	1.39	0.009	0.0648	0.002	0.0327	0.001	0.0262
100	2.78	0.006	0.06	0.001	0.0262	0	0.0262
150	4.17	0.006	0.0593	0	0.0262	0	0.0262
200	5.56	0.005	0.0583	0	0.0262	0	0.0262
250	6.94	0.005	0.0577	0	0.0262	0	0.0262

[1] Rain is assumed to occur at the same rate every 10th day – i.e., 36 rainfall events per year.

Table 4-2: Summary of borax toxicity values used in ecological risk assessment [1]

Organism	Endpoint	Toxicity Value	Reference, Species
Terrestrial Species			
mammals			
acute (rats)	NOAEL	10.3 mg B/kg/day	Allen et al. 1996, U.S. EPA 2004
chronic (rats)	NOAEL	10.3 mg B/kg/day	Allen et al. 1996, U.S. EPA 2004
birds			
acute (bobwhite quail)	NOAEL	136 mg B/kg/day	Reinart and Fletcher 1977
chronic (rats) [2]	NOAEL	10.3 mg B/kg/day	see Section 4.3.2.2.
terrestrial invertebrates - honey bee			
acute	NOAEL	677 mg B/kg	Atkins 1987, as cited in U.S. EPA 1993b
terrestrial plants			
acute			
sensitive (potato)	NOAEC	5 mg B/kg soil	Kluge 1990, as cited in ECETOC 1997
tolerant (sugarbeet)	NOAEC	20 mg B/kg soil	Kluge 1990, as cited in ECETOC 1997
Aquatic Species			
fish			
cute			
sensitive (razorback sucker swimup fry)	96-hour LC_{50}	233 ppm B	Hamilton 1995
tolerant (rainbow trout)	96-hour LC_{50}	>1100 ppm B	LaLievre 1988, as cited in U.S. EPA 1993b
chronic			
sensitive (goldfish)	NOAEC	0.5 ppm B	Birge and Black 1977
tolerant (rainbow trout and channel catfish)	NOAEC	1.0 ppm B	Birge and Black 1977

aquatic invertebrates			
acute			
sensitive (*Daphnia magna*)	48-hour LC_{50}	133 ppm B	Gerisch 1984
tolerant (*Chironomas decorus*)	48-hour LC_{50}	1376 ppm B	Maier and Knight 1991
chronic			
sensitive (*Daphnia magna*)	NOAEC	6 ppm B	Lewis and Valentine 1981
sensitive (*Chironomas decorus*)	NOAEC	61.8 ppm B	surrogate value derived from acute exposure data [3]
amphibians			
acute (leopard frog)	NOAEC	1.0 ppm B	Birge and Black 1977
aquatic macrophytes			
acute			
sensitive (watermilfoil and waterweed)	21-day EC_{50} for photosynthesis	5 ppm B	Nobel 1981, as cited in WHO 1998
tolerant (water buttercup)	21-day EC_{50} for photosynthesis	10 ppm B	Nobel 1981, as cited in WHO 1998
chronic (common reed)	NOAEC	4 ppm B	Bergmann et al. 1995, as cited in ECETOC 1997
algae			
sensitive (*Scenedesmus subpicatus*)	72-hour NOAEC	10 ppm B	Bringmann and Kuhn 1978, as cited in ECETOC 1997
tolerant (*Microcystis aeruginosa*)	72-hour NOAEC	20.3 ppm B	Bringmann and Kuhn 1978, as cited in ECETOC 1997
aquatic microorganisms			
sensitive (*Entosiphon sulfacum*)	72-hour NOAEC	0.3 ppm B	Bringmann and Kuhn 1980, as cited in WHO 1998
tolerant (*Pseudomonas putida*)	72-hour NOAEC	291 ppm B	Schoberl and Huber 1988, as cited in WHO 1998

[1] See Sections 3.3 and 4.3 for discussion on the selection of toxicity values
[2] See Section 4.3.3.2 for discussion of the selection of this toxicity value
[3] Surrogate chronic NOAEC derived due to lack of chronic toxicity data in a tolerant species. See Section 4.3.3.2 for details regarding derivation of this surrogate value.

Table 4-3: Risk Characterization for Terrestrial Plants

Application Rate (lb Sporax/acre)		Lower Exposure Estimate (ppm B) [1]	Lower HQ	Upper Exposure Estimate (ppm B) [2]	Upper HQ	Toxicity Value (ppm B) [3]
0.1 [4]						
	Sensitive (potato)	0.00262	5.2e-04	0.04576	9.2e-03	5
	Tolerant (sugarbeet)	0.00262	1.3e-04	0.04576	2.3e-03	20
1.0						
	Sensitive (potato)	0.0262	5.2e-03	0.4576	9.2e-02	5
	Tolerant (sugarbeet)	0.0262	1.3e-03	0.4576	2.3e-02	20
5.0 [5]						
	Sensitive (potato)	0.1310	2.6e-02	2.2880	0.46	5
	Tolerant (sugarbeet)	0.1310	6.6e-03	2.2880	0.11	20

1 This value is the lowest peak soil concentration of boron based on GLEAMS modeling. The lowest exposure estimate is associated with annual rainfalls of 100 inches or more in loam and 50 inches or more in sand. See Table 4-3.

2 This value is the highest peak soil concentration of boron based on GLEAMS modeling. The highest exposure estimate is associated with the maximum value in clay for an annual rainfall of 5 inches. See Table 4-3.

3 See Section 4.3.2.4

4 Table 4-3 gives the GLEAMS modeling soil concentrations for an application rate of 1 lb Sporax/acre. To calculate soil concentrations for the application rate of 0.1 lb Sporax/acre, soil concentrations were multiplied by 0.1.

5 Table 4-3 gives the GLEAMS modeling soil concentrations for an application rate of 1 lb Sporax/acre. To calculate soil concentrations for the application rate of 5 lb Sporax/acre, soil concentrations were multiplied by 5.

Table 4-4: Risk Characterization for Acute exposure of Aquatic Microorganisms

Species	Central Exposure Estimate (ppm B)	Central HQ	Lower Exposure Estimate (ppm B)	Lower HQ	Upper Exposure Estimate (ppm B)	Upper HQ	Toxicity Value (ppm B) [1]
Accidental Spill Scenario [2]							
Sensitive	0.6418	2.1	0.3209	1.1	1.2837	4.3	0.3
Tolerant	0.6418	2.2e-03	0.3209	1.1e-03	1.2837	4.4e-03	291
Short-term peak exposure from run-off [3]							
Sensitive	0.03	1.0e-01	0.006	2.0e-02	0.1	3.3e-01	0.3
Tolerant	0.03	1.0e-04	0.006	2.1e-05	0.1	3.4e-04	291

1 See Section 4.2.2.5.
2 See Worksheet D02. For exposure values, central estimate is based on spill of 12.5 pounds of Sporax, lower estimate based on spill of 6.24 pounds of Sporax, and upper estimate based on spill of 25 pounds of Sporax.
3 Exposure values for an application rate of 5 lb Sporax/acre. See Worksheet G03c

APPENDICES

Appendix 1: Toxicity of borax to experimental mammals

Animal	Dose/Exposure	Response	Reference
ORAL			
Acute Oral			
rats, Sprague-Dawley (SD) and Long-Evans (LE)	single doses of **borax and boric acid** administered in aqueous solutions by gavage. Dose range not reported	Borax SD (males): LD_{50} = 4.50 g/kg (0.51 g B/kg) (CL 4.14-5.01) SD (females): LD_{50} = 4.98 g/kg (0.56 g B/kg) (CL 4.31-5.76) LE (males): LD_{50} = 6.08 g/kg (0.69 g B/kg) (CL 3.54-10.4) Boric acid SD (males): LD_{50} = 3.450 g/kg (0.60 g B/kg) (CL .295-4.04) SD (females): LD_{50} = 4.08 g/kg (0.71 g B/kg) (CL 3.64-4.56) LE (males): LD_{50} = estimate 3.16 g/kg (0.55 g B/kg) Signs of toxicity similar for both borax and boric acid: depressions, ataxia, convulsions, death.	Weir and Fisher 1972
dogs	oral administration of **borax** (1.54-6.51 g borax/kg or 0.174-0.736 g B/kg) and **boric acid** (1.0-3.98 g boric acid/kg or 0.175-0.697 g B/kg) by capsule, followed by 14 day observation period	for both borax and boric acid, no deaths during 14-day observation period for all at doses tested. Except at lowest doses, administration of test compounds produced strong dose-related emetic response within 1 hour of dosing	Weir and Fisher 1972
Subchronic Oral			

Appendix 1: Toxicity of borax to experimental mammals

Animal	Dose/Exposure	Response	Reference
rats	1 g/kg **borax and boric acid** for 1-3 weeks administered by gavage. Rats were sacrificed when clinical signs of toxicity were observed.	In borax treated rats, decrease in body weight after 1 week of treatment. After 3 weeks, clinical signs of toxicity (not specified) were observed. Analysis of liver tissue shows significant inhibition of DNA synthesis.	Dani et al. 1971
dogs	90-day dietary exposure of dogs to **borax** at concentrations of 0, 0.0154%, 0.154%, and 1.54% B According to U.S. EPA 1993c, daily doses are - Males: 0, 3, 35, and 268 mg borax/kg/day; Females: 0, 2, 22, and 192 mg borax/kg/day	No treatment-related effect for any blood or urine values in males. In females, decreased hematocrit and hemoglobin in the 1.54% treatment group In the 1.54% treatment group, decrease testicular weights, testicular atrophy, and "alterations" in the seminiferous tubules. For males - NOAEL = 35 mg borax/kg/day (3.97 mg B/kg/day LOAEL = 268 mg borax/kg/day (33.80 mg B/kg/day) For females - NOAEL = 22 mg borax/kg/day (2.50 mg B/kg/day LOAEL = 192 mg borax/kg/day (21.78 mg B/kg/day)	Paynter 1963 MRID 406923-07
rats	70-day to **borax** in exposure in drinking water at concentrations of 0, 150 and 300 mg B/L	Compared to controls, rats in the 150 and 300 mg B/L treatment groups had decreased body weights. Weights of seminal vesicle and testes decreased in both borax treatment groups. Inhibition of spermatogenesis in both treatment groups. NOAEL <150 mg B/L in drinking water (authors did not calculate mg B/kg/day)	Seal and Weeth 1980

Appendix 1: Toxicity of borax to experimental mammals

Animal	Dose/Exposure	Response	Reference
rats, Sprague-Dawley	90 day dietary exposure to **borax and boric acid** at concentrations in food ranging of 52.5, 175, 525, 1750, and 5250 ppm boron equivalents	borax: No signs of toxicity up to concentrations of 525 ppm. At 1750 and 5250 ppm, signs of toxicity included rapid respiration, inflamed eyes, swollen paws and desquamated skin. All rats in 5250 group died within 3-6 wks of treatment. Food consumption and body wt decreased for males at 1750 and 5250 ppm and for females at 5250 ppm. At lower doses, some organ weights were increased compared to controls. For males in the 1750 group, decrease in weights of testes, liver, spleen, kidneys and brain. In females, in the 1750 ppm group, decrease in wts of liver, spleen and ovaries. Gross pathology of dead animals from the 5250 ppm group showed congestion of liver and kidneys, bright red lungs, swollen appearance of brain, small testes and thickened pancreas. Microscopic pathology showed dose-related atrophy of testes, with complete atrophy in the 1750 ppm group. 4 males in the 525 ppm group showed partial atrophy of testes and spermatogenic arrest (NOAEC = 175 ppm). boric acid: No signs of toxicity up to concentrations of 525 ppm. At 1750 and 5250 ppm, signs of toxicity included rapid respiration, inflamed eyes, swollen paws and desquamated skin. All rats in 5250 group died within 3-6 wks of treatment. Food consumption and body wt decreased for males and females at 1750 and 5250 ppm.	Weir and Fisher 1972

Appendix 1: Toxicity of borax to experimental mammals

Animal	Dose/Exposure	Response	Reference
dogs (5M/5F)	90 day dietary exposure to **borax and boric acid** at concentrations in food of 17.5, 175 and 1750 ppm boron equivalents	Borax With one exception (1 dog in 1750 borax group died of severe diarrhea), no signs of toxicity were observed in any treatment group. Hematology, biochemistry and urinalysis parameters normal except for decreased packed cell volume and hemoglobin in the 1750 ppm borax group. Testes and thyroid size significantly decreased in 1750 ppm group. Severe testicular atrophy, complete degeneration of spermatogenic epithelium in 1750 ppm group Boric acid Observations similar to borax	Weir and Fisher 1972

Chronic Oral

Appendix 1: Toxicity of borax to experimental mammals

Animal	Dose/Exposure	Response	Reference
rats (Sprague-Dawley)	2-year dietary exposure to **borax and boric acid** at concentrations in food of 117, 350 and 1170 ppm boron equivalents According to U.S. EPA 1989, these doses are equivalent to 5.9, 17.5, and 58.5 mg B/kg/day	For both borax and boric acid for the 117 and 350 ppm exposure groups, no effects of treatment were observed (**NOAEC = 350 ppm boron equivalents**). In the 1170 ppm groups clinical signs of toxicity included coarse hairs, scaly tails, hunched posture, swelling and desquamation of the pads of paws, shrunken scrotum in males, and inflamed eyes with bloody discharge. Lower packed cell volume and hemoglobin in 1170 ppm group. In the 1170 ppm group, atrophy of testes observed, including decreased testes weight, atrophied seminiferous epithelium and decreased tubular size (**LOAEC for testes effects = 1170 ppm boron equivalents**). No evidence of carcinogenesis in any treatment group.	Weir and Fisher 1972

Appendix 1: Toxicity of borax to experimental mammals

Animal	Dose/Exposure	Response	Reference
dogs (4M and 4 F per dose group)	2-year dietary exposure to **borax and boric acid** at concentrations in food of 58, 117 and 350 ppm boron equivalents. An additional group received 38-week exposure to 1170 ppm (boron equivalents) borax or boric acid According to U.S. EPA 1989, the 350 ppm concentration is equivalent to a daily dose of 8.8 mg B/kg/day and the 1170 ppm concentration is equivalent to 28 mg B/kg/day	No clinical signs of toxicity in any treatment group. No change in body weight, gross pathology, or hematological or biochemical parameters in any group. No testicular changes in any treatment group [**NOAEC = 350 ppm boron equivalents (8.8 mg B/kg/day)**]. Exposure to 1170 ppm produced testicular atrophy in both borax and boric acid groups [**LOAEC for testes effects = 1170 ppm boron equivalents (28 mg B/kg/day)**]. Severe testicular atrophy was observed, with spermatogenic arrest observed in 2 dogs sacrificed at 26 weeks. Microscopic examination revealed atrophy of the seminiferous epithelium of the tubules. Changes appear reversible - when dogs were placed back on control diet for 25 days from the boric acid group, testicular changes returned to control or nearly control levels. No other adverse effects were observed in any treatment group. No evidence of carcinogenesis in any treatment group.	Weir and Fisher 1972

Appendix 1: Toxicity of borax to experimental mammals

Animal	Dose/Exposure	Response	Reference
dogs (beagles) (8M/8F); 8 dogs (4M/4F) in each treatment group	1.03% sodium tetraborate decahydrate in diet (100% a.i. **borax**) for 38 weeks. Control group included. 25-day recovery period following 38-week treatment period. Average daily dose of test material was approximately 378 mg borax/kg/day (43 mg boron equivalents /kg/day). Averages calculated from weekly compound consumption and boron equivalents consumption for each dog (displayed in Table 1 of fiche)	No difference in treatment groups for weight or general appearance. No differences for hematology, biochemistry or urinalysis. In borax-treated males, testicular atrophy, with microscopic pathology revealing spermatogenic arrest at the spermatocyte stage, progressing to complete atrophy of the seminiferous epithelium. No change in reproductive organs of female dogs. No tissue accumulation of boron observed. No evidence of carcinogenesis in any treatment group.	Wier 1967 MRID 00005620 *appears to be same results as reported in Weir and Fisher 1972*
Reproduction Studies			
rats, males, Sprague-Dawley	single doses of **borax** (45, 1590, and 450 mg B/kg)	No effects on male fertility for any dose tested (measured as % fertile by assessing spermatozoa, spermatids, spermatocytes and spermatogonia).	Dixon et al. 1976

Appendix 1: Toxicity of borax to experimental mammals

Animal	Dose/Exposure	Response	Reference
rats, males, Sprague-Dawley	exposure to **borax** in drinking water for 30, 60, and 90 days. Concentrations in drinking water 0, 0.3, 1 and 6 mg/L. According to U.S. EPA 1989, these doses are equivalent to 0.02, 0.072, and 0.426 mg/kg/day).	At all borax exposure levels, seminal vesicle weight was significantly decreased compared to controls after 30 and 90 days of exposure, but not after 60-day exposure (table 5, p. 66 of paper). However, authors state that treatment with borax had no affect on body weight, or weight of testis, prostate or seminal vesicles. According to U.S. EPA 1989, **NOAEL is 0.426 mg B/kg/day (HDT)**. Plasma levels of FSH and LH unaffected by treatment In forced breeding, no effect in fertility at any dose level	Dixon et al. 1976
rats, Sprague-Dawley	90-day dietary exposure to **borax** in diet at concentrations of 0, 500, 1000, and 2000 ppm boron equivalents. According to U.S. EPA 1989, these doses are equivalent to 25, 50, and 100 mg B/kg/day).	No effects noted at the 500 ppm exposure level. At concentrations of 1000 and 2000 ppm, decreased weights of liver and testes. Testicular atrophy, decrease in seminiferous tubular diameter, and marked reduction in spermatocytes and spermatogenic cells. Decreased fertility (as measured by percentage of pregnant females). At 1000 ppm, most effects reversible within 5 weeks of discontinuation of treatment. At 2000 ppm, sterility was not reversed after 5 weeks. No dose-related decrease in litter size or fetal death, indicating that effects of boron were due to germinal aplasia, and not a dominant lethal effect. NOAEL = 25 mg B/kg/day LOAEL = 50 mg B/kg/day	Dixon et al. 1979

Appendix 1: Toxicity of borax to experimental mammals

Animal	Dose/Exposure	Response	Reference
rats	**boric acid** in feed (0, 0.1, 0.2, or 0.4%) throughout gestation (days 0-20) or 0.8% pm gestational days 6-15. Equivalent to daily doses of 0, 78, 163, 330, and 539 mg **BA**/kg/day (0, 13.6, 28.5, 57.7, and 94.3 mg B/kg/day).	For maternal toxicity: no effect noted in the 13.6 mg B/kg/day. At doses of 28.5 mg B/kg/day and higher, increased liver and kidney weight. At doses of 57.7 mg B/kg/day and greater, altered food and/or water intake. For highest dose only, decreased weight gain. For fetal toxicity: Increased fetal deaths (NOAEL 57.7 mg B/kg/day; LOAEL 94.3 mg B/kg/day) **decreased fetal body weight (NOAEL < 13.6 mg B/kg/day**; LOAEL13.6 mg B/kg/day) increase in fetal malformations (anomalies of the eyes, CNS, cardiovascular system, and axial skeleton) (NOAEL 13.6 mg B/kg/day; LOAEL 28.5 mg B/kg/day).	Heindel et al. 1992, 1994
mice	**boric acid (BA)** in feed (0, 0.1, 0.2, or 0.4%) throughout gestation (days 0-17). Equivalent to daily doses of 248, 452, and 1003 mg **BA**/kg/day (0, 43.3, 79.0, 175 mg B/kg/day).	For maternal toxicity: mild renal lesions, increased kidney wt, decreased wt gain for all boron treatment groups. For fetal toxicity: **Increased fetal deaths (NOAEL 79 mg B/kg/day**; LOAEL 175 mg B/kg/day) decreased fetal body weight (NOAEL 43.3 mg B/kg/day; LOAEL 79mg B/kg/day) **increase in fetal malformations (short rib XIII and other skeletal anomalies pertaining to ribs) (NOAEL 79 mg B/kg/day**; LOAEL 175 mg B/kg/day)	Heindel et al. 1992, 1994

Appendix 1: Toxicity of borax to experimental mammals

Animal	Dose/Exposure	Response	Reference
rabbits	oral exposure (gavage) to **boric acid (BA)** 0, 62.5, 125, or 250 mg **BA**/kg/day (0, 10.9, 21.8, or 43.7 mg B/kg/day) on gestational days 6-19.	For maternal toxicity: At highest exposure level only, decreased food consumption and vaginal bleeding associated with pregnancy loss. For fetal toxicity: Increased fetal deaths (NOAEL 21.8 mg B/kg/day; LOAEL 43.7 mg B/kg/day) cardiovascular malformations (NOAEL 21.8 mg B/kg/day; LOAEL 43.7 mg B/kg/day)	Heindel et al. 1994
rats	dietary exposure to dietary **boric acid** at 0, 0.025, 0.050, 0.075, 0.1, or 0.2% in feed on gestational days 0-20 (approximately equivalent to 18.6, 36.2, 55.1, 75.9, and 142.9 mg **BA**/kg/day or 3.3, 6.3, 9.6, 13.3, and 25 mg B/kg/day)	For maternal toxicity: No maternal deaths or signs of toxicity in any boron treatment group. Only effect was Increased kidney wt in 0.2% group. NOAEL = 13.3 mg B/k/day. LOAEL = 25 mg B./kg /day For fetal toxicity: Fetal viability unaffected. Fetal weight significantly decreased in 0.1 (94% of control) and 0.2% (88% of control) groups. Increased wavy rib in 0.1 and 0.25 groups. Rib malformation reversed by post-natal day 21. For developmental toxicity (skeletal malformations and reduced fetal weight): NOAEL = 9.6 mg B/kg/day LOAEL = 13.7 mg B/kg/day	Price et al. 1996a

Appendix 1: Toxicity of borax to experimental mammals

Animal	Dose/Exposure	Response	Reference
rabbits	oral exposure (gavage) to **boric acid** (62.6, 125, or 250 mg boric acid/day) on gestational days 6-19. Doses equivalent to 10.9, 21.8, or 43.7 mg B/kg/day.	For maternal toxicity: In 21.8 and 43.7 mg B/kg/day groups, decreased body wt and wt gain, decreased gravid uterus wt, decrease number of ovarian corpus lutea. In 43.7 mg B/kg/day group, increase in kidney wt, but no treatment-related renal pathology observed. For fetal toxicity: In 43.7 mg B/kg/day group, increased fetal resorptions (90% for B, 6% for control, reduction in litter size, and increase in malformed fetuses (cardiovascular malformation of interventricular septal defect). Slight decreased in fetal wt, but not statistically significant. For developmental toxicity: NOAEL = 21.8 mg B/kg/day LOAEL = 43.7 mg B/kg/day	Price et al. 1996b

Appendix 1: Toxicity of borax to experimental mammals

Animal	Dose/Exposure	Response	Reference
rats, male	exposure to borax in feed at concentrations of 0, 500, 1000, and 2000 ppm boron equivalents for 30 and 60 days. According to U.S. EPA 1989, these doses are equivalent to 25, 50, and 100 mg/kg/day).	No adverse effects observed in the 500 ppm exposure group for either 30- or 60-day exposure. In the 1000 and 2000 ppm groups, dose-related testicular atrophy, with complete depletion of germ cells within 60 days of exposure in the 2000 ppm group. In both groups, decrease in seminiferous tubular diameter and accumulation of testicular boron. Reduction in activities of enzymes that are markers of post-meiotic germ cell activity. Time- and dose-dependent increases in plasma FS and LH, but normal plasma concentrations of testosterone. Serial mating studies show decreased fertility without change in copulatory behavior. Dose-dependent decrease in fertility. No litters produced in the 2000 ppm group. In the 2000 ppm group, infertility persisted for 8 months following the cessation of treatment. No other clinical signs of systemic toxicity were observed in any treatment group. For male reproductive effects - NOAEL = 25 mg B/kg/day LOAEL - 50 mg B/kg/day	Lee et al. 1978

Appendix 1: Toxicity of borax to experimental mammals

Animal	Dose/Exposure	Response	Reference
rats (albino)	Reproduction study. Rats exposed to **borax** (sodium tetraborate decahydrate) at concentrations of 0, 0.103, 0.308, and 1.030% in diet. Exposure period was for 3 generations, through the weaning of the second litter of the 3rd generation. Average daily dose of test material were approximately 70, 200 and 700 mg borax/kg/day (8, 24, and 80 mg boron equivalents/kg/day). Averages calculated from weekly compound consumption and boron equivalents consumption for each treatment group (displayed in Tables 6 and 7 of fiche)	No effects on reproduction in 0.103 and 0.308% groups compared to control. Mating of animals in the 1.03% test group was discontinued due to failure to produce litters.. Microscopic evaluation of males showed lack of viable sperm and grossly atrophied testes in all males of this group. Evidence of decreased ovulation noted in females of this group. When females of this group were mated with control males, no litters were produced. Possible causes could be adverse effects on ovum, implantation, or gestation after implantation. In 1.03% test group, decreased body weight gain. No alterations in behavior in any test group. For male reproductive effects: NOAEL = 24 mg B/kg/day LOAEL = 80 mg B/kg/day	Wier 1966 MRID 00005623 *appears to be same data as presented in Weir and Fisher 1972 and Weir and Crews 1972 (MRID 406923-11)*

Appendix 1: Toxicity of borax to experimental mammals

Animal	Dose/Exposure	Response	Reference
rats	**Borax and boric acid** in diet at concentrations of 117, 350, and1170 ppm (boron equivalents) for 14 weeks prior to mating. Diets continued through 3 generations According to U.S. EPA 1989, these doses are equivalent to 5.9, 17.5, and 58.5 mg B/kg/day	No effects on reproduction (fertility index, lacation index or live birth index) in the 117 or 350 ppm diets for either borzx or boric acid. **NOAEC for reproductive effects = 350 ppm (17.5 mg B/kg/day)** In the 1170 ppm group for both borax and boric acid, no litters were produced. Mating of treated females with untreated males was not successful. Microscopic examination showed lack of viable sperm and atrophied testes in males. Evidence of decreased ovulation in females. **LOAEC for reproductive effects = 1170 ppm (58.5 mg B/kg/day)**	Weir and Fisher 1972
DERMAL			
rabbits (10 White New Zealand)	Acute dermal toxicity test of **borax** (sodium tetraborate decahydrate) (purity not reported). Single dose of test substance applied to clipped skin at 2.0 g/kg and occluded. Test substance removed after 2 hours. Animals observed for 15 days after application.	No mortalities. LD_{50} >2.0 g/kg Clinical observations: anorexia, decreased activity, diarrhea, soft stools, and nasal discharge. Gross pathological examination revealed no significant findings. No control group.	Reagan 1985a MRID 43553200

Appendix 1: Toxicity of borax to experimental mammals

Animal	Dose/Exposure	Response	Reference
rabbits (White New Zealand)	Primary dermal irritation study of **borax** (sodium tetraborate decahydrate) (purity not reported). Single dose of 0.5 g applied to shaved skin and occluded. Animals observed for 28, 52, and 76 hours after application.	No irritation noted. Mean primary irritation score = 0.	Reagan 1985b MRID 43553203
guinea pigs (10)	Dermal sensitization test for **borax** (sodium tetraborate decahydrate) (98% pure) repeated exposure to once weekly for 3 weeks, followed by challenge test. Concentrations tested: 25%, 50%, 75% and 95%.	Challenge test revealed no sensitizing effect. No irritation noted at any test site.	Wnorowski 1994b MRID 34500802
rats (5M/5F)	Acute dermal toxicity study of **borax** (sodium tetraborate decahydrate) (100% pure). Single dermal application of 5000 mg/kg to shaved skin and occluded for 24 hours. Animals observed for 12 days after exposure.	No mortalities. LD_{50} > 5000 mg/kg. On days 1 and 2 after application, dermal irritation was noted in all animals. Irregular breathing in one male. On necropsy, red lungs were noted in all animals. No control group.	Wnorowski 1996 MRID 44048603

EYES

Appendix 1: Toxicity of borax to experimental mammals

Animal	Dose/Exposure	Response	Reference
rabbits (6 White New Zealand)	0.1g **borax** (sodium tetraborate decahydrate) instilled in one eye of each rabbit. Material was not washed out. Animals observed for 72 hours post-treatment.	Severe irritation observed, including irritation of the iris, corneal opacity and conjunctival redness, chemosis, and discharge.	Reagan 1985c MRID 43553202

Appendix 1: Toxicity of borax to experimental mammals

Animal	Dose/Exposure	Response	Reference
INHALATION			
rats (5M/5F)	4- hour inhalation exposure to 2.0 mg/L **borax** (sodium tetraborate decahydrate) for 14 days. Measured concentration = 2.03 mg/L. Animals observed for 14 days after exposure.	No mortalities. 4-hour LC_{50} > 2.03 mg/L. During 1st hour of exposure, ocular discharge, hypoactivity and hunched posture were observed. After removal from chamber, ocular discharge persisted and 2/10 rats had nasal discharge. All symptoms resolved by day 7 after exposure. No significant finding on gross pathological exam.	Wnorowski 1994a MRID 43500801

Appendix 2: Toxicity of borax and boric acid to birds

Species	Nature of Exposure	Exposure Time	Effects	Reference
Single Dose				
Bobwhite quail (age: 5 months	single oral doses (0, 398, 631, 1000, 1590, and 2510 mg/kg) of **borax** (sodium tetraborate decahyrate, 100% a.i.) administered by gavage	single oral dose. Birds observed for 14 days after dosing	LD_{50} > 2510 mg borax/kg (equivalent to > 284 mg B/kg). One mortality in the 2510 mg/kg group. No mortalities in any other treatment group. No behavioral changes in any treatment group. Slight loss of body weight during the first 3 days after treatment in the 1590 and 2510 mg/kg treatment groups.	Fink et al. 1982a, MRID 001000657
Acute Dietary				
Bobwhite quail (10-15 days old)	dietary exposure to **borax** (sodium tetraborate decahyrate (100% a.i.) at concentrations of 0, 312.5, 625, 1250, 2500, 5000 ppm. Average body weight: 43 g average food: consumption: 10.4 g/bird/day	5-day dietary exposure. Birds observed for total of 8 days.	LC_{50} > 5000 ppm borax (equivalent to >567 ppm B) One mortality (10%) in the 5000 ppm treatment group. 10% and 20 % mortality observed in 2/4 control groups. No abnormal behavior observed in any group. No change in mean body weight in treatment groups compared to controls.	Reinart and Fletcher 1977 MRID 00149195

Appendix 2: Toxicity of borax and boric acid to birds

Species	Nature of Exposure	Exposure Time	Effects	Reference
Reproduction Studies				
mallard ducks	dietary exposure to **boric acid** in feed at concentrations of 0, 30, 300 and 1000 ppm B.	3 weeks of treatment prior to mating. Treatment continued through 21-days after ducklings hatched.	<u>Hatchlings</u> decrease in hatching, post-hatching growth and survival following exposure to 1000 ppm. NOAEL = 300 ppm B LOAEL = 1000 ppm B <u>Adults</u> No effect of treatment on adult survival or egg fertility NOAEL >1000 ppm	Smith and Anders 1989
broiler chickens	dietary exposure **borax**, 0 and 250 ppm B equivalents. Average weight of male birds = 5,667 g Average food consumption g/bird/day = 146 g/bird/day	Females were exposed for 28 days, during which egg production was recorded. Males were exposed for 28 days	In exposed females mated with unexposed males, no effect on body weight, egg production, or fertility. Hatchability was significantly decreased (to approximately 75% of control value) in borzx group. In exposed males, increase in number of damaged spermatozoal cells in boron-treated birds (approached statistical significance $p \leq 0.051$)	Rossi et al. 1993

Appendix 3: Toxicity of boric acid to terrestrial invertebrates

Species	Exposure	Effects	Reference
honey bee	acute topical exposure to **boric acid** (362.58 µg/bee)	No mortality. LD_{50} >362.58 µg boric acid/bee (or 41.1 µg B/bee) Boric acid is rated as essentially non-toxic	Atkins 1987 MRID 402692-01

Appendix 4: Toxicity of borax and boric acid to terrestrial plants

Species	Exposure	Effects	Reference
potatoes, winter wheat, and sugarbeet	boron (added as **boric acid**) in soil. Concentration range not specified.	Greenhouse study to determine the threshold soil concentrations of boron for producing phytotoxicity. Soil types were described as "light" and "heavy" soils. In "light soils:, the NOEAC for phytotoxic effects: potatoes: 5.0 - 7.5 mg B/kg soil winter wheat: 9 - 13 mg B/kg soil sugarbeet: 20 - 35 mg B/kg soil Higher values observed in "heavy" soils	Kluge 1990, as cited in ECETOC 1997
poppy (*Papaver somniferum*)	**borax** at concentrations of 1 to 32 ppm B in soil	NOEAC = 8 ppm B LOAEC = 16 ppm B Signs of phytotoxicity included decline in plant development, yellow leaves, late flowering, and reduction of mitotic frequency in root tip cells.	Sopova et al. 1981
Oat and turnip	**borax** added to soil at concentrations of 1, 10, 100 and 1000 mg/kg dry soil (added prior to planting)	Greenhouse study. EC_{50} values (based on fresh weight of 21-day old plants) Oats: 310 mg borax /kg soil (35.2 mg B/kg soil) turnip: 115 mg borax /kg soil (13.0 mg B/kg soil) NOAEC values not reported	Stanley and Tapp 1982, as cited in Windeatt et al. 1991

Appendix 5: Toxicity of borax and boric acid to fish and amphibians

Species	Nature of Exposure	Exposure Time	Effects	Reference
		FISH		
Acute				
rainbow trout	**Borax**, concentration range not reported	24- and 48-hour exposure	24-hr LC_{50} = 602.0 mg B/L 48-hr LC_{50} = 387.0 mg B/L	Alabaster 1969, as cited in Hovatter and Ross 1995
Bluegill sunfish	acute toxicity test of boric acid	96-hour	96-hour LC_{50} >1021 ppm B/L	LaLievre 1998 MRID 40594602, as cited in U.S. EPA 1993b
rainbow trout	acute toxicity test of boric acid	96-hour	96-hour LC_{50} >1100 ppm B/L	LaLievre 1998 MRID 40594602, as cited in U.S. EPA 1993b
Colorado squawfish, razorback sucker, and bonytail (all endangered fish collected from the Green River, Utah	acute toxicity test with **boric acid**	96-hour exposure	all values expressed as mg B/L <u>Colorado squawfish</u> 96-hr LC_{50} for – swimup fry = 279 small juvenile > 100 larger juvenile = 527 <u>razorback sucker</u> 96-hr LC_{50} for – swimup fry = 233 small juvenile = 279 larger juvenile > 100 <u>bonytail</u> 96-hr LC_{50} for – swimup fry = 280 small juvenile = 552 larger juvenile = 337	Hamilton 1995

Appendix 5: Toxicity of borax and boric acid to fish and amphibians

Species	Nature of Exposure	Exposure Time	Effects	Reference
Young salmon fry (Chinook and Coho)	static acute toxicity test for boron in water - **boric acid**	up to 96 hour exposure	Chinook Salmon 24-hr LC_{50} >1000 mg B/L 96-hr LC_{50} = 600 mg B/L For eyed egg and alevin, 24- and 96 hr LC_{50} >1000 mg B/L Coho Salmon 24-hr LC_{50} >1000 mg B/L 96-hr LC_{50} = 447 mg B/L	Hamilton and Buhl 1990
Western mosquitofish	**borax**, concentration range not reported	24-, 48-, and 96-hour exposure	24-hr LC_{50} =1361 mg B/L 48-hr LC_{50} = 930 mg B/L 96-hr LC_{50} = 408 mg B/L	Wallen et al,. 1957, as cited in Hovatter and Ross 1995

Appendix 5: Toxicity of borax and boric acid to fish and amphibians

Species	Nature of Exposure	Exposure Time	Effects	Reference
Longer Term				
Rainbow trout	Exposure from before fertilization to 4 days post-hatch, in hard and soft water. **Borax** concentrations: 0.001 to 300 ppm boron	up to 28 days	*All numbers expressed as boron equivalents* Authors note that no consistent effect of water hardness no boron toxicty was observed. The following LC_x values represent the combined response for embryonic mortality, embryogenic teratogenesis and posthatch mortality. <u>Borax</u> LC_1 in soft water ($CaCl_2$ 50 ppm) = 0.07 ppm B **LC_{50} in soft water ($CaCl_2$ 50 ppm) = 27 ppm** B LC_1 in hard water ($CaCl_2$ 200 ppm) = 0.07 ppm B LC_{50} in hard water ($CaCl_2$ 200 ppm) = 54 ppm B NOAEC (% mortality) = 1.0 ppm Boron LOAEC (% mortality) = 10.0 ppm boron (NOAECs and LOAECs estimated based on tabular results. No statistics were performed in this study)	Birge and Black 1977

Appendix 5: Toxicity of borax and boric acid to fish and amphibians

Species	Nature of Exposure	Exposure Time	Effects	Reference
channel catfish	Exposure to 0.001 to 300 ppm B (as **borax**) from before fertilization to 4 days post-hatch.	9 days	LC_{50} = 71 Boron ppm NOAEC (% mortality) = 1.0 ppm Boron LOAEC (% mortality) = 5.0 ppm boron (NOAECs and LOAECs estimated based on tabular results. No statistics were performed in this study)	Birge and Black 1977
Goldfish	Exposure to 0.001 to 300 ppm B (as **borax**) from before fertilization to 4 days post-hatch.	7 days	LC_{50} = 59 Boron ppm NOAEC (% mortality) = 0.5 ppm Boron LOAEC (% mortality) = 1.0 ppm boron (NOAECs and LOAECs estimated based on tabular results. No statistics were performed in this study)	Birge and Black 1977
Field/Mesocosm Bioconcentration Studies				
Western mosquito fish (*Gambusia affinis*)	Field study. Fish collected from various waters in California. Surface water boron concentrations ranged from 7.4-20 mg B/L	Chronic exposure. Field study.	Bioconcentration factors ranged from 0.08 to 0.2. No evidence of bioconcentration	Ohlendorf et al.1986, as cited in ECETOC Working Group 1997

Appendix 5: Toxicity of borax and boric acid to fish and amphibians

Species	Nature of Exposure	Exposure Time	Effects	Reference
Bluegill sunfish (*Lepomis macrochirus*)	Field study. Fish collected from waters in the San Joaquin Valley, CA, Surface water boron concentrations ranged from 1.1-3.1 mg B/L	Chronic exposure. Field study.	Bioconcentration factors ranged from 0.16 to 0.78. No evidence of bioconcentration	Klasing and Pilch 1988, as cited in ECETOC Working Group 1997
Common carp (*Cyprinus carpio*)	Field study. Fish collected from waters in the San Joaquin Valley, CA, Surface water boron concentrations ranged from 1.1-3.1 mg B/L	Chronic exposure. Field study.	Bioconcentration factors ranged from 0.1 to 1.25. No evidence of bioconcentration	Klasing and Pilch 1988, as cited in ECETOC Working Group 1997
		AMPHIBIANS		
Leopard Frog	Exposure to 0.001 to 300 ppm B (as **borax**) from before fertilization to 4 days post-hatch (7.5 days)	7.5 days	LC_{50} = 47 ppm Boron NOAEC (% mortality) = 1.0 ppm Boron LOAEC (% mortality) = 5.0 ppm boron (NOAECs and LOAECs estimated based on tabular results. No statistics were performed in this study)	Birge and Black 1977

Appendix 5: Toxicity of borax and boric acid to fish and amphibians

Species	Nature of Exposure	Exposure Time	Effects	Reference
Wood Frog	eggs exposed to borax (0, 50, or 100 mg/L) until hatch	13-23 days	Dose-dependent increase in proportion of deformed larvae (crescent shaped bodies). No effect of boron exposure on proportion of eggs hatching.	Lapsota and Dunson 1998
Jefferson Salamander	eggs exposed to borax (0, 50, or 100 mg/L) until hatch	17-35 days	Dose-dependent increase in proportion of deformed larvae (crescent shaped bodies). No effect of boron exposure on proportion of eggs hatching.	Lapsota and Dunson 1998
Spotted Salamander	eggs exposed to borax (0, 50, or 100 mg/L) until hatch	38-44 days	Dose-dependent increase in proportion of deformed larvae (swollen thoracic region and enlarged, shortened gills). No effect of boron exposure on proportion of eggs hatching.	Lapsota and Dunson 1998
American toad	eggs exposed to borax (0, 50, or 100 mg/L) until hatch	15-23 days	Dose-related decrease in proportion of eggs hatching in boron treatment groups.	Lapsota and Dunson 1998

Appendix 6: Toxicity of borax and boric acid to aquatic invertebrates

Species	Exposure Time	Effects[a]	Reference
Acute			
Daphnia magna	48-hour exposure to **borax**	48-hr LC_{50} = 141 mg B/L	Maier and Knight 1991
Chironomas decorus (a freshwater benthic invertebrate)	48-hour and 96-hour exposure to **borax**	48-hr LC_{50} = 1376 mg B/L 96-hour NOAEC (for decreased growth) 10 mg B/L 96-hour LOAEC (for decreased growth) 20 mg B/L No 96-hour LC_{50} reported	Maier and Knight 1991
Daphia magna	24-hour exposure to **borax**. Concentration range not reported	24-hr LC_{50} = 73 mg B/L	Bringmann and Kuhn 1977, as cited in Hovatter and Ross 1995
Daphia magna	48-hour exposure to **boric acid**. Concentration range not reported	48-hr LC_{50} = 133.0 mg B/L	Gersich 1984,
Daphia magna	48-hour exposure to **boric acid.** Concentration range not reported	48-hr LC_{50} = 226.0 mg B/L	Lewis and Valentine 1981
Longer Term			

Appendix 6: Toxicity of borax and boric acid to aquatic invertebrates

Species	Exposure Time	Effects[a]	Reference
Daphia magna	21-day exposure to **boric acid**, 6-106 mg B/L	21-day LC_{50} = 53.2 mg B/L (based on adult mortality) NOEAC (decreased length) = 27 mg B/L LOAEC (decreased length) = 53 mg B/L NOEAC (decreased brood size) = 6 mg B/L LOAEC (decreased brood size) = 13 mg B/L	Lewis and Valentine 1981
Daphnia magna	21-day exposure to **boric acid** at concentrations ranging from 6.3-59.3 mg B/L	21-day LC_{50} = 52.2 mg B/L (based on adult mortality) NOAEC (for reproductive parameters) = 6.4 mg B/L LOAEC (for reproductive parameters) = 13.6 mg B/L	Gerisch 1984

Appendix 7: Toxicity of borate compounds to aquatic plants

Species	Exposure	Effects [a]	Reference
		ALGAE	
green algae (*Scenedesmus quadricauda*)	72-hour exposure (borate compound not specified)	72-hour EC_3 = 16 mg B/L	Bringmann and Kuhn 1978, as cited in ECETOC Working Group 1997
blue-green algae (*Microcytsis aeruginosa*)	72-hour exposure (borate compound not specified)	72-hour EC_3 = 20.3 mg B/L	Bringmann and Kuhn 1978, as cited in ECETOC Working Group 1997
green algae (*Scenedesmus subpicatus*)	72-hour exposure (borate compound not specified)	72-hour EC_{10} = 10 mg B/L 72-hour EC_{50} = 34 mg B/L 72-hour EC_{100} = 100 mg B/L	Guhl 1992, as cited in ECETOC Working Group 1997
green algae (*Scenedesmus subpicatus*)	72-hour exposure (borate compound not specified)	72-hour EC_{10} = 24 mg B/L 72-hour EC_{50} = 52 mg B/L	Kopf and Wilk 1995, as cited in ECETOC Working Group 1997
		MACROPHYTES	
Short-term Exposure			
watermilfoil	21-day exposure to **boric acid** at concentrations of 0, 1, 2, 10 mg B/L	21-day EC_{50} for decreased photosynthesis = 5 mg B/L	Nobel 1981, as cited in WHO 1998
water buttercup	21-day exposure to **boric acid** at concentrations of 0, 1, 2, 10 mg B/L	21-day EC_{50} for decreased photosynthesis = 10 mg B/L	Nobel 1981, as cited in WHO 1998

Appendix 7: Toxicity of borate compounds to aquatic plants

Species	Exposure	Effects [a]	Reference
waterweed	21-day exposure to **boric acid** at concentrations of 0, 1, 2, 5, 10 and 250 mg B/L	21-day EC_{50} for decreased photosynthesis= 5 mg B/L	Nobel 1981, as cited in WHO 1998
Long-term Exposure			
Common reed (*Phragmites australis*)	**boric acid** in concentrations of 1. 0.5, 1.0, 2.0, 4.0, 8.0, 16.0 mg B/L for 2-3 months or 2 years A "pot study" - water concentrations maintained the indicated concentrations	NOAEC (2-3 months) for visual damage to that plant = 8 mg B/L NOAEC (2 years) for visible damage to the plant = 4 mg B/L	Bergmann et al. 1995, as cited in ECETOC Working Group 1997 and WHO 1998