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Sporax® and Cellu-Treat®
(Selected Borate Salts)
Human Health and Ecological Risk Assessment
FINAL REPORT

Submitted to:
Dr. Harold Thistle
USDA Forest Service
Forest Health Technology Enterprise Team
180 Canfield St.
Morgantown, WV 26505
Email: hthistle@fs.fed.us

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Submitted by:
Patrick R. Durkin
Syracuse Environmental Research Associates, Inc.
8125 Solomon Seal
Manlius, New York 13104

E-Mail: **SERA_INC@msn.com**
Home Page: **www.sera-inc.com**

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ACRONYMS, ABBREVIATIONS, AND SYMBOLS

ACGIH	American Conference of Governmental Industrial Hygienists
AEL	adverse-effect level
a.e.	acid equivalent
a.i.	active ingredient
a.k.a.	also known as
a.s.	active substance
AHETF	Agricultural Handlers Exposure Task Force
APHIS	Animal and Plant Health Inspection Service
ATSDR	Agency for Toxic Substances and Disease Registry
ASAE	American Society of Agricultural Engineers
BCF	bioconcentration factor
bw	body weight
calc	calculated value
CAT	Californians for Alternatives to Toxics
CBI	Confidential Business Information
CEQ	Council on Environmental Quality
CI	confidence interval
cm	centimeter
CNS	central nervous system
COC	crop oil concentrates
DAA	days after application
DAT	days after treatment
DER	Data Evaluation Record
d.f.	degrees of freedom
DOT	disodium octaborate tetrahydrate
dpf	days post-fertilization (term used in fish embryo assays)
EC	emulsifiable concentrate
EC_x	effective concentration causing X% inhibition of a process
EC_{25}	effective concentration causing 25% inhibition of a process
EC_{50}	effective concentration causing 50% inhibition of a process
ECOTOX	ECOTOXicology (database used by U.S. EPA/OPP)
EDSP	Endocrine Disruptor Screening Program
EFED	Environmental Fate and Effects Division (U.S. EPA/OPP)
ExToxNet	Extension Toxicology Network
F	female
FH	Forest Health
FIFRA	Federal Insecticide, Fungicide and Rodenticide Act
FQPA	Food Quality Protection Act
g	gram
GD	gestation day
GLP	Good Laboratory Practices
ha	hectare
hpf	hours post-fertilization (term used in fish embryo assays)
HED	Health Effects Division (U.S. EPA/OPP)
HQ	hazard quotient

HRAC	Herbicide Resistance Action Committee
IARC	International Agency for Research on Cancer
IRED	Interim Reregistration Eligibility Decision
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
LOAEC	lowest-observed-adverse-effect concentration
LOAEL	lowest-observed-adverse-effect level
LOC	level of concern
LR_{50}	50% lethal response [EFSA/European term]
m	meter
M	male
MEI	Most Exposed Individual
mg	milligram
mg/kg/day	milligrams of agent per kilogram of body weight per day
mL	milliliter
mM	millimole
mPa	millipascal, (0.001 Pa)
MOE	Margin of Exposure
MOS	Margin of Safety
MRID	Master Record Identification Number
MRL	minimum risk level
MSDS	material safety data sheet
MSO	methylated seed oil
MTDC	Missoula Technology and Development Center
MW	molecular weight
NAWQA	USGS National Water Quality Assessment
NCI	National Cancer Institute
N.D.	not determined
NEPA	National Environmental Policy Act
NIOSH	National Institute for Occupational Safety and Health
NIS	nonionic surfactant
NOAEL	no-observed-adverse-effect level
NOAEC	no-observed-adverse-effect concentration
NOEC	no-observed-effect concentration
NOEL	no-observed-effect level
NOS	not otherwise specified
N.R.	not reported

OM	organic matter
OPP	Office of Pesticide Programs
OPPTS	Office of Pesticide Planning and Toxic Substances
OSHA	Occupational Safety and Health Administration
Pa	Pascal
PBPK	Physiologically Based Pharmacokinetic
PHED	Pesticide Handlers Exposure Database
ppm	parts per million
RBC	red blood cells
RED	re-registration eligibility decision
RfD	reference dose
RQ	risk quotient
SERA	Syracuse Environmental Research Associates
TEP	typical end-use product
TRED	Tolerance Reassessment Eligibility Decision
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
VMD	volume median diameter (for droplet size distributions)
WCR	water contamination rate (mg/L per lb/acre)
WEPP	Water Erosion Prediction Project
WHO	World Health Organization
WSSA	Weed Science Society of America

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℃+32
centimeters	inches	0.3937
cubic meters (m^3)	liters (L)	1,000
Fahrenheit	centigrade	0.556℉-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

Boric acid and boric acid salts are effective fungicides which are applied to recently cut conifer stumps to control the spread of heterobasidion root disease. This risk assessment covers the use of two formulations designated by the Forest Service: Sporax® (a.i. sodium tetraborate decahydrate) and Cellu-Treat® (a.i. disodium octaborate tetrahydrate). These and other borates are naturally occurring compounds that are converted predominantly to boric acid. Thus, exposure to boron, primarily in the form of boric acid, is unavoidable, and the issue with the use of borates in Forest Service activities involves an assessment of the extent to which normal exposures to boron may be increased significantly by Forest Service activities. Following a convention used in most risk assessments on borates, both the exposure assessments and dose-response assessments developed in the current risk assessment are based on boron (B) equivalents.

In both the human health and ecological risk assessments, the quantitative expression of the risk characterization is the hazard quotient (HQ), the ratio of the anticipated dose or exposure to the RfD (human health) or no-observed-effect level or concentration (ecological effects) using 1 as the level of concern—i.e., an HQ of < 1 is below the level of concern.

The toxicity values used in the human health risk assessment are a surrogate acute RfD of 3.5 mg/kg bw/day and a longer-term RfD of 0.088 mg/kg bw/day. The HQs for workers (Worksheet E02) and members of the general public (Worksheet E04) are summarized in the attachments to this risk assessment—i.e., Attachment 1 for liquid applications of Cellu-Treat, Attachment 2 for liquid applications of Sporax, and Attachment 3 for dry applications of Sporax.

Exposure of workers involved in dry applications of Sporax® over a prolonged period is the only exposure scenario in the human health risk assessment for which the HQs exceed the level of concern. For this scenario, the HQs are 0.6 (0.1 to 6) with only the upper bound of the HQ exceeding the level of concern. This exposure scenario involves a deposition-based exposure assessment developed by EPA which is based on inhalation exposures. A major reservation with this exposure scenario is that the EPA applied the same exposure rates for both indoor (confined spaces) and outdoor dust applications. The extent to which the use of the same exposure rates for indoor and outdoor dust applications may overestimate exposures for forestry workers involved in stump applications is unclear. While the upper bound HQ of 6 indicates that extreme exposures would be considered generally unacceptable, it is not clear that these exposure levels would lead to overt toxic effects.

The only other exposure scenario that approaches the level of concern is the upper bound HQ of 0.9 for a small child who consumes Sporax® directly from a treated stump after a dry application. The upper bound HQ of 0.9 is associated with a dose 3.1 mg B/kg bw. This dose is slightly below the level of concern (HQ=1) and below the anticipated adverse effect level by a factor of over 6.

The registration for stump applications of Sporax® is no longer supported. While the Forest Service may continue to use existing stocks of Sporax, stump treatments will be limited to liquid applications of Cellu-Treat, once the existing stocks of Sporax® are exhausted. For liquid applications of Cellu-Treat, non-accidental HQs are below the level of concern by a factor of

over 300 for workers and over 100 for members of the general public. The highest accidental HQ (i.e., consumption of contaminated water by a small child) is below the level of concern by a factor of 100.

In the ecological risk assessment, most of the exposure assessments involve boron concentrations in surface water that are directly proportional to the application rate in units of lb B/acre. These application rates are virtually identical for both Cellu-Treat® (0.105 lb B/acre) and Sporax® (0.113 lb B/acre). Thus, for exposures involving surface water, there are no remarkable differences in HQs for Cellu-Treat® and Sporax®. The only exposure scenarios not dependent on application rates in units of lb B/acre are the exposure assessments for terrestrial organisms consuming borates from treated stumps. These exposure assessments are dependent on the stump application rate—i.e., 0.000525 lb B/ft^2 for Cellu-Treat® and 0.00226 lb B/ft^2 for Sporax®. Thus, the HQs for Sporax® involving the consumption of borates from tree stumps are a factor of about 4 greater than the corresponding HQs for Cellu-Treat®. Qualitatively, these differences are insignificant in that none of the HQs exceeds the level of concern.

For aquatic organisms, the highest non-accidental HQ is 0.07, the upper bound HQ for acute exposures in sensitive species of aquatic invertebrates following applications of Sporax®. This HQ is below the level of concern by a factor of about 14 [$1 \div 0.07 \approx 14.2857$]. The corresponding HQ for Cellu-Treat® is only marginally lower than the HQ for Sporax—i.e., 0.06, which is below the level of concern by a factor of about 17 [$1 \div 0.06 \approx 16.666\ldots$]. This benign risk characterization is consistent with the recent EPA ecological risk assessment, which describes risks to aquatic organisms as *Predominant Evidence of Negligible Risk* (U.S. EPA/OPP/EFED 2015a, p. 9).

The risk characterization for mammals and birds involving exposures to boron in surface water is similarly benign. The highest HQ is 0.002, the longer-term HQ for small birds consuming contaminated water as well as piscivorous birds consuming fish over a longer period of time. This HQ is below the level of concern by a factor of 500 [$1 \div 0.002$].

The risk characterization for mammals and birds consuming borates from treated stumps is somewhat more nuanced in that the exposure assessments have a high degree of uncertainty. The exposure assessment for the 70 kg mammal (deer) consuming borates from a treated stump is the only exposure scenario supported by direct observations—i.e., that deer may lick treated stumps. For this exposure assessment, the central estimate of the HQ for Sporax® is 0.04, and the central estimate of the HQ for Cellu-Treat® is 0.01. These central estimates are based on the assumption that a deer will consume all of the borate from a 1 ft^2 treated stump. Thus, to reach the level of concern, a deer must consume all of the borates applied to 25 ft^2 of stumps treated with Sporax® or 100 ft^2 of stumps treated with Cellu-Treat®. In the absence of information indicating that deer or other terrestrial vertebrates are attracted to stumps treated with borates, there is no compelling basis to assert that adverse effects in these animals are likely.

Stump applications of borates will not substantially increase concentrations of boron in soil, with the exception of areas immediately adjacent to treated stumps. Consequently, there is no basis for asserting that stump applications of borates would cause adverse effects in terrestrial plants, invertebrates, or microorganisms through soil exposures. The potential for adverse effects

associated with foliar exposures also appears to be remote. Liquid stump applications are likely to lead to lower levels of foliar exposure relative to standard backpack foliar applications of herbicides because the borate solution will be applied essentially at ground level (i.e., the height of the treated stump); hence off-site drift should be minimal. Nonetheless, HQs for terrestrial plants based on estimates of drift lead to HQs that are substantially below the level of concern. An HQ of 4 is estimated for direct spray of a terrestrial plant. This HQ, however, is based on a study in which an adverse effect level was not defined. Thus, the HQ of 4 should not be interpreted as an indication that adverse effects in plants would be anticipated, because the levels of exposure causing adverse effects following foliar exposures have not been defined.

Although the EPA considers risks to terrestrial insects because borates are registered as insecticides, Forest Service applications to stumps will limit any exposures of insects to incidental events that should not have a substantial impact on insect populations.

1. INTRODUCTION

1.1. Chemical Specific Information

This document provides human health and ecological risk assessments of the environmental consequences of using borax and related compounds in Forest Service programs to control heterobasidion root disease, also known as annosum root disease (e.g., Schmitt et al. 2000). This risk assessment is an update to the previous USDA Forest Service risk assessments on borax (SERA 2006a). The previous risk assessment considered only Sporax®, a formulation of borax (i.e., sodium tetraborate decahydrate). The current updated risk assessment includes the use of both Sporax® and Cellu-Treat® DOT Wood Preservative, a formulation of disodium octaborate tetrahydrate.

As discussed further in Section 2.2, borax (i.e., tetraborate decahydrate), disodium octaborate tetrahydrate, and other borates dissociate in the environment, particularly in aqueous solutions, and the species of boron containing compounds that will exist in the environment will depend on the pH of the aqueous solution and the concentration of boron compounds in solution (ATSDR 1992, p. 53, 2010, p. 24; HERA 2005, p. 5). 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 the relevant boric acid rather than boron equivalents. 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). This approach is essentially the same one used by the U.S. EPA/OPP in the re-registration of boric acid/sodium borate salts (U.S. EPA/OPP 1993a, 2006a; U.S. EPA/OPP/HED 2005a,b, 2006a; U.S. EPA/OPP/EFED 2006a) and results in conclusions similar to those reached by other governmental and related organizations (e.g., ECHA 2010, 2013; EFSA 2009, 2013; European Commission 2009a,b; HERA 2005; HSDB 2014; IPCS/WHO 1998; U.S. EPA/OW 2008; WHO 1998a,b).

Borates have been used by humans for over 4000 years (Woods 1994). The relatively recent formal literature on borates is robust and extends well into the late 1800s (Meacham et al. 2010) and early 1900s (e.g., Tunnicliffe and Rosenheim 1901). More recently, numerous studies have been submitted to regulatory agencies in both the United States and Europe in support of the registration of borax. The registrant studies are classified as Confidential Business Information (CBI) and are not publically available. In the previous Forest Service risk assessment (SERA 2006a), full text copies of the most relevant studies [n=52] were kindly provided by the U.S. EPA Office of Pesticide Programs. The U.S. EPA/OPP no longer provides full copies of registrant studies for risk assessments conducted in support of activities outside of U.S. EPA/OPP and the CBI studies provided for the 2006 risk assessment are not available for the current update. Consequently, summaries of the registrant-submitted studies from SERA (2006a) are included in the current Forest Service risk assessment. These studies are cited in the bibliography (Section 5) as RA2006 and are identified in the citation by MRID (Master Record Identification Number). In the interest of transparency, information on registrant studies based either on copies of full studies or DERs is cited in the standard author/date format, supplemented by the MRID number. Information taken only from EPA documents is cited using the MRID number and a reference to the EPA document in which the information is summarized.

The U.S. EPA/OPP is in the process of reviewing the registration of many pesticides (http://www.epa.gov/oppsrrd1/registration_review) including borax and related borates. Several documents relating to the registration review have been developed by EPA (U.S. EPA/OPP 2009b; U.S. EPA/OPP/EFED 2009a; U.S. EPA/OPP/HED 2009a,b). The EPA risk assessments for human health effects (U.S. EPA/OPP/HED 2015a) and ecological effects (U.S. EPA/OPP/EFED 2015a) are used extensively in the current risk assessment as the most definitive summary of registrant submitted studies on boric acid and sodium borate salts. In addition to the EPA registration review, the EPA has published a TRED (Tolerance Reassessment Eligibility Decision) and related documents (U.S. EPA/OPP 2006a; U.S. EPA/OPP/HED 2005a,b,c) since the previous Forest Service risk assessment.

It is common for EPA to reassess studies during registration reviews and tolerance reassessments. Except as specifically noted to the contrary, the current Forest Service risk assessment uses the most recent EPA evaluations of studies from the most recent EPA documents. Thus, summaries of some studies in the previous Forest Service risk assessment (SERA 2006a) have been modified in this revised risk assessment to reflect changes in study evaluations from EPA.

In addition to the activities of EPA, regulatory reviews are available from the European community. The European regulatory literature is significant in that European regulatory bodies often require assays of species not covered in EPA testing requirements. As with EPA risk assessments, the European risk assessments will cite registrant studies that are not publically available. These studies are summarized in the current Forest Service risk assessment based on and referenced to the appropriate documents from the European community (e.g., ECHA 2010, 2013; EFSA 2013; European Commission 2009a,b). Reviews in the open literature are also consulted (e.g., Beyond Pesticides 2006; Butterwick et al. 1989; Cal EPA 2013; Institute of Medicine 1997, 2001; Lloyd 1998; Moore 1997; Meacham et al. 2010; Pahl et al. 2005; Tyl et al. 2007). Because of the extensive literature on boron, it is not practical to provide a comprehensive review of all of the primary open literature on boron. As in the previous Forest Service risk assessment (SERA 2006a), reviews on boron are used directly for some summaries of the open literature, although relevant primary literature on boron has been reviewed and summarized as appropriate. Summaries of information on boron taken substantially from reviews are noted specifically as appropriate in the current risk assessment.

In addition to the new regulatory literature, the newer open literature is identified through literature searches of TOXLINE and ECOTOX covering the period from 2004 to present. The year 2004 is chosen as the reference point for newer literature because the previous Forest Service risk assessment was finalized early in 2006 and the literature search was conducted in 2005. Commonly, there is about a 1-year lag time for some journals included in databases such as TOXLINE and ECOTOX. In addition to the newer literature, focused searches were conducted on the earlier literature and some relevant older studies not included in the SERA (2006a) risk assessment are included in the current updated risk assessment.

1.2. General Information

This document has four chapters, including the introduction, program description, risk assessment for human health effects, and risk assessment for ecological effects or effects on wildlife species. Each of the two risk assessment chapters has four major sections, including an identification of the hazards, an assessment of potential exposure to this compound, an assessment of the dose-response relationships, and a characterization of the risks associated with plausible levels of exposure.

This is a technical support document which 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 2014a). The human health and ecological risk assessments presented in this document are not, and are not intended to be, comprehensive summaries of all of the available information. As discussed in the previous Forest Service risk assessment (SERA 2006a), there is an extremely large and diverse literature on borax and related borates. As with the previous risk assessment, no attempt is made to encompass all of the studies on borates. Doing so would not be justified in terms of the required resources and potential impact on the risk assessment. Nonetheless, 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 an independent review of the risk analyses.

As noted in Section 1.1, studies submitted by registrants in support of the registration of borates are used extensively in this risk assessment based on information publically available from the U.S. EPA. In any risk assessment based substantially on registrant-submitted studies, the Forest Service is sensitive to concerns of potential bias. The general concern might be expressed as follows:

> *If the study is paid for and/or conducted by the registrant, the study may be designed and/or conducted and/or reported in a manner that will obscure any adverse effects that the compound may have.*

This concern is largely without foundation. While any study (published or unpublished) can be falsified, concerns with the design, conduct and reporting of studies submitted to the U.S. EPA for pesticide registration are minor. The design of the studies submitted for pesticide registration is based on strict guidelines for both the conduct and reporting of studies. These guidelines are developed by the U.S. EPA and not by the registrants. Full copies of the guidelines for these studies are available at http://www.epa.gov/ocspp/pubs/frs/home/guidelin.htm. Virtually all studies accepted by the U.S. EPA/OPP are conducted under Good Laboratory Practices (GLPs). GLPs are an elaborate set of procedures which involve documentation and independent quality control and quality assurance that substantially exceed the levels typically seen in open literature publications. As a final point, the EPA reviews each submitted study for adherence to the relevant study guidelines. These reviews most often take the form of Data Evaluation Records (DERs). While the nature and complexity of DERs varies according to the nature and complexity of the particular studies, each DER involves an independent assessment of the study to ensure that the EPA Guidelines are followed and that the results are expressed accurately. In

many instances, the U.S. EPA/OPP will reanalyze raw data from the study as a check or elaboration of data analyses presented in the study. In addition, each DER undergoes internal review (and sometimes several layers of review). The DERs prepared by the U.S. EPA form the basis of EPA risk assessments and, when available, DERs are used in Forest Service risk assessments.

Despite the real and legitimate concerns with risk assessments based largely on registrant-submitted studies, data quality and data integrity are not substantial concerns. The major limitation of risk assessments based substantially on registrant-submitted studies involves the nature and diversity of the available studies. The studies required by the U.S. EPA are based on a relatively narrow set of criteria in a relatively small subset of species and follow standardized protocols. The relevance of this limitation to the current risk assessment on borates is noted in various parts of this risk assessment as appropriate. Overall, as discussed in Section 1.1, the open literature on borates is robust, and this literature is used quantitatively in the current risk assessment as needed and as appropriate.

The Forest Service periodically updates pesticide risk assessments and welcomes input from the general public and other interested parties on the selection of studies included in risk assessments. This input is helpful, however, only if recommendations for including additional studies specify why and/or how the new or not previously included information would be likely to alter the conclusions reached in the risk assessments.

As with all Forest Service risk assessments, 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 quite 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 which are relatively simple. Simple calculations are included in the body of the document [typically in brackets]. The results of some calculations within brackets may contain an inordinate number of significant figures in the interest of transparency—i.e., to allow readers to reproduce and check the calculations. In all cases, these numbers are not used directly but are rounded to the number of significant figures (typically two or three) that can be justified by the data.

Some of the calculations, however, are cumbersome. For those calculations, EXCEL workbooks (i.e., sets of EXCEL worksheets) are included as attachments to this risk assessment. The workbooks included with the current risk assessment are discussed in Section 2.4. The worksheets in these workbooks provide the detail for the estimates cited in the body of the document. Documentation for the use of these workbooks is presented in SERA (2011a).

The EXCEL workbooks are integral parts of the risk assessment. The worksheets contained in these workbooks are designed to isolate the numerous calculations from the risk assessment narrative. In general, all calculations of exposure scenarios and quantitative risk characterizations are derived and contained in the worksheets. In these worksheets as well as in the text of this risk assessment, the hazard quotient is the ratio of the estimated exposure to a toxicity value, typically a no adverse effect level or concentration (i.e., NOAEL or NOAEC). Note that the use of the terms *NOAEL* (no-observed-adverse-effect level) and *NOAEC* (no-

observed-adverse-effect concentration) are sometimes used interchangeably. Following the general practice of the U.S. EPA/OPP, the term *NOAEC* is used in the current risk assessment for exposures associated with concentrations in water, food, or soil. The term *NOAEL* is used more generally for other types of exposures – e.g., doses in units of mg/kg bw or application rates in units of lb/acre. Both the rationale for the calculations and the interpretation of the hazard quotients are contained in this risk assessment document.

2. Program Description

2.1. Overview

Boric acid and boric acid salts are effective fungicides, and the Forest Service applies these fungicides to recently cut conifer stumps to control the spread of heterobasidion root disease. This updated risk assessment covers the use of two formulations: Sporax® (a.i. sodium tetraborate decahydrate or borax) and Cellu-Treat® (a.i. disodium octaborate tetrahydrate or DOT). Sporax® and Cellu-Treat® contain different active ingredients, which has a minimal impact on the current risk assessment because both active ingredients are converted to boric acid, which may be viewed as the toxic agent of concern. Following a convention used in virtually all risk assessments on borates, both the exposure assessments and dose-response assessments developed in the current risk assessment are based on boron (B) equivalents.

Labelled application rates for Sporax® and Cellu-Treat® are expressed in units of lb/ft^2 of treated stump surface. The recommended labelled application rate for stump applications of Sporax® is 0.02 lb a.i./ft^2 of stump surface. An 8-fold lower rate of 0.0025 lb a.i./ft^2 is recommended on the product label for Cellu-Treat®. In terms of boron equivalents, the stump application rate for Cellu-Treat® (0.000525 lb B/ft^2) is less than the stump application rate for Sporax® (0.00226 lb B/ft^2) by a factor of about 4.3 [0.00226 lb B/ft^2 ÷ 0.000525 lb B/ft^2 ≈ 4.3048].

While application rates in units of lb/ft^2 are most germane to applications of these borates to stump surfaces, application rates in terms of lb/acre are required for several of the exposure assessments developed in this risk assessment. As with the previous risk assessment on Sporax, the typical application rate is taken as 1 lb borax/acre. Application rates for Cellu-Treat® units of lb DOT/acre are not well documented and the Forest Service has limited experience with the Cellu-Treat® formulation. For the current risk assessment, the Forest Service has indicated that an application rate of 0.5 lb/acre should be used. In terms of boron, these two application rates are virtually identical – i.e., 0.105 lb B/acre for Cellu-Treat® at 0.5 lb a.i./acre and 0.113 lb B/acre for Sporax® at 1 lb a.i./acre.

2.2. Chemical Description and Commercial Formulations

Boric acid and several boric acid salts are registered by the U.S. EPA for the control of mites, algae, fungi, plants, and insects (e.g., U.S. EPA/OPP/EFED 2009a, 2015a; U.S. EPA/OPP/HED 2015a). As in the previous Forest Service risk assessment on borax (SERA 2006a), the only use of boric acid salts in Forest Service programs involves the control of heterobasidion root disease. Heterobasidion root disease was formerly referenced as *annosum root disease*, and this term is still used in the literature as well as on the most recent EPA labels for Sporax® (Wilbur-Ellis 2013) and Cellu-Treat® (Nisus 2015). Heterobasidion root disease is a fungal disease in conifers caused by the fungi *Heterobasidion irregulare* or *Heterobasidion occidentale* (Bakke 2016a). The fungi infect conifer stumps following forest thinning (e.g., Aho et al. 1983; Edmonds et al. 1989; Lehtijarvi et al. 2011; Schmitt et al. 2000). The disease may then spread to healthy uncut confers via existing root grafts between healthy tree roots and the roots of cut, infected stumps (http://dnr.wi.gov/topic/foresthealth/annosumrootrot.html). Borax is also used in Europe for the control of various *Heterobasidion* species (Nicolotti and Gonthier 2005). While most efficacy studies have focused on borax (Findlay 1953, 1960; Graham 1970), DOT has been found to be

effective for the control of *Heterobasidion* species (Lloyd 2012; Lloyd and Pratt 1997; Pratt and Quill 1996; Westlund and Nohrstedt 2000).

The previous Forest Service risk assessment covered only Sporax, a formulation of borax (sodium tetraborate decahydrate) labeled for the control of heterobasidion root disease. The current risk assessment covers both Sporax® and Cellu-Treat®. In this risk assessment, the terms "*borax*" and "*DOT*" rather than the longer chemical names are used, unless otherwise warranted. As with Sporax, Cellu-Treat® is labeled for the control of heterobasidion root disease. Differences in the application methods for the two formulations are discussed in Section 2.3.

The recent ecological risk assessment in support of the registration review of boric acid and sodium borate salts indicates that the spot treatment of stumps is permitted only for DOT (U.S. EPA/OPP/EFED 2015a, p. 19):

> *Forest trees:*
>
> *This use is only for disodium octaborate tetrahydrate (PC code 011103). It is for spot treatment on stumps, and can be applied with either a backpack sprayer or a hand held sprayer when needed.*

Notwithstanding the above statement, the most recent label for Sporax® available at the EPA's pesticide label system (http://www3.epa.gov/pesticides/chem_search/ppls) is dated January 31, 2013 and indicates that Sporax® is labeled for stump treatments for the control of annosum root disease. Based on the above note from EPA and comments from the Forest Service, it appears that the registration for stump treatments with Sporax® is being dropped. While the Forest Service may continue to use existing stocks of Sporax, stump treatments will be limited to Cellu-Treat® once the existing stocks of Sporax® have been exhausted.

Based on product labels in the EPA's pesticide label system, Cellu-Treat® has the same registration number as Nibor® Borate Insecticide and Fungicide. The earliest product label for this pesticide specifically permitting stump applications for the control of *annosum root disease* was approved by the U.S. EPA on July 13, 2005 (Nisus 2005). The earliest EPA approved label at the EPA site specifying Cellu-Treat® as a formulation name is dated September 24, 2015 (Nisus 2015), although Nisus has used this trade name on formulations of DOT since 2010 (Nisus 2010). Based on the Nisus (2015) general use label, acceptable formulation names for Cellu-Treat® include the following: Cellutreat, Tim-Bor Professional, Nibor-D, and Nibor D.

An overview of the formulations and the corresponding active ingredients explicitly covered in the current risk assessment is given in Table 1 along with some corresponding information on boron and boric acid. 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/neutral boric acid [$B(OH)_3$]. As discussed specifically for DOT,

> *The water solubility, dissociation constant, partition coefficient, and surface tension for disodium octaborate tetrahydrate as such cannot be determined*

> *because disodium octaborate tetrahydrate is converted into boric acid/borate upon dissolution in water:* $Na_2B_8O_{13}.4H_2O + 9H_2O \leftrightarrow 2NaB(OH)_4 + 6\ B(OH)_3$. *The water solubility, dissociation constant, partition coefficient, and surface tension found will be the ones for an equivalent amount of boric acid in the presence of sodium ions.*
>
> European Commission 2009b, p 6.

Since borax, DOT, as well as other borate salts in water transform to boric acid, many standard physical/chemical properties of borate salts are not available or relevant.

Because of the conversion of borate salts to boric acid, as discussed further in the exposure assessments for human health effects (Section 3.2) as well as ecological effects (Section 4.2), the exposure assessments for both borax and DOT are based on the chemical properties of boric acid.

Another factor in the risk assessment of borates is the conversion of borates to boric acid in organisms.

> *At the low concentrations and near-neutral pH found in most biological fluids, monomeric* $B(OH)_3$ [i.e., boric acid] *will be the predominant species present (with some* $B(OH)_4^-$ [i.e., tetrahydroxyborate], *regardless of whether the boron source is boric acid or one of the borates. This is because boric acid is a very weak acid (*pK_a *9.15).*
>
> WHO 1998, Section 1.1.1

In other words, dilute solutions of boric acid consist almost completely of un-ionized boric acid, $B(OH_3)$ and the tetrahydroxyborate anion $[B(OH_4)^{-1}]$ (Woods 1994). More specifically, the proportion of a weak acid that is un-ionized (*P*) may be calculated from the pK_a for the weak acid and the pH of the media in which the acid occurs as (e.g., U.S. EPA/OSWER 1996, Eq. 72, p. 146):

$$P = \frac{1}{1+10^{(pH-pK_a)}} \qquad (1)$$

Taking a pH of 7 as representative of most biological fluids and the pK_a of 9.15 for boric acid, the proportion of boric acid in the un-ionized/neutral form is about 0.99 $[1/(1+10^{(7-9.15)}) \approx 0.99297]$.

Another important factor in this risk assessment is that borates are naturally occurring compounds. As summarized in Table 2, boron is found in the earth's crust at concentrations of 5 to 100 mg/kg with a mean value of about 10 mg/kg and normal concentrations of boron in freshwater, primarily in the form of boric acid, are typically below 1 mg B/L in freshwater and about 4.5 mg/L in ocean water. Given the natural occurrence and ubiquity of boron, exposure to boron is unavoidable. As discussed further in Section 3.2 (Exposure Assessment), the primary route of background exposures to boron involve dietary intake with typical intakes in the U.S. of about 1 to 3 mg B/day. In addition, boron is essential to higher plants (e.g., Kabu and Akosman 2013; Kato et al. 2009; Roessner et al. 2006; WHO 1998), aquatic vertebrates and invertebrates

(U.S. EPA/OPP/EFED 2015a) and appears to be a beneficial micronutrient in some terrestrial vertebrates (Meacham et al. 2010; U.S. EPA/OPP/EFED 2009a, 2015a). As discussed further in Section 3.1.2 (Mechanism of Action), boron is not considered to be an essential micronutrient in vertebrates but typical background levels of exposure may be beneficial.

Given the above, the central issue with the use of borates in Forest Service activities involves an assessment of the extent to which normal exposures to boron may be increased significantly by Forest Service activities. As noted in the recent EPA ecological risk assessment:

> *Considering the amounts of borate ion found naturally in the environment (30 to 100 ppm in soil, 1 to 200 ppb in fresh water, and 4.5 ppm in ocean water), the spot treatments on aquatic areas, forest trees, and premises/structures are not expected to meaningfully impact background borate concentrations.*
>
> U.S. EPA/OPP/EFED 2015a, p. 19

This issue is addressed further in the exposure assessments for human health (Section 3.2) and ecological effects (Section 4.2). The consequences of such exposures are discussed in the risk characterizations for human health (Section 3.4) and ecological effects (Section 4.4).

Risk assessments on borate salts have adopted the convention of expressing exposure and toxicity values in terms of boron equivalents (ECHA 2010, 2013; EFSA 2013; European Commission 2009a,b; HERA 2005; HSDB 2014;U.S. EPA/OPP 1993a, 2006a; U.S. EPA/OPP/HED 2006a, 2015a; U.S. EPA/OPP/EFED 2006a, 2015a; WHO 1998b). As with the previous Forest Service risk assessment, this convention is adopted in the current risk assessment. The boron equivalents for boric acid, borax, and DOT are given in Table 1. The boron equivalents are calculated as the molar weight of boron in boric acid or the borate salt divided by the total molecular weight of boric acid or the borate salt. In the terms of the development of hazard quotients—i.e., the ratio of the exposure to toxicity values—the use of boron equivalents versus reasonable alternative equivalents (e.g., boric acid or boric oxide) is incidental in that any of these measures leads to identical hazard quotients.

2.3. Application Methods

Both Sporax® and Cellu-Treat® are applied to recently cut tree stumps. No broadcast application methods are used in forestry applications of these borates. Coupled with the natural occurrence of boron (Section 2.2), this limited use of borates is a limiting factor in risks potentially posed by the use of borates in Forest Service programs.

Sporax® can be applied as a solid (dry application) or mixed with water for spray application. Specific application rates are discussed in the following section. When applied dry, Sporax® is sprinkled onto the cut tree stump with a “salt-shaker” style applicator. For large scale mechanical operations with a feller-buncher, the Forest Service’s Missoula Technology and Development Center (MTDC) developed a mechanical dry borax applicator (Karsky 1999; Karsky et al. 1998).

Cellu-Treat® is labelled only for liquid application. As indicated on the product label for Cellu-Treat, this formulation is applied using a backpack sprayer or hand held sprayer. The U.S. EPA/OPP/EFED (2015a, p. 19) provides a similar description of the application method. In

larger scale applications, Cellu-Treat® may be applied by the mechanical harvester if set up to apply as part of the tree cutting process. This method appears to be similar to MTDC dry applicator discussed above for Sporax, however, a more detailed description of large scale application equipment for Cellu-Treat® was not encountered in the literature other than a note indicating that liquid applications of Cellu-Treat® are used particularly for cutting with masticators (http://www.fs.usda.gov/detail/r5/forest-grasslandhealth/insects-diseases/?cid=stelprdb5329386).

2.4. Mixing and Application Rates

For Sporax, the product label specifies that stump applications are made at a rate of 1 lb/50 ft^2 of stump surface. This rate is also specified in the EPA's RED for borax (U.S. EPA/OPP 2993a, p. 9), the recent human health risk assessment (U.S. EPA/OPP/HED 2015a), and equivalently as 20 lbs/1000 ft^2 (U.S. EPA/OPP 2003a, Appendix A, p. 2). This application rate corresponds to 0.02 lb/ft^2. All of these rates are given in units of borax (sodium tetraborate decahydrate). As indicated in Table 1, a factor of $0.113_{B/Borax}$ is used to convert borax to boron equivalents. Thus, an application rate of 0.02 lb borax/ft^2 is equivalent to 0.00226 lb B/ft^2 [0.02 lb borax/ft^2 x $0.113_{B/Borax}$]. As noted in Section 2.3, Sporax® may be applied dry (no mixing) or wet. For nominal *dry* applications, the product label clearly indicates that …*moisture in the exposed wood from freshly cut stumps, dew or rain, will dissolve the product and leach it into the wood*. For liquid applications, the amount of water to be used is not specified on the product label except with the following general guidance: *enough water to adequately spray 50 square feet of stump surfaces*. While borax may be mixed with water prior to application and sprayed on the stumps, Smith (1970) noted that dry applications of borax appeared to be somewhat more effective than wet applications – i.e., 0/50 white fir stumps infected following a dry application and 2/50 stumps infected following a wet application as a 10% borax solution. Note, however, the difference between the two methods is not statistically significant using a one-tailed Fischer Exact Test (p=0.247475).

Cellu-Treat® is not labeled for dry application and must be mixed with water. The most recent product label for Cellu-Treat® at the EPA pesticide label site is dated September 24, 2015 (Nisus 2015). The label specifies several formulation names: Nibor®, Tim-Bor® Professional, Nibor®-D, Nibor® D, Cellutreat®, and Cellu-Treat®. The product label specifies a concentration for stump applications of 5% as mixing 0.5 lb formulation per gallon of water and indicates that one gallon will treat 200 ft^2. Note that the mixing directions of 0.5 lb (≈226.796 g) and 1 gallon of water (≈3785.41 mL) corresponds to a nominal concentration of about 0.0559 g/mL or about a 6% w/v solution [226.796 g ÷ 3785.41 mL ≈ 0.059913 g DOT/mL] or about [59.913 mg/L x $0.21_{B/DOT}$ ≈ 12.582 mg B/mL]. These calculations, however, do not consider the impact of the dissolved DOT on the volume of the solution. In any event, the recommended concentration of 5% DOT is the lowest concentration associated with 0% infection in spruce stumps (Lloyd and Pratt 1997, p. 137, Table 1). The application rate of 0.5 lb/200 ft^2 is equivalent to 0.0025 lb DOT/ft^2 of stump surface [0.5 lb DOT ÷ 200 ft^2] or 0.000525 lb B/ft^2 [0.0025 lb DOT/ft^2 x $0.21_{B/DOT}$ = 0.000525 lb B/ft^2]. In terms of formulations, the application rate for Cellu-Treat® is less than the application rate for Sporax® by a factor of about 8 [0.02 lb Sporax®/ft^2 ÷ 0.0025 lb Cellu-Treat®/ft^2]. In terms of boron equivalents, the stump application rate for Cellu-Treat® is less than the stump application rate for Sporax® by a factor of about 4.3 [0.00226 lb B/ft^2 ÷ 0.000525 lb B/ft^2 ≈ 4.3048].

The most recent ecological risk assessment from U.S. EPA specifies a stump application rate for Cellu-Treat® of "1.225 lb/ 1K sq. ft" (U.S. EPA/OPP/EDED 2015a, Table 2.5, p. 18) for stump treatments of DOT. This designation is mixed terminology for 1.225 lb per 1000 square feet. This is equivalent to 0.001225 lb DOT/ft^2 or about 0.00026 B/ft^2 [0.001225 lb DOT/ft^2 x $0.210_{B/DOT} \approx 0.0002625$ B/ft^2]. The reason for the discrepancy in the rate given in the recent EPA product label – i.e., 0.000525 lb B/ft^2 as discussed above – and the lower maximum rate specified in U.S. EPA/OPP/EDED (2015a, Table 3.5, p. 18) is not apparent. In the absence of additional information, the product label is viewed as the more definitive and legally binding document.

Application rates for pesticides applied by broadcast or directed foliar applications are typically expressed in units of lbs a.i./acre. These application rates are then used in the risk assessment to estimate exposure levels for workers (Section 3.2.2), members of the general public (Section 3.2.3), and various groups of non-target species (Section 4.2). An application rate expressed in units of lbs a.i./acre is a particularly significant and, in some respects, a controlling parameter as input for environmental fate models commonly used to estimate pesticide concentrations in ambient water (Section 3.2.3.4). Application rates in units of lb a.i./acre for stump applications, however, are not specified on the product labels for either Sporax® (Wilbur-Ellis 2013) or Cellu-Treat® (Nisus 2010, 2015); moreover, application rates in units of lb a.i./acre are not specified by the EPA for stump applications (e.g., U.S. EPA/OPP 1993a; U.S. EPA/OPP/HED 2015a).

In the previous Forest Service risk assessment on Sporax® (SERA 2006a), an application rate of 1 lb/acre Sporax® was used as a typical application rate, and application rates of 0.1 lb/acre to up to 5 lb/acre were considered in the risk characterization. As discussed further in Section 2.5, these estimates are based on Forest Service use reports of Sporax® applications over the period from 2000 to 2002. Based on more recent use data from the Forest Service as well as use data from California (Section 2.5), the estimates of application rates for borax from the previous risk assessment are maintained in this updated risk assessment.

The potential application rates in terms of lb/acre for Cellu-Treat® are less certain. In assigning the current risk assessment, the Forest Service indicated that a conservative (upper bound) application of Cellu-Treat® would involve about 1 gallon of a 5% solution per acre. This rate corresponds to about 0.5 lb/acre. The Forest Service, however, expresses low confidence in this estimate: "*At this time we don't have a lot of experience in terms of the actual application rate that would be done in real world situations, so label numbers will have to suffice*". As detailed above, the "*label numbers*" do not translate to an application rate in units of lb/acre. Given the differences between Sporax® and Cellu-Treat® in the lb/ft^2 application rates discussed above, it could be reasonable to reduce the estimated application rates for Cellu-Treat® by a factor of 8 relative to the lb/acre application rates for Sporax® – i.e., application rates for Cellu-Treat® of 0.125 (0.0125-0.625) lb/acre. The Forest Service, however, does not have substantial experience with the use of Cellu-Treat® and there is uncertainty in the functional application rate in terms of lb/acre. The best estimate of the application rate for Cellu-Treat® from the Forest Service is 0.5 lb/acre (Bakke 2016a).

As with the previous Forest Service risk assessment on borax, the current risk assessment is accompanied by EXCEL workbooks detailing the more complex calculations involved in the risk

assessment. As discussed in Section 1.2, these workbooks follow the general structure and conventions common to workbooks made with WorksheetMaker (SERA 2011a). Because of differences in the application rates to stumps between Sporax® and Cellu-Treat® as well as differences in some exposure rates as well as exposure scenarios for liquid versus dry applications, three EXCEL workbooks are included with this risk assessment:

Attachment 1: Cellu-Treat® (Liquid Applications)
Attachment 2: Sporax® (Liquid Applications)
Attachment 3: Sporax® (Dry Applications)

These workbooks are more customized than most workbooks developed with WorksheetMaker. At detailed in Worksheet A01 of these workbooks, each workbook can be readily modified to include liquid or dry applications of either formulation. Note that an attachment for dry applications of Cellu-Treat® is not included with this risk assessment because Cellu-Treat® is not labelled for dry application. Nonetheless and to cover the possibility that dry applications of Cellu-Treat® may be permitted in the future, Worksheet A01 may be modified to accommodate dry applications of Cellu-Treat®.

2.5. Use Statistics

Forest Service risk assessments attempt to characterize the use of an herbicide or other pesticide in Forest Service programs relative to the use of the herbicide or other pesticide in agricultural applications. Forest Service pesticide use reports up to the year 2004 are available on the Forest Service web site (http://www.fs.fed.us/ foresthealth/pesticide/reports.shtml). While these use reports may not reflect current or future use, the reports are the most recent information available. The Forest Service use reports do not include any information on applications of DOT. Applications of borax are detailed in Table 3 for years 2000 to 2004. As discussed in the previous Forest Service risk assessment (SERA 2006a), the summaries in Table 3 and Table 4 do not include a reported application of 8380 lbs to 838 acre in Forest 14 of Forest Service Region 5 (Pacific Southwest) in 2000. 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.

The data on Forest Service applications in Table 3 are summarized in Table 4 by Forest Service region. The various regions designated by the Forest Service are illustrated in Figure 1. Only three regions report the use of borax: Region 5 (Pacific Southwest), Region 6 (Pacific Northwest), and Region 8 (Southeast). The largest use of borax is reported for Region 5 and involves the application of 81,731.3 lbs to 86,138.7 acres for an average application rate of 0.95 lbs/acre with a range of 0.1 to 1.9 lbs/acre. Applications in Region 6 are fewer (i.e., 6 in Region 6 vs 47 in Region 5) involving only 886 lbs applied to 4291 acres for an average application rate of 0.21 lbs/acre with range of 0.1 to 0.5 lbs/acre. Only two applications are reported in Region 8 for a total of 57 lbs applied to 37 acres for an average application rate of 1.54 lbs/acre with range of 0.7 to 3.3 lbs/acre. Over the 5-year period from 2000 to 2004, the Forest Service used a total of 82,674.3 lbs (average annual use of about 16,534.86 lbs/year) applied to a total of 90,466.7 acres (average application rate of about 0.91 lbs/acre).

In addition to the use statistics from the Forest Service, detailed pesticide use statistics are compiled by the state of California. The use statistics from California for 2013, the most recent year for which statistics are available, indicate a total use of borax of 134,344.77 lbs. Of this

amount, 31,483.28 lbs were applied to 32,494.50 acres of timberland for an average application rate of about 1 lb/acre [31,483.22 lbs ÷ 32,494.50 acres ≈ 0.969 lb/acre]. An additional forestry related use involves the application of 100,582.94 lbs to rights-of-way (CDPR 2015, p. 218). Thus, forestry related uses of borax accounted for about 98% of the borax use in California [(31,483.28 lbs + 100,582.94) ÷ 134,344.77 ≈ 0.98304].

The California pesticide use report also includes DOT (CDPR 2015, p.246). In 2013, a total of 316,028.04 lbs of DOT was applied in California. Of this amount, 9901.75 lbs were applied to rights-of-way accounting for about 3% of the total use of DOT [9901.75 lbs ÷ 316,028.04 lbs ≈ 0.03133]. As with the statistics for borax, the number of acres treated in the rights-of-way applications is not specified. No other forestry related uses for DOT are given in the California report.

For comparisons of agricultural to forestry related applications, Forest Service risk assessments often cite information on the agricultural use of pesticides compiled by the U.S. Geological Survey (USGS) (http://water.usgs.gov/nawqa/pnsp/usage/maps/). USGS, however, does not provide agricultural use statistics for borax or DOT.

Based on the use statistics from California, it appears that forestry related uses account for the majority of the use of borax as a pesticide (≈98%) but only a small proportion (≈3%) of the use of DOT as a pesticide. The extent to which this pattern would hold for other areas of the United States is not clear.

3. HUMAN HEALTH

3.1. HAZARD IDENTIFICATION

3.1.1. Overview

While only two borates are used in the formulations covered in this risk assessment, namely, borax and DOT, each of these as well as many other borate compounds are considered toxicologically equivalent because they are converted to boric acid. Thus, this hazard identification considers studies on boric acid and the specific borates covered in this risk assessment as well as other related borates. In order to facilitate any comparisons between borax, DOT, other borates, and boric acid, toxicity data are expressed in terms of the dose or concentration in units of boron equivalents (B). While the toxicology of borates is extensively documented, most of the available data involves boric acid and borax with relatively little data specific to DOT.

Because of the stability of the boron-oxygen bond, borates are not metabolized beyond the conversion to boric acid. Boric acid is readily absorbed following oral exposures but poorly absorbed following dermal exposure. The absorption of borates following inhalation exposure is not well characterized, and the current Forest Service risk assessment is consistent with the most recent EPA risk assessment in using the assumption of 100% absorption for inhalation exposures (U.S. EPA/OPP/HED 2015a, p. 9).

The primary endpoints of concern involve reproductive effects. Results of subchronic and chronic toxicity studies show that the testes are 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. Results of one study in rats indicate that borax exposure may also reduce ovulation in female rats. Developmental studies in rats and mice indicate that borates cause skeletal and soft-tissue malformations. The mechanism of toxic action, however, is not well understood. Borates can suppress cell division/cell proliferation, and this general mechanism appears relevant to developmental and other reproductive effects.

Because borates occur naturally, human exposure to borates is unavoidable. As discussed further in Section 3.2 (exposure assessment), median intakes of boron by the general population in the range of 1.0 to 2 mg B/day (≈0.01 to 0.03 mg B/kg bw/day) are not associated with adverse effects. As discussed in Section 3.3 (Dose-Response Assessment), the Institute of Medicine of the U.S. National Academies of Sciences proposed that doses of up to 20 mg B/day or about 0.3 mg/kg bw/day should not be harmful.

The borates also appear to have beneficial effects, specifically in reducing or mitigating oxidative damage. Some researchers suggest that boron may be an essential micronutrient in mammals as well as plants in regulating cell proliferation. Although boron is not currently recognized as an essential element for humans—i.e., reference values and reference daily intakes for boron by humans have not been proposed by the U.S. Food and Drug Administration—an evolving body of literature involving both experimental mammals and epidemiology studies indicates that low levels of exposure to boron are beneficial.

The EPA uses a ranking system for acute responses ranging from Category I (most severe response) to Category IV (least severe response). Based on standard acute toxicity studies, boric acid and borax are classified as Category III for acute oral and dermal toxicity, Category IV (borax) or Category III (boric acid) for dermal irritation, and Category III for acute inhalation toxicity. Borax is classified as a severe eye irritant (Category I); however, boric acid is classified as only a moderate eye irritant (Category III). Eye irritation was noted also in humans following inhalation exposures to borate dusts.

In longer-term studies, the borates do not appear to be specific neurotoxins or immunotoxins. Borates do not appear to have a direct impact on endocrine function; nonetheless, changes in hormone status are noted in some recent studies. Pending a further evaluation in EPA's Endocrine Disruptor Screening Program (EDSP), potential for boric acid and related borates to affect endocrine function is indeterminate. The EPA classifies borates as "*Not Likely to be Carcinogenic to Humans*." Moreover, there is a substantial body of literature indicating that borates may reduce the activity of known carcinogens.

3.1.2. Mechanism of Action

The toxicology of boron and related borates is well characterized. As discussed further in Section 3.1.9, the reproductive system is the primary target for boron toxicity, with testicular toxicity, abnormal development of sperm, and developmental effects as the predominant findings. As discussed in the ecological risk assessments, similar effects (i.e., impaired sperm development and developmental abnormalities) were observed in birds (Section 4.1.2.2) and amphibians (Section 4.1.3.2). No specific receptor or even cellular level mechanisms are clearly identified for the developmental and reproductive effects of boron (decreased fetal weight and skeletal malformations) and testicular damage. As discussed in Section 3.1.8, borates can affect hormonal levels, particularly in decreasing testosterone; however, this effect may be due to direct testicular damage rather than endocrine disruption (Fail et al. 1998; Linder 1990; Ku and Chapin 1994; Treinen and Chapin 1991; U.S. EPA/OPP/HED 2006a).

One possible mechanism for the reproductive effects of boron involves effects on cell division/cell proliferation. Boron has a clear role in cell division/proliferation which is particularly well documented in plants, for which boron is an essential element (Section 4.1.2.5). Optimal levels of boron will enhance cell division in plants; while, higher or lower levels of boron will impair cell division (IPCS/WHO 1998; Kabu and Alkosman 2013; Stangoulis and Reid 2002). This pattern of favorable biological responses to low exposures to toxins and other stressors is common in toxicology and is sometimes referenced as hormesis (e.g., Calabrese 2010, 2013). For essential or at least beneficial elements, a common dose-response pattern is U-shaped, as illustrated in Figure 2, in which low exposures result in adverse effects due to insufficiency and higher doses result in adverse effects due to toxicity. This type of U-shaped dose-response curve for boron is not demonstrated explicitly in mammals but has been observed in fish (Rowe et al. 1998).

Although boron is not currently recognized as an essential element for humans—i.e., reference values and reference daily intakes for boron by humans have not been proposed by the U.S. Food and Drug Administration (FDA 2013)—an evolving body of literature indicates that exposures to low levels of boron are clearly beneficial (Dinca and Score 2013; Institute of Medicine 2001;

Meacham et al. 2010; Nielsen 1997; Spears 1999). As discussed further in Section 3.2 (exposure assessment), median intakes of boron in the range of 1.0 to 2 mg B/day are not associated with adverse effects in the general population, and, as discussed in Section 3.3 (Dose-Response Assessment), the Institute of Medicine of the U.S. National Academies of Science proposes that doses of up to 20 mg B/day should not be harmful (Institute of Medicine 2001).

Fail et al. (1998) suggest that high doses of boron may impact fetal growth and development through the inhibition of mitosis, as noted in U.S. EPA/OPP/HED (2006a, p. 13). Within the context of an interference with normal development, an inhibition of mitosis may be considered an adverse effect. Similarly, boron has been shown *in vitro* to inhibit the proliferation of bone marrow cells (Ying et al. 2011), human melanoma cells (Acerbo and Miller 2009), and prostate cancer cells (e.g., Barranco and Eckhert 2006a,b). Consistent with the biphasic pattern illustrated in Figure 2, Park et al. (2004, Figure 6) note that while low concentrations of borate (<0.01 to about 1 mM) will stimulate cell growth, higher concentrations will inhibit cell growth. Furthermore, mammals have a borate transporter (termed NaBC1) that is analogous to the more extensively studied borate transporter in plants (i.e., AtBor1 as discussed further in Section 4.1.2.5). In both plants and animals, these transporters are involved in the maintenance of intracellular boron levels. Given the similarities in function of the boron transporters in plants and mammals, some researchers suggest that boron may be an essential micronutrient in mammals as well as plants in regulating cell proliferation (Devirian and Volpe 2003; Hunt 1998; Park et al. 2004, 2005). Setting aside the issue of essentiality, the supposition that boron may affect development in mammals by the inhibition of mitosis (and consequently cell proliferation) seems reasonable.

As discussed further in Section 4.1, borates cause signs of oxidative stress in both insects (Buyukguzel et al. 2013; Hyrsl et al. 2007) and plants (Cervilla et al. 2007; Esim et al. 2013). Oxidative stress is a general metabolic imbalance causing an increase in reactive oxidant compounds and a decrease in antioxidant compounds that leads to cellular and organ level damage. Oxidative stress is a common manifestation of general toxicity seen with many pesticides as well as other toxic agents (Abdollahi et al. 2004).

At least in mammals, and consistent with the U-shaped dose-response relationship for the effects of boron on cell proliferation, the effects of boron on oxidative stress appear to be biphasic. Based on *in vitro* studies with human blood cell cultures at boric acid and borax concentrations in the range of 15, 50, and 500 mg/L, Turkez et al. (2007, Tables I and II) noted that the lowest concentration enhanced several biochemical markers of antioxidant capacity (a beneficial effect); whereas, the two higher concentrations of the boron compounds enhanced signs of oxidative stress. Similarly, as summarized in Appendix 1 (Table A1-2), *in vivo* subchronic studies in rats demonstrate that boron supplementation of the diet (i.e., 100 mg B/kg bw) increased measures of antioxidant capacity, compared with rats on a standard diet (i.e., 6.4 mg B/kg bw) (Ince et al. 2010). Furthermore, as discussed in Section 3.1.16 (Toxicological Interactions), there are several studies indicating that borates antagonize the toxicity of numerous agents that typically act by inducing oxidative damage. With the exception of the study by Turkez et al. (2007) which noted signs of oxidative stress at high boron concentrations, the literature on boron clearly suggests that boron is typically protective of anti-oxidant toxins.

3.1.3. Pharmacokinetics and Metabolism

Pharmacokinetics involves the quantitative study of the absorption, distribution, metabolism, and excretion of a compound. The pharmacokinetics of borate compounds have been extensively studied in both humans and laboratory animals, with several reviews available in the published literature (ATSDR 2010; Beyer et al. 1983; ECETOC 1995; Fail et al. 1998; Hubbard 1998; Hubbard and Sullivan 1996; Meacham et al. 2010; Moore 1997; Murray 1995, 1998; IPCS/WHO 1998) as well as reviews and risk assessments by the EPA (e.g., U.S. EPA/OPP/HED 2006a). Absorption is particularly important to exposure assessments and is discussed in Section 3.1.3.2. Excretion is important in terms of likely body burdens in longer-term exposure scenarios and is discussed in Section 3.1.3.3.

3.1.3.1. General Considerations

Borates are inorganic compounds; therefore, normal metabolic processes (e.g., oxidation, reduction, and hydroxylation) are not relevant to the borates (ATSDR 2010, p. 90). More specifically, the boron-oxygen bond is stable with a bond energy of about 523 kJ/mole (Meacham et al. 2010; Murray 1998), relative to the carbon-oxygen bond which has an average bond energy of about 358 kJ/mole (http://www.wiredchemist.com/chemistry/data/bond_energies_lengths.html). While boric acid will not undergo classical metabolism, boric acid can form reversible complexes with a variety of substituents commonly found in biological molecules, like hydroxyl, amino, and thiol groups (Moore 1997; ESFA 2013). The available literature on borates does not indicate that these reversible and highly labile complexes have any discrete biological activity or effect.

As discussed in Section 2.2, the pK_a for boric acid is about 9.15 suggesting that about 99% boric acid will exist in the un-ionized/neutral form ($B(0H)_3$) in water at a physiologic pH of 7. Blood and body tissues are much more complex than water, but the proportion of neutral boric acid in biological fluid is about 98.4% (Devirian and Volpe 2003), very similar to that suggested by simple approximation using the pK_a in an aqueous solution.

Because boric acid is a small and predominately neutral molecule, the distribution of boric acid in mammals is governed largely by passive diffusion (e.g., IPCS/WHO 1998, p. 145; Murray 1998). As discussed further in Section 3.1.3.3, boric acid is excreted primarily by the kidneys, and high levels of boric acid can occur in the kidneys (e.g., Sabuncuoglu et al. 2006). The only other notable exception is bone tissue. Boron levels in humans indicate a concentration of boron in bone tissue, relative to blood, ranges from a factor of about 4 (Murray 1998) to a factor of about 6 (Moseman 1994, Table 2, [0.90 ppm ÷ 0.14 ppm ≈ 6.429]). While the mechanism of boron concentration in bone is not understood (ATSDR, 2010, p.95), the concentration of boron in bone does not appear to be an indication of a target tissue. To the contrary, several studies indicate that boron may promote normal bone growth and health (Kabu and Akosman 2013). In a recent review, however, the European Food Safety Authority (EFSA 2009) expresses skepticism that boron can be used as a supplement to promote bone health. While the macro-distribution of boron in mammals may be predominantly due to passive diffusion, recent studies suggest that boron transporters may be involved in the regulation of boron levels at the cellular level—i.e., NaBC1 transporters in mammals, as discussed in Section 3.1.2.

As discussed in Section 2.2 and summarized in Table 2, boron is a naturally occurring compound, and exposures to background levels of boron are unavoidable. In a non-

occupationally exposed group of men in the United States, the average blood boron level was about 0.114 mg B/L with a range of 0.039 to 0.365 mg B/L (Imbus et al. 1963, p.118). In a Japanese population, typical concentrations of boron in blood are about 0.0567 mg B/L (median) with a range of 0.0084 to 0.1704 mg B /L (Abou-Shakra et al. 1989, Table 3). In a control population in China (i.e., individuals not subject to occupational exposures), mean blood boron levels are reported as 0.0221 mg B/L with a range of 0.014 to 0.0332 mg B/L (Zing et al. 2008, Table II). Based on these studies, typical background blood boron levels in humans are about 0.1 mg B/L with a range from about 0.01 to 0.4 mg B/L. These background levels of boron in blood are substantially below boron blood levels in human poisoning incidents—i.e., up to about 300 mg B/L, as discussed further in Section 3.1.4.2.

Boron levels in blood are similar to boron levels in other tissue, except for bone (Moore 1997; ATSDR 2010). Consistent with the rapid elimination rate of boron, as discussed further in Section 3.1.3.3, boron reaches steady state within 3 to 4 days (e.g., Treinen et al. 1991; Ku and Chapin 1994).

As discussed further in Section 3.1.9.3, high doses of boron are associated with testicular atrophy and an inhibition of normal spermatogenesis. Pharmacokinetic studies in rats, however, clearly indicate that boron is not concentrated in the testes (Ku and Chapin 1994; Treinen et al. 1991). Similarly, as discussed further in Section 3.1.9, a subchronic reproductive study in rats found that boron concentrations in the testes were not substantial, relative to concentrations in plasma (Dixon 1979).

Based on exposure studies in humans conducted in China, boron may be modestly concentrated in semen, relative to blood (Robbins et al. 2010; Xing et al. 2008). In workers with mean blood boron levels of 0.2048 mg/L, the mean concentration in semen was about 0.5187 mg B /L—i.e., higher by a factor of about 2.5 [0.5187 mg B/L ÷ 0.2048 mg B/L ≈ 2.533]. In a control group with a mean blood boron level of 0.0221 mg B/L, the concentration of boron in semen was 0.0866 mg B/L—i.e., higher by a factor of about 4 [0.0866 mg B/L ÷ 0.0221 mg B/L ≈ 3.919]. In another study from China, Robbins et al. (2010, Table 1) noted greater concentrations of boron in semen relative to blood—i.e., a factor of about 1.6 for workers [0.785 mg B/L semen ÷ 0.4992 mg/L blood ≈ 1.574] and about 4.5 for controls [0.214 mg B/L semen ÷ 0.0479 mg/L blood ≈ 4.468].

3.1.3.2. Absorption

Boric acid is a small neutral molecule that is readily absorbed following oral administration (Jansen et al. 1984b; Litovitz et al. 1988; Moseman 1994; Institute of Medicine 2001). Boric acid is a weak acid. In nonlethal exposures, boric acid does not have a corrosive effect on the gastrointestinal tract, at least in rats (Ince et al. 2011). In a suicidal and fatal exposure, however, severe stomach damage may occur (Rani and Meena 2013).

Several exposure assessments for the borates involve dermal exposure. These scenarios involve estimates of the first order dermal absorption rate coefficients (k_a) expressed in units of hour^{-1} and skin permeability coefficient (K_p) expressed in cm/hour. Both parameters can be estimated from the study by Wester et al. (1998) which measured the dermal absorption of a 5% solution of boric acid, a 5% solution of borax, and a 10% solution of DOT in eight volunteers with and without pretreatment with a surfactant (2% sodium lauryl sulfate). The surfactant had no

significant effect on boron absorption and there were no significant differences between the three boron solutions (Wester et al. 1998, Table 2). Using the central value for the 5% borax solution, the proportion of the applied dose absorbed over the 24-hour exposure period was 0.0021 (0.00048-0.00372). These values correspond to first-order dermal absorption rate coefficients of about 0.0000876 (0.00002-0.000155) $hour^{-1}$ [$k_a = -Ln(1-prop) \div t$]. These values are rounded to two significant places in the workbooks. Based on the central estimate of the proportion absorbed over the 24-hour period (i.e., 0.00210), Wester et al. (1998, Table 3) derive a K_p of 1.8×10^{-7} cm/h. Using the confidence interval on this proportion (i.e., 0.00048 to 0.00372), the corresponding confidence interval on the K_p is taken as 4.1×10^{-8} to 3.2×10^{-7} [1.8×10^{-7} cm/h x (0.00048 to 0.00372) ÷ 0.00210].

In the absence of experimental data, Forest Service risk assessments use quantitative structure activity relationships, described in SERA (2014a) to estimate the k_a and K_p. These methods are based on the K_{ow} and the molecular weight. In the interest of transparency, these models are implemented in Worksheets B03a (K_p) and B03b (k_a) using the K_{ow} of 0.175 (Barres 1967) and the molecular weight for boric acid of 61.8317 g/mole (Table 1). As summarized in these worksheets, the estimated K_p is about 0.00023 (0.000097-0.00054) cm/hour and the estimated k_a is about 0.0095 (0.0018-0.050) $hour^{-1}$. These estimates are much higher than those from Wester et al. (1998), but the experimental measurements clearly take precedence over the QSAR methods, particularly because the QSAR methods are based exclusively on data for organic compounds.

Other estimates of the dermal absorption of borates range from 0.5 to 10% (EFSA 2013; European Commission 2009a,b). These estimates appear to be judgmental approximations which are not supported by experimental data. ECHA (2010) notes that the dermal absorption of borates is likely to be very low. This supposition is supported by Wester et al. (1998) and by Krieger et al. (1996) which indicate that there was no significant uptake of boron via dermal contact with rugs contaminated with DOT. The study by Draize and Kelley (1959, Table 1 of paper) notes that boric acid is absorbed to a greater extent across mildly abraded skin but that the increase is not toxicologically significant. These investigators observed much greater dermal absorption of boric acid across severely burnt or partially denuded skin; however, this observation would be true for many chemicals—i.e., severely damaged skin is a less effective barrier to dermal absorption.

As discussed in Section 3.2.2.1, standard worker exposure rates for stump applications have not been developed for the Forest Service (i.e., SERA 2014b). Consequently, the current Forest Service risk assessment adopts the worker exposure assessment methods for stump applications used by the U.S. EPA (U.S. EPA/OPP/HED 2015a, p. 37). For granular applications, the method is based predominantly on inhalation exposure, for which there is little information on the absorption of borates. Nonetheless, as discussed in Section 3.2, occupational monitoring studies clearly indicate that exposure to borates, predominantly by inhalation, increases its levels in both the blood and urine of workers. As noted by ATSDR (2010), these increases clearly suggest that borates will be absorbed and distributed through the body following inhalation exposures. The U.S. EPA/OPP/HED (2015a, p. 9) assumes 100% absorption for inhalation exposures.

3.1.3.3. Excretion

As detailed in several reviews, boric acid in mammals is rapidly excreted in the urine (ATSDR 2010; Draize and Kelly 1059; Institute of Medicine 2001; Moore 1997; Moseman 1994). Reported half-lives in rats range from about 8.43 hours (Tagawa et al. 2000) to about 20 hours (Ku et al. 1991). Reported half-lives in humans range from about 8.55 hours (Naderi and Palmer 2006) to about 21±4.9 hours (Jansen et al., 1984a). In a review of human poisoning incidents, Litovitz et al. (1988, Table 3 of paper) report half-lives of 10.4±4.8 hours in patients not receiving dialysis. Based on the data in humans from Jansen et al. (1984a) and the data on rats from Ku et al. (1991), the review by the Institute of Medicine (2001) indicates that rats may excrete boric acid more rapidly than humans do. Considering the additional human data from Litovitz et al. (1988) and Naderi and Palmer (2006), however, the differences in the rate of elimination of boric acid by humans and rats do not seem remarkable.

Although excretion rates are not used directly in either the dose-response assessment or risk characterization, excretion half-lives can be used to infer the effect of longer-term exposures on body burden, based on the *plateau principle* (e.g., Goldstein et al. 1974, p. 320 ff.). Under the assumption of first-order elimination, the first-order elimination rate coefficient (***k***) is inversely related to the half-life ($\boldsymbol{T_{50}}$) [$\boldsymbol{k} = \ln(2) \div \boldsymbol{T_{50}}$]. If a chemical with a first-order elimination rate constant of ***k*** is administered multiple times at a fixed time interval (***t****) between doses, the body burden after the $\boldsymbol{N^{th}}$ dose ($\boldsymbol{X_{N\ Dose}}$), relative to the body burden immediately following the first dose ($\boldsymbol{X_{1\ Dose}}$) is:

$$\frac{X_{N\,Dose}}{X_{1Dose}} = \frac{(1-\left(e^{-kt*}\right)^{N})}{1-e^{-kt*}} \tag{2}$$

As the number of doses (***N***) increases, the numerator in the above equation approaches a value of 1. Over an infinite period of time, the plateau or steady-state body burden ($\boldsymbol{X_{Inf}}$) can be calculated as:

$$\frac{X_{Inf}}{X_1} = \frac{1}{1-e^{-kt*}} \tag{3}$$

Whole-body half-lives are most appropriate for estimating steady-state body burdens.

Taking the average half-life for boric acid of 10.2 hours or about 0.54 days from Litovitz et al. (1988), the first-order elimination coefficient is approximately 1.28 days^{-1} [$k = \ln(2) \div t_{½}$]. Using this elimination coefficient in the above equation for the plateau assuming a daily dosing, the estimated plateau for boric acid is about 1.39. Thus, over prolonged periods of exposure, boric acid is not likely to accumulate substantially in mammals, including humans.

3.1.4. Acute Oral Toxicity

3.1.4.1. Animal Studies

Standard acute oral toxicity studies are typically used to determine LD_{50} values—i.e., the treatment dose estimated to be lethal to 50% of the animals. LD_{50} values are not used directly to derive toxicity values as part of the dose-response assessment in Forest Service risk assessments.

LD_{50} values as well as other measures of acute toxicity discussed in following sections are used by the U.S. EPA/OPP to categorize potential risks. U.S. EPA/OPP uses a ranking system for responses ranging from Category I (most severe response) to Category IV (least severe response). Details of the EPA system of categorization are detailed in SERA (2014a, Table 4) as well as in U.S. EPA/OPP (2010a), the label review manual.

The acute oral LD_{50} values for boric acid, borax, and DOT are summarized in Appendix 1, Table A1-1. For all borates, signs of toxicity include depression, irregular breathing, diarrhea, and red crusts on the eye (U.S. EPA/OPP/HED 2015a, p. 9). Both boric acid and borax are classified as Category III for acute oral toxicity (U.S. EPA/OPP/HED 2015a, p. 61). The classification for boric acid is based on the gavage LD_{50} of 3450 mg/kg bw in male rats (MRID 00006719) and the classification for borax is based on the gavage LD_{50} of 4550 mg/kg bw in male rats (MRID 40692303). The EPA human health risk assessments do not cite an oral LD_{50} value for DOT (U.S. EPA/OPP/HED 1993, 2006a, 2015a). The review by the European Commission (2009b) specifies an oral LD_{50} value of 2550 mg/kg bw (p. 25), which is also specified on the MSDS for Cellu-Treat® (Nisus 2009). Based on this LD_{50}, DOT would also be classified as Category III. As specified in Appendix I, Table A1-1, the confidence limits of the LD_{50} values expressed as boron equivalents for boric acid and borax overlap and the LD_{50} value for DOT expressed in units of boron equivalents falls within the range of the comparable LD_{50} values for boric acid and borax. In other words, the available information on the acute oral toxicity data for boric acid, borax, and DOT does not indicate significant differences in toxicity among the three agents.

In addition to the LD_{50} values in rats, as also summarized in Appendix 1, Table A1-1, some acute toxicity data are available in dogs and mice. No definitive LD_{50} values are available in dogs. The indefinite LD_{50} values of >631 mg/kg bw for boric acid (MRID 00064208) and >974 mg/kg bw for borax (MRID 40692304) cited by EPA (U.S. EPA/OPP/HED 2006a) appear to be essentially identical to Weir and Fisher (1972) in which no mortality was noted in dogs given capsule administrations of both agents. Except at the lowest doses of boric acid (≈1000 mg/kg bw) and borax (1540 mg/kg bw), dogs vomited within 1 hour of dosing. Thus, these studies are not useful in assessing the sensitivity of dogs, relative to rats. Soriano-Ursua et al. (2014) conducted an acute toxicity study of boric acid in male mice by intraperitoneal injection and estimated an LD_{50} of 2150 mg/kg bw, equivalent to about 376 mg B/kg bw. This LD_{50} is somewhat below the acute oral LD_{50} in rats of 3450 mg/kg (MRID 00006719); however, the difference could be attributed to the difference in the route of administration, differences in species sensitivity, or a combination of these two factors.

As discussed further in Section 3.3 (dose-response assessment), U.S. EPA/OPP/HED (2015a) uses an acute NOAEL of 350 mg B/kg bw from an acute LD_{50} study in rats (MRID 40692303) with an uncertainty factor of 100 for risk characterization of acute exposures in humans. This approach is equivalent to using an acute RfD of 3.5 mg B/kg bw. As discussed further in the following section, this approach is supported by early studies in humans in which borates were administered therapeutically.

As discussed further in Section 3.1.5, repeated-dose studies in borates indicate that the testes, specifically in terms of sperm development, are a key target tissue in mammals. In rats, a single gavage dose of up to 450 mg B/kg bw did not cause signs of testicular toxicity, based on sperm

development (Dixon 1976), as summarized at the end of Appendix 1, Table A1-1. A later single-dose study by Linder (1990), however, notes slight decreases in testes weights following a single gavage dose of 350 mg B/kg followed by a 57-day observation period—i.e., acute exposure and subchronic observations. In a subsequent single-dose study in rats with a 14-day observation period, also conducted by Linder (1980), abnormal sperm morphology was observed at doses of 175 and 300 mg B/kg bw. As discussed further in Section 4.1.3.2, testicular toxicity and abnormal sperm development due to boron exposure was observed also in amphibians.

3.1.4.2. Human Case Reports

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; IPCS/WHO 1998):

> *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).*
>
> IPCS/WHO 1998, p. 100

This statement refers to *clinical symptoms* rather than serious adverse effects, and the range is sufficiently broad to be of little use in assessing potential serious adverse effects. Assuming a 70 kg body weight, the above exposures would correspond to doses of about 1.6 to 793 mg/kg/day, in terms of boric acid. Using a conversion factor of 0.175 for boron equivalents (Table 1) would result in corresponding doses of 0.28 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 derived in U.S. EPA/ORD (2004). Thus, while the upper range of exposure—i.e., 55.5 g of boric acid—may be a useful estimate of a dose likely to be associated with adverse effects, the lower range reported by IPCS/WHO (1998) appears to be an artifact of uncertainties in the exposure assessment; accordingly, this lower bound is not useful for estimating the plausibility of adverse effects.

Nevertheless, other case reports and analyses of boron toxicity in humans are available and can be used to approximate dose-response relationships for acute toxicity. These selected studies are summarized in Table 5. Some of the data in Table 5 are taken from several detailed reviews (ATSDR 2010; Institute of Medicine 2001; IPCS/WHO 1998), as indicated in the last column. For data taken from reviews, the entries in Table 5 specify both the review used as the information source as well as the specific studies cited in the reviews.

As reviewed by IPCS/WHO (1998) as well as Culver and Hubbard (1996), boric acid and borax have been used to treat chest pain, epilepsy, malaria, tumors (B^{10} therapy), as well as urinary tract and other infections (IPCS/WHO 1998). Although many of the incidents summarized in Table 5 involve attempted suicides or accidental exposures, the studies by Jansen et al. (1984a,b) involve the intentional intravenous administration of borates as part of a pharmacokinetic study. The studies by Jansen et al. (1984a,b) indicate that intravenous doses in the range of 1.4 to 2 mg B/kg bw are not associated with adverse effects in humans. The upper bound of this range is close to the acute RfD of 3.5 mg B/kg bw, as noted in Section 3.1.4.1 and discussed further in Section 3.5. Moreover, as discussed in Section 3.1.5, the acute RfD of 3.5 mg B/kg bw is further

supported by longer-term exposures in humans in which doses of 2.5 mg B/kg bw/day are not associated with adverse effects (Culver and Hubbard 1996, Table IV, p. 180).

Intravenous doses of 19 to 46 mg B/kg bw as well as a subcutaneous dose of 70 mg B/kg bw are associated with adverse effects including nausea, skin reactions, and vomiting in humans (Locksley and Farr 1955). The lowest reported lethal dose for borates in humans is 640 mg boric acid/kg bw (≈112 mg B/kg bw) (Stokinger 1981), which is more than 30 times greater than the acute RfD [112 mg B/kg bw ÷ 3.5 mg/kg bw = 32].

As summarized in Table 5, the study by Naderi and Palmer (2006) is somewhat unusual in that it reports an apparent suicide attempt involving co-exposure to boric acid and cocaine in which the subject may have consumed up to 75 g of boric acid. Using a 70 kg body weight, the maximum dose could have been about 187 mg B/kg bw [$0.175_{B/BA}$ x 75,000 mg BA ÷ 70 kg bw ≈ 187.5 mg B/kg bw]. Although this dose might have been lethal, the individual received aggressive medical care and survived.

Wong et al. (1964) report an incident in which 11 infants were inadvertently given formula prepared with a 2.5% solution of boric acid. Five of the infants died. Relatively good estimates of doses are available for two of the fatally exposed infants. One infant (Case 1 in the paper) weighed 7 lbs. 6 oz. (≈3.345 kg) and consumed about 14 g of boric acid. Using the conversion factor of $0.175_{B/BA}$, this exposure corresponds to a dose of about 735 mg B/kg bw [14,000 mg BA x $0.175_{B/BA}$ ÷ 3.345 kg ≈ 735 mg B/kg bw]. The other infant (Case 3 in the paper) weighed 7 lbs. 2 oz. (≈3.232 kg) and consumed about 9.25 g of boric acid. This exposure corresponds to a dose of about 500 mg B/kg bw [9,250 mg BA x $0.175_{B/BA}$ ÷ 3.232 kg ≈ 500.87 mg B/kg bw]. Both of these infants died despite aggressive medical intervention. A dose of about 187 mg B/kg bw can be estimated for a third infant (Case 11) who survived and showed only mild signs of possible toxicity. This case is not summarized in Table 5 because Wong et al. (1964) suggest that the laboratory results for this infant may have been contaminated.

3.1.5. Subchronic or Chronic Systemic Toxic Effects

As discussed in SERA (2014a, Section 3.1.5), *subchronic* and c*hronic* are somewhat general terms that refer to studies involving repeated dosing. Some repeated dose studies are designed to detect specific toxic endpoints, like reproductive, development, and neurological effects. Except for some comments in this subsection on general signs of toxicity, these more specialized studies are discussed in subsequent subsections of this hazard identification.

The subchronic and chronic toxicity studies on the borates are summarized in Appendix 1, Table A1-2. Table 5 presents an overview of the studies in which doses can be expressed in units of mg B/kg bw/day. While the available data are not amenable to quantitative duration-response assessment, there is an apparent, albeit not pronounced, duration-response relationship in NOAELs for rats. Dogs appear to be more sensitive than rats, based on both 90-day and 2-year NOAELs. Based on longer-term (≥266 days) LOAELs, however, there are no marked differences in the responses of dogs, rats, and mice. Possibly, what appears to be greater sensitivity in dogs, relative to rats, based on NOAELs, is an artifact of the dose spacing used in the dog studies. As discussed further in Section 3.3 (dose-response assessment), the U.S. EPA derived RfDs for borates based on a dietary study in dogs that resulted in the NOAEL of 8.8 mg B/kg bw/day (MRID 40692310).

In addition to the studies summarized in Table 5, other subchronic exposures of rats and dogs to borates in food and drinking water resulted in testicular toxicity characterized by atrophy of the testes, degeneration of the spermatogenic epithelium and spermatogenic arrest (Appendix 1, Table A1-2). 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.

Additionally, Culver and Hubbard (1996, Table IV, p. 180) summarize several case reports involving human exposures to borates. No adverse effects are noted at doses up to 2.5 mg B/kg bw/day. Doses ranging from 5 to about 7 mg B/kg bw/day are associated with nausea and skin reactions. In one male, a dose of about 25 mg B/kg bw/day (as a treatment for epilepsy) was associated with hair loss, anemia, skin reactions, and general weakness. While these are not controlled studies, the minimal responses to doses of up to 7 mg B/kg bw/day suggest that human sensitivity to borates is not remarkably different from that of dogs (dog NOAEL = 8.8 mg B/kg bw/day).

3.1.6. Effects on Nervous System

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. As defined, neurotoxicants, which act directly on the nervous system (direct neurotoxicants), are different from those agents (indirect neurotoxicants), which may cause neurological effects secondary to other forms of toxicity. Practically any chemical will cause signs of neurotoxicity in severely poisoned animals, and, therefore, can be classified as an indirect neurotoxicant. U.S. EPA/OPP (2013a) defines general protocols for assessing neurotoxicity, which include assays for sensory effects, neuromuscular effects, learning and memory, and histopathology of the nervous system.

As discussed in Section 3.1.4.1, acute exposure to lethal doses of borax causes depression, ataxia, and convulsion in rats (Weir and Fisher 1972). These findings, however, do not implicate borates as a direct neurotoxicant. No studies designed specifically to detect impairments in motor, sensory, or cognitive functions in animals or humans exposed to borax were identified in the available literature. Regardless, there is no evidence that borax produces direct effects on the nervous system. Also, the most recent EPA human health risk assessment affirms there was a … *lack of toxicity observed in the rat acute neurotoxicity screening study at the highest dose level of 350 mg/kg boron equivalents* (U.S. EPA/OPP/HED 2015a, p. 9). The EPA risk assessment does not provide a reference to or further description of the screening study, which may refer to the study by Linder (1990), as summarized in Appendix 1, Table A1-1. As reviewed by both ATSDR (2010, p. 112-113) and U.S. EPA/OPP/HED 2006a, p. 21), potential signs of

neurotoxicity were observed in human poisoning incidents and an animal study but only at high doses in which the signs of neurotoxicity could be secondary to other toxic effects. In any event, neurotoxicity is not a sensitive endpoint for exposures to borates.

3.1.7. Effects on Immune System

There are various methods for assessing the effects of chemical exposure on immune responses, including assays of antibody-antigen reactions, changes in the activity of specific types of lymphoid cells, and assessments of changes in the susceptibility of exposed animals to resist infection from pathogens or proliferation of tumor cells. As with neurotoxicity, the EPA has a series of screening tests for immunotoxicity involving assays for humoral or cell-mediated immune function as well as a consideration of data from standard subchronic and chronic studies that could indicate immunotoxicity – e.g., spleen and thymus weights or pathology and changes in hematological parameters (U.S. EPA/OPP 2013a, pp. 8-9).

As summarized in Appendix 1, Table A1-2, changes in spleen weight or appearance were observed in one study in dogs (MRID 40692307) and in another study in rats (Weir and Fisher 1972). A decrease in hematocrit was observed in the study in dogs (MRID 40692307) but this effect has not direct implications for immunologic effects. These effects are not reported in other studies. As summarized by HSDB (2014), Sylvain et al. (1998) observed thymus pathology in rats treated with dietary doses of borax at 350 ppm boron equivalents. In an *in vitro* study using human lymphocytes, Pongsavee (2009a) observed a dose-related inhibition of lymphocyte proliferation at borax concentrations of 100 to 600 mg borax/L—i.e., equivalent to 17.5 to 105 mg B/L—over a 72-hour exposure period. As discussed in Section 3.1.3.1, these concentrations are substantially above normal concentrations of blood boron—i.e., 0.1 (0.01 to 4 mg B/L)—but in the range of blood boron levels in cases of human poisoning—i.e., up to 315 mg B/L, as summarized in Table 5.

The risk assessments from EPA (U.S. EPA/OPP/HED 1993, 2006a, 2015a) and WHO (IPCS/WHO 1998, WHO 1998) do not directly address effects on immune function. Citing the lack of effects on lymph nodes and spleen in the inhalation study by Wilding et al. (1959), discussed further below in Section 3.1.13, ATSDR (2010, p. 113) concludes that: *Results of chronic studies do not suggest that the immune system is a potential target for boron toxicity*. The ATSDR document, however, does not address the studies by Sylvain et al. (1998) or Pongsavee (2009a). Nonetheless, there is no clear indication that borates will have a direct impact on immune function. While the effect on lymphocyte proliferation from Pongsavee (2009a) is noteworthy, it appears to be consistent with the observations on the general effect of boron on cell proliferation (Section 3.1.2) and may not reflect a direct effect on immune competency. In the absence of additional information, the conclusion from ATSDR (2010) appears to be correct.

3.1.8. Effects on Endocrine System

The *endocrine system* assists 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 Section 3.1.5 and summarized in Table 6, subchronic exposure to borax results in testicular atrophy/pathology, decreased testosterone, and abnormal sperm development. As noted further in Section 3.1.9, longer-term exposures to borax can lead to sterility in male rats and decreased ovulation in female rats. It is most likely that the adverse effects of borax on testosterone are due to a direct testicular effect rather than an endocrine effect (ATSDR 2010; ECETOC 1995, Fail et al. 1998; El-Dakdoky and Abd El-Wahab 2013). Wang et al. (2008) indicate that boric acid may mimic estrogen in ovariectomized female rats but does not affect the level of estradiol in serum.

Lee et al. (1978) noted time- and dose-dependent decreases in plasma luteinizing hormone (LH) and follicle stimulating hormone (FSH) levels in rats exposed to borax in the diet (daily doses of 35 and 50 mg B/kg/day). These effects, however, were not observed at doses of up to 350 mg B/kg bw in the study by Linder (1990).

In a recent study in rats, Kucukkurt et al. (2015) observed that boron supplemented diets (100 mg B/kg) resulted in an increase in triiodothyronine (T_3), a decrease in insulin, but no significant effect on thyroxine (T_4), relative to rats on a standard laboratory diet containing 6.4 mg B/kg over a 28-day exposure period.

As discussed further in Section 4.1.2.3, Fort et al. (2002) noted no effect of boron on endocrine function in frog embryos.

Citing studies concerning the impact of borates on testosterone, U.S. EPA/OPP/HED (2006a, p. 39) notes that these effects cannot be attributed directly to an impact on endocrine function; however, an endocrine mediated mechanism cannot be ruled out. Although effects on endocrine function are not specifically addressed in the most recent EPA human health risk assessment (U.S. EPA/OPP/HED 2015a), the recent EPA ecological risk assessment (U.S. EPA/OPP/EFED 2015a) notes that boric acid and sodium borate salts are subject to EPA's Endocrine Disruptor Screening Program (EDSP). The most recent report from this program does not indicate that boric acid or related borates have been assayed under this program (U.S. EPA 2014).

Until additional information is available, the potential for boric acid and related borates to affect endocrine function is indeterminate.

3.1.9. Reproductive and Developmental Effects

3.1.9.1. Developmental Studies in Experimental Mammals

Developmental studies are used to assess the potential of a compound to cause malformations and signs of toxicity during fetal development. These studies typically entail gavage administration of the chemical compound to pregnant rats or rabbits on specific days of gestation. Teratology assays as well as studies on reproductive function (Section 3.1.9.2) are generally required by the EPA for the registration of pesticides. Accordingly, EPA has established specific protocols for developmental and reproduction studies (U.S. EPA/OPPTS 2000).

The available studies on developmental and reproductive effects are summarized in Appendix 1, Table A1-3, and an overview of these studies is presented in Table 7. Developmental studies are available on mice (n=2), rabbits (n=1), and rats (n=5). Several of these studies, including some from the published literature (Heindel et al. 1992, 1994) were submitted to the U.S. EPA and are reviewed in the EPA risk assessments (U.S. EPA/OPP/HED 2009a, 2015a). Other open literature publications of developmental studies in rats that were not reviewed by EPA (i.e., Harrouk et al. 2005; Wise and Winkelmann 2009; El-Dakdoky and Abd El-Wahab 2013) are generally consistent with the registrant-submitted studies; nevertheless, the studies submitted to the EPA provide the most sensitive endpoints—i.e., the lowest NOAEL/LOAEL combinations.

Several of the studies provide multiple sets of NOAELS and LOAELs based on different endpoints—i.e., fetal, paternal, and maternal. The fetus is the most sensitive receptor in five of the eight studies, one in mice (Heindel et al. 1992, 1994, MRID 41725402) and four in rats (Price et al. 1996a/MRID 43340101; Heindel et al. 1992, 1994/MRID 41725401; Harrouk et al. 2005; Wise and Winkelmann 2009). In other words, adverse effects on the fetus were demonstrated at dose levels lower than those that cause signs of maternal or paternal toxicity. The only study reporting what might be viewed as an opposite pattern is the study by El-Dakdoky and Abd El-Wahab (2013) which notes a decrease in testosterone in paternal rats at a dose (21.9 mg B/kg bw/day) that did not adversely affect the fetus. In terms of overt toxic effects, however, El-Dakdoky and Abd El-Wahab (2013) note fetal mortality but only a decrease in paternal testes weight at a dose of 43.75 mg/kg bw/day. Based on a dose-severity comparison, the fetal response is clearly more severe than the paternal response. In the two other studies, one on mice (MRID 41589101) and the other in rabbits (Price et al. 1996b, MRID 42164202), the fetal and parental NOAELs and LOAELs are identical.

Unlike the case with subchronic and chronic toxicity in which no clear species differences are apparent (Section 3.1.5), rats appear to be the most sensitive species in terms of developmental effects. As summarized in Table 7, Price et al. (1996a) report a LOAEL for rats of 13.7 mg B/kg bw/day based on fetal mortality and malformations. This LOAEL is below the NOAELs for rabbits (21.8 mg B/kg bw/day) and mice (27 and 43.3 mg B/kg bw/day). The only reservations with this comparison are that more studies are available on rats (n=5) than are available on mice (n=2) or rabbits (n=1) and that some of the NOAELs for fetal mortality in rats (e.g., 57.5 mg B/kg bw/day from Heindel et al. 1992, 1994) are below the LOAEL of 13.7 mg B/kg bw/day from Price et al. (1996a). In other words, the apparently greater sensitivity of rats may be an artifact of the greater number of studies available on rats relative to mice and rabbits.

Notwithstanding the above, as discussed further in Section 3.3, the rat study by Price et al. (1996a) was used by the Institute of Medicine (2001) to derive a surrogate RfD for boron. Furthermore, the rat study by Price et al. (1996a) and the rat study by Heindel et al. (1992, 1994) were used also by Allen et al. (1996), which in turn served as the basis for the boron RfD derived by U.S. EPA/OPP/NCEA (2004).

As discussed in Section 3.1.2, borates have a well-documented impact on cell development and proliferation. Although borates may be important for normal cell growth, they may also inhibit cell division at toxic doses. According to Tyl et al. (2007), the cellular target for borates is unclear. Di Renzo et al. (2006, 2007), however, note that boric acid inhibits embryonic histone deacetylases which may in turn inhibit normal cell growth and differentiation. This inhibition could be involved in the development of malformations induced by borates. Based on histological findings showing degeneration of the spermatogenic epithelium (e.g., Weir and Fisher 1972), it has been proposed that the Sertoli cell is the most likely target for borate compounds at the cellular level (ECETOC 1995, Fail et al. 1998, WHO 1998).

3.1.9.2. Reproduction Studies in Experimental Mammals

Reproduction studies involve exposing one or more generations of the test animal to a chemical compound. Generally, the experimental method involves dosing the parental (P or F_0) generation (i.e., the male and female animals used at the start of the study) to the test substance prior to mating, during mating, after mating, and through weaning of the offspring (F_1). In a 2-generation reproduction study, this procedure is repeated with male and female offspring from the F_1 generation to produce another set of offspring (F_2). During these types of studies, standard observations for gross signs of toxicity are made. Additional observations often include the length of the estrous cycle, assays on sperm and other reproductive tissue, and number, viability, and growth of offspring. Typically, the EPA requires one acceptable multi-generation reproduction study for pesticide registration (U.S. EPA/OPPTS 2000).

As summarized in Table 7 and detailed in Appendix 1, Table A1-3, there are two reproduction studies involving the exposure of rats to borax. The study by Dixon (1979) does not appear to have been submitted to EPA and is not covered in EPA risk assessments. The open literature publication by Weir and Fisher (1972) was submitted to and reviewed by the U.S. EPA and is designated as MRID 40692311 in U.S. EPA/OPP/HED (2009a). Separate entries for Weir and Fisher (1972) and MRID 40692311 are given in Appendix 1, Table A1-3, because of minor differences in exposures between the open literature publication and the EPA summary of the submission. These types of differences are common and occur during the EPA study review. In Table 7, only the EPA reviewed data from MRID 40692311 are listed.

The NOAELs from the developmental studies reviewed by EPA—i.e., 9.6 mg B/kg bw/day from MRID 43340101 and 13.6 mg B/kg bw/day from MRID 41725401—are below the NOAEL of 25 mg B/kg bw/day from the reproduction study reviewed by EPA. This is not an unusual pattern and may reflect the difference in the route of administration—i.e., gavage in the developmental studies and dietary in the reproduction study. At least in terms of endpoints, the two types of studies are consistent with adverse effects noted in both parental animals (i.e., testicular atrophy, uterine effects, and reduced fertility) and offspring (i.e., decreased survival).

3.1.9.3. Human Data

Due to the prevalence of boron exposures (Sections 2 and 3.2), there is a substantial body of human experience with borates. As reviewed by Meacham et al. (2010), borax was used as a component in a contraceptive pill to control female fertility as early as 500 BC. More recently, borates have been used vaginally to treat various vaginal infections (Muzny et al. 2012; Ray et al. 2007; Savini et al. 2009). One study from Hungary suggests a weak association between vaginal boric acid use during pregnancy and the development of congenital abnormalities (Acs et al. 2006). In this study, risks are expressed as odds ratios – i.e., prevalence in the boric acid treated group divided by the prevalence in the untreated group. Based on total congenital abnormalities, the odds ratio was marginally significant—i.e., 1.6 (1.0-2.4)—but the odds ratio for congenital abnormalities of the skeletal system was 7.1 (1.7-29.5). These findings are consistent with the prevalence of skeletal abnormalities in animal studies (Section 3.1.9.1.1). Nonetheless, Acs et al. (2006) was a relatively small study in terms of the number of treated mothers—i.e., 43 mothers who received boric acid treatment during pregnancy and 38,151 control mothers who did not.

A series of worker exposure studies conducted in Turkey failed to note signs of reproductive effects in workers—i.e., effects on semen morphology and/or testosterone levels (Basaran et al. 2012; Bolt et al. 2012; Duydu et al. 2011; Duydu et al. 2012a,b). As discussed further in Section 3.2, the highest mean exposure in these groups of workers was 41.2 mg B/day (Xing et al. 2008, Table III, p. 145). Xing et al. (2008) do not provide information on the ages or body weights of the workers. Data from Gu et al. (2006, Table 1) suggests that a standard body weight of 70 kg may be a reasonable approximation. Using a body weight of 70 kg, the average dose for the highly exposed workers from the study by Xing et al. (2008) is 0.6 mg B/kg bw. As summarized in Table 7, this dose is a factor of 16 below the lowest NOAEL [9.6 mg B/kg bw ÷ 0.6 mg B/kg bw = 16] and a factor of about 23 below the lowest LOAEL [13.7 mg B/kg bw ÷ 0.6 mg B/kg bw ≈ 22.83…] for developmental and reproductive effects in experimental mammals, which is consistent with assessments by Bolt et al. (2012) and Duydu et al. (2011, 2012a) that even extreme occupational exposures are substantially below those associated with adverse effects in experimental mammals.

3.1.10. Carcinogenicity and Mutagenicity

As summarized Table 6 and detailed further in Appendix 1, Table A1-2, standard chronic carcinogenicity studies are available in rats (MRID 40692309) and mice (MRID 41863101). No carcinogenic responses were observed in either bioassay. In addition, as summarized in Appendix 1, Table A1-8, standard *in vitro* mutagenicity bioassays required by the EPA are negative. Based on these data, the most recent human health risk assessment from EPA has indicated that boric acid and associated borates are classified as "*Not Likely to be Carcinogenic to Humans*" (U.S. EPA/OPP/HED 2015a, p. 5).

As noted in Section 3.1.2, boron inhibits the proliferation of human melanoma cells (Acerbo and Miller 2009), and prostate cancer cells (e.g., Barranco and Eckhert 2006a,b). In addition, epidemiology studies suggest that boron intake is negatively correlated with cancer risk in human populations. In a study conducted in Turkey, women (n=472) with a mean dietary intake of 8.41 mg B/day had a decreased risk of cervical cancer, relative to women (n=587) who consumed 1.26 mg B/day. In an epidemiology study conducted in Texas involving 763 women with lung cancer and 838 women without lung cancer, a significant negative association between

cancer risk and boron exposure was noted over a range of boron intake rates from <0.78 mg/day (highest risk) to >1.2 mg B/day (lowest risk) (Mahabir et al. 2008, Table 2). Finally, a somewhat smaller study of prostate cancer risk in the United States—i.e., comparing 95 prostate cancer cases with that of 8720 controls—noted a negative correlation between boron consumption and prostate cancer over a range of 0.62 to 1.36 mg B/day (Cui et al. 2004). The concordance of the *in vitro* studies and the epidemiology studies appear to support the assessment that boron may have a protective effect for at least some forms of human cancers (Henderson et al. 2015).

Some *in vitro* studies in the open literature indicate that borax may be associated with chromosomal damage (Pongsavee 2009a,b; Turkoqlu 2007); whereas, other studies have failed to confirm evidence of genotoxicity (Geyikoglu and Turkez 2008; Turkez et al. 2007). While these studies are noted for the sake of completeness, the *in vivo* bioassays reviewed by EPA and the epidemiology studies from the open literature support the assessment that carcinogenicity is not an endpoint of concern for the hazard identification of boric acid and related borates.

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

As with acute oral toxicity, the U.S. EPA/OPP requires acute assays for skin irritation, skin sensitization, and eye irritation and uses a ranking system for responses ranging from Category I (most severe response) to Category IV (least severe response) for skin and eye irritation. Skin sensitization is classified simply as occurring or not occurring. For each type of assay, the EPA has developed standard protocols (U.S. EPA/OCSPP 2014).

3.1.11.1. Skin Irritation

As summarized in Appendix 1, Table A1-4, standard skin irritation studies in rabbits indicate that borax is not a skin irritant (Category IV) and that boric acid is a mild skin irritant (Category III). As also summarized in Appendix 1, an early open literature study by Roudabush et al. (1965) indicates that neither boric acid nor borax would be classified as primary skin irritants, based on skin irritation studies in both rabbits and guinea pigs.

Boric acid preparations have been used for the treatment of external or middle ear infections. Ozturkcan et al. (2009) assayed a 4% solution of boric acid applied to the middle ear of guinea pigs. While not specifically designed as a skin irritation assay, Ozturkcan et al. (2009) report no indication of damage to the ear.

Although standard animal assays for skin irritation do not suggest that boric acid and related borates are strong skin irritants, Weir and Fisher (1972) observed that chronic exposure to dietary concentrations of 1750 and 5250 mg B/kg food caused swollen paws and desquamation of the skin in rats. Also, human incident reports suggest that the borates may cause skin irritation under extreme exposure conditions. As summarized in Table 5, incidents involving intravenous dosing (Locksley and Farr 1955), subcutaneous dosing (Peyton and Green 1941), and oral dosing (ATSDR 2010; Lung and Clancy 2009; Webb et al. 2013) are associated with severe skin reactions. The study by Lung and Clancy (2009) provides a detailed description of the adverse skin reaction they called a “Boiled lobster” rash characterized by redness and peeling of the skin. The serum borate level (>13,000 µg B/dL or 130 mg B/L), however, clearly indicated a gross overexposure. As discussed in Section 3.1.3.1, typical blood boron levels in humans are about 0.1 mg B/L with range from about 0.01 to 0.4 mg B/L. A recent case report from Jirakova et al. (2015) describes a severe skin reaction (erosions, crusts, edema, and

exudation) in a 2-year old child who was treated with a 2% boric acid solution (pH 3.6-4.2) 10 times per day for 14 days. Also, U.S. EPA/OPP/HED (2009b) briefly summarizes five human incident reports, two of which include an indication of dermal irritation (rash in one incident and blisters of the tongue in another). The human experience with borates suggests that skin irritation may be of concern.

3.1.11.2. Skin Sensitization

As with skin irritation, the EPA typically requires assays for skin sensitization in guinea pigs (U.S. EPA/OPPTS 2003). As summarized in the previous Forest Service risk assessment on borax (SERA 2006a) and included in Appendix 1, Table A1-4 of the current risk assessment, a standard dermal challenge study in guinea pigs found no indication that borax causes skin sensitization effect (Wnorowski 1994b, MRID 34500802). This study, however, is not cited in the EPA documents on borates, which indicate that skin sensitization studies are not required (U.S. EPA/OPP 1993, p. 23-24; U.S. EPA/OPP/HED 2006a, p. 14). The most recent EPA human health risk assessment (U.S. EPA/OPP/HED 2015a), the recent review from ATSDR (2010), and the review by the European Food Safety Authority (EFSA 2013) do not address skin sensitization. HSDB (2014) summarizes a human study of a "hair preparation" containing 3.2% sodium borate indicating that the product was not a skin sensitizer. Based on these admittedly scant data, skin sensitization does not appear to be an endpoint of concern for borates.

3.1.11.3. Ocular Effects

Eye irritation studies are summarized in Appendix 1, Table A1-5. Based in a study in which borax was directly instilled into the eyes of rabbits (Reagan 1985c, MRID 43553202), borax is classified as a Category I severe eye irritant. This study involved the direct instillation of borax powder (0.1 g) into the eyes of the rabbits. Based on a study in boric acid (MRID 00064209), details of which are not available, boric acid is classified as Category III for eye irritation (U.S. EPA/OPP/HED 2015a, p. 8). An eye irritation study on DOT, the active ingredient in Cellu-Treat, has not been identified. The MSDS for Cellu-Treat® indicates that this product caused only mild eye irritation in rabbits (Nisus 2009). Nonetheless, the product labels for both Cellu-Treat® (Nisus 2015) and Sporax® (Wilbur-Ellis 2013) indicate that protective eyewear is required when handling these products.

As discussed further in Section 3.1.13, eye irritation was observed in experimental mammals during inhalation exposures to boron oxide (i.e., boron oxide dusts). It seems reasonable to speculate that the severe eye irritation for borax may be limited to exposures involving borax (or other borate) particles. Nonetheless, the severe eye irritation noted in the study on borax and the cautionary language on the product labels for both Sporax® and Cellu-Treat® suggest that eye irritation should be considered an endpoint of concern with respect to handling borates, particularly as particulates.

3.1.12. Systemic Toxic Effects from Dermal Exposure

The acute dermal toxicity studies on borates are summarized in Appendix 1, Table A1-6. As with acute irritant effects to the skin and eyes (Section 3.1.11), the U.S. EPA/OPP requires acute dermal toxicity studies classifies the potential for acute dermal toxicity using a Category I (most hazardous) to Category IV (least hazardous) classification system (SERA 2014a, Table 4).

Based on acute dermal LD_{50} values of >2000 mg/kg bw in rabbits, the EPA classifies both borax (MRID 43553201) and boric acid (MRID 00106011) as Category III (U.S. EPA/OPP/HED 2015a, p. 8). The indefinite LD_{50} of >2000 mg/kg bw cited as MRID 43553201 in the EPA risk assessments is identical to the study by Reagan (1985a, MRID 43553200) summarized in the previous Forest Service risk assessment (SERA 2006a). Also available is a study reporting an acute dermal LD_{50} of >5000 mg/kg bw in rats (Wnorowski 1996, MRID 44048603), as summarized in the previous Forest Service risk assessment (SERA 2006a). Even though rats are an acceptable test species for acute dermal studies (U.S. EPA/OPPTS 1998a), the study by Wnorowski (1996) is not cited in the EPA risk assessments on borates (U.S. EPA/HED 1993, 2006a, 2015a).

As discussed in Section 3.1.3.2, boric acid is not well absorbed following dermal exposure; moreover, the available dermal toxicity studies on borates do not suggest a high potential hazard. Nonetheless, dermal exposures may occur in the normal use of borates in Forest Service applications. Consequently, dermal exposures are considered quantitatively in the current Forest Service risk assessment.

3.1.13. Inhalation Exposure

The standard acute toxicity studies are required by U.S. EPA/OPP in support of the registration of borates, and these studies are summarized in Appendix 1, Table A1-7. Following standard EPA protocols, these acute studies were conducted with rats using an exposure period of 4 hours (U.S. EPA/OPPTS 1998b).

As summarized in Table A1-7, the most recent EPA human health risk assessment classifies both borax and boric acid as Category III, based on inhalation LC_{50} values of >2.03 mg/L (U.S. EPA/OPP/HED 2015a, p. 8). The indefinite LC_{50} values correspond to >229 mg B/m^3 for borax (MRID 43500801, Wnorowski 1994a) and >355 mg B/m^3 for boric acid (MRID 43500701). The full study by Wnorowski (1994a) using borax was available for the conduct of the previous Forest Service risk assessment (SERA 2006a). As indicated in Table A1-7, sublethal effects noted in this study include ocular and nasal discharges and hypoactivity, which were reversible by 7 days after exposure. The EPA summary of the study on boric acid indicates only that no mortalities occurred during the study.

The previous EPA human health risk assessment (U.S. EPA/OPP/HED 2006a, the science chapter for the TRED) does not cite the study on boric acid used by U.S. EPA/OPP/HED (2015a). Instead, U.S. EPA/OPP/HED (2006a, p. 14) cites another rat inhalation study on boric acid reporting an indefinite LC_{50} of >0.16 mg/L (MRID 00005592), corresponding to >28 mg B/m^3. Based on this toxicity value, U.S. EPA/OPP/HED (2006a) designates boric acid as Category II for acute inhalation toxicity. This lower LC_{50} is not cited in the 2015 EPA assessment, and the higher LC_{50} used in the 2015 EPA assessment is not cited in the EPA 2006 assessment. U.S. EPA/OPP/HED (2006a) does not provide many details but the EPA assessment does note that no mortality occurred at 0.16 mg boric acid/L (28 mg B/m^3).

Short-term studies with volunteers exercising during controlled exposures to boric acid and disodium borate dust report effects that include nasal irritation and discharge, throat irritation, and eye irritation (Cain et al. 2004, 2009). As discussed further in Section 3.3 (Dose-Response Assessment), ATSDR (2010) jointly assessed both of these studies and identified a NOAEL of

0.8 mg B/m3 (boric acid from Cain et al. 2008) and a LOAEL of 1.5 mg B/m^3 (sodium borate from Cain et al. 2004). As indicated in Appendix 1, Table A1-7, these calculations appear reasonable with minor differences probably due to rounding. Note that the signs of eye and nasal irritation in humans are consistent with the signs in rats from the study by Wnorowski (1994a, MRID 43500801). Also notable is the NOAEL for irritation in humans of 0.8 mg B/m^3 is substantially below the NOAEL for mortality in rats of 28 mg B/m^3 (MRID 00005592).

The EPA sometimes requires subchronic inhalation studies (U.S. EPA/OPPTS 1998c), and U.S. EPA/OPP/HED (2006a, p. 55) notes that a 28-day inhalation study in rats *…is required at this time to better characterize risk from inhalation exposure*. Nevertheless, the most recent EPA human health risk assessment indicates that the requirement for a subchronic inhalation study was waived (U.S. EPA/OPP/HED 2015a, p. 9).

Chronic inhalation studies using boron oxide were conducted in rats and dogs (Wilding et al. 1959). As with both borax and boric acid, boron oxide is rapidly converted to boric acid (ATSDR 2010, p. 24). As summarized in Appendix 1, Table A1-7, the NOAEL for rats is about 11.6 mg B/m^3 for a 20-week exposure with a corresponding LOAEL of about 26.4 mg B/m^3 for a 12-week exposure. In the Wilding et al. (1959) study, all exposures were conducted for 6 hours/day, 5 days/week. No signs of systemic toxicity other than a decrease in body weight were observed in rats. The primary observation involved signs of nasal irritation. The NOAEL of 11.6 mg B/m^3 in rats from the Wilding et al. (1959) study is substantially below the LOAEL for irritation in humans cited in Cain et al. (2004).

In addition to the controlled studies discussed above, several occupational studies indicate that inhalation of dust containing boron causes irritation to the nasal mucosa and respiratory tract in humans (Garabrant et al. 1985; Hu et al. 1992; Woskie et al, 1994, 1998). The study by Woskie et al. (1998) is particularly noteworthy in that it documents concentrations of "sodium borate" of about 1.5 mg/m^3 for non-responders (i.e., individuals without nasal irritation) and about 1.69 to 3.73 mg/m^3 for workers with signs of nasal irritation. The precise form of sodium borate is not specified by Woskie et al. (1998). Using a conversion factor of 0.151 for disodium borate pentahydrate (ATSDR 2010, p. 10), these concentrations correspond to a boron equivalent NOAEL of about 0.22 mg B/m^3 and boron equivalent LOAELs of about 0.26 to 0.56 mg B/m^3. These LOAELs are somewhat below the acute LOAEL of 1.5 mg B/m^3 for sodium borate cited in Cain et al. (2004).

While nasal and throat irritation are viewed as endpoints of concern in the hazard identification, all of the LOAELs are far below estimated levels of exposures for workers involved in stump applications, as discussed further in Section 3.2.

3.1.14. Adjuvants and Other Ingredients

As discussed in Section 2.2 and summarized in Table 1, the borate formulations consist only of the technical grade borates—i.e., 100% borax in Sporax® and 98% DOT in Cellu-Treat®. Adjuvants are not used with either formulation.

3.1.15. Impurities and Metabolites

As also summarized in Table 1, Sporax® contains 100% borax (sodium tetraborate decahydrate) and Cellu-Treat® contains 98% DOT (disodium octaborate tetrahydrate). Based on the product label for Cellu-Treat® (Nisus 2010, 2015), the remaining 2% in Cellu-Treat® consists of absorbed water.

3.1.16. Toxicological Interactions

As discussed in Section 3.1.10 (Carcinogenicity and Mutagenicity), there is a substantial literature indicating that boron decreases the activity of carcinogens/mutagens including vanadium tetraoxide (Geyikoglu and Turkez 2008), carbon tetrachloride (Ince et al. 2012), titanium dioxide (Turkez 2008), paclitaxel (Turkez et al. 2010), aluminum (Turkez et al. 2013), and aflatoxin b_1 (Turkez and Geyikoglu 2010). Boron also appears to reduce the toxic effects of heavy metals, including lead (Turkez et al. 2012b; Ustundaq et al. 2014). As discussed in Section 3.1.2 (Mechanism(s) of Action), the mechanism for these beneficial effects appears to involve an inhibition of cell proliferation and as well as antioxidant activity. While both of these mechanisms may lead to toxicity at high levels of exposure, the anti-carcinogenic and antioxidant activity of borates can clearly be beneficial.

There is no evidence in the available literature that borates will synergize adverse effects of other agents.

3.2. EXPOSURE ASSESSMENT

3.2.1. Overview

As discussed in Section 2.2, boron is a naturally occurring element, which makes human exposure to boron unavoidable. As summarized in Table 8, estimates of human exposure to boron are extensively documented and, for the most part, remarkably consistent. Non-occupational exposures to boron are generally in the range of 1 to 3 mg B/day. A notable exception is Turkey, which has more than 70% of the earth's documented boron reserves. In Turkey, boron exposure levels typically range from about 6 to 8 mg B/day. In the United States, high levels of boron occur in California, particularly in the Mojave Desert and Death Valley (ATSDR 2010; National Boron Research Institute 2016). Worker exposures to boron are highly variable. In the United States, average levels of exposure to boron range from about 4 to nearly 25 mg B/day for workers involved in handling or shipping borax (Culver et al. 1994).

An obvious concern in dealing with these exposure estimates is the extent to which Forest Service uses may contribute substantially to normal background levels of boron exposure. While the estimates of human exposure given in the literature are expressed in terms of mg B/day, the exposure estimates developed in the current risk assessment are expressed in terms of mg B/kg bw/day. For the sake of comparisons, an upper bound background exposure of 3 mg B/day and a body weight of 70 kg are used to estimate a reference background dose of about 0.04 mg B/kg bw/day [3 mg B/day ÷ 70 kg ≈ 0.04286].

Worker exposures to boron following liquid stump applications of either Cellu-Treat® or Sporax® are far below background exposures. The highest worker exposures are associated with the accidental spill of a Sporax® solution on to the lower legs. As detailed in Attachment 2, Worksheet C03b, the upper bound dose estimate associated with this exposure scenario is about 0.0005 mg B/kg bw, below the reference background exposure by a factor of 80 [0.04 mg/kg bw/day ÷ 0.0005 mg B/kg bw = 80]. Workers involved in dry applications of borax, however, may be subject to substantially higher exposures. Based on the methods used by EPA, the estimated non-accidental exposures for workers involved in the dry application of Sporax® to tree stumps is about 0.013 (0.003 to 0.13) mg/kg bw/day. The upper bound of this exposure exceeds the reference background exposure by a factor of about 3 [0.13 mg/kg bw/day ÷ 0.04 mg/kg bw/day = 3.25].

A standard set of exposure assessments for members of the general public are included in the exposure assessment for borates, except for the scenarios associated with the consumption of contaminated vegetation. As with the previous Forest Service risk assessment on borax, scenarios associated with the consumption of contaminated vegetation are not included for the borates because these compounds are applied directly to tree stumps and the likelihood of contaminating edible vegetation is minimal. All of the non-accidental exposure scenarios for members of the general public lead to dose estimates that are far below the reference background exposure of about 0.04 mg/kg bw/day. The highest non-accidental exposure estimate is about 0.0055 mg/kg bw/day—the peak expected exposure associated with the consumption of contaminated water. This exposure level is below the reference background dose by factor of about 7 [0.04 mg/kg bw/day ÷ 0.0055 mg/kg bw/day ≈ 7.2727…].

The only substantial exposure for members of the general public involves the accidental consumption of Sporax® dust by a small child, which leads to dose estimates of 1.2 (0.5 to 3) mg/kg bw/day. For liquid applications of Cellu-Treat® or Sporax, the highest estimated dose for an accidental exposure is about 0.06 mg/kg bw—i.e., the upper bound exposure for a child drinking contaminated water following an accidental spill. This dose estimate is only marginally higher than the reference background exposure of 0.04 mg/kg bw/day.

3.2.2. Workers

All general exposures for workers are calculated as the amount of a.i. handled by a worker in a single day multiplied by a worker exposure rate (in units of mg agent/kg bw per lb agent handled). Forest Service risk assessments typically use relatively well-documented worker exposure rates based on studies in which worker exposures are estimated from biomonitoring studies—i.e., absorption-based methods (SERA 2014b). The U.S. EPA typically uses deposition-based exposure estimates from the Pesticide Handlers Exposure Database (PHED) or the Agricultural Handlers Exposure Task Force (AHETF) (U.S. EPA/OPP 2013b). Because the standard Forest Service methods do not specifically address stump applications, both absorption-based methods and deposition-based methods are considered in the current risk assessment.

3.2.2.1. General Exposures

3.2.2.1.1. Liquid Stump Applications

3.2.2.1.1.1. Absorption-Based Methods

For stump applications, Cellu-Treat® is labelled only for liquid applications; while, Sporax® may be applied as either a liquid or solid. Thus, the liquid application exposure scenario applies to both Cellu-Treat® (Attachment 1) and Sporax® (Attachment 2) and is implemented in Worksheet C01a of these attachments.

As discussed in Section 2.3, liquid applications are made with a backpack sprayer or hand-held sprayer. While standard Forest Service methods do not specifically address stump applications, absorption-based worker exposure rates for backpack applications are well documented (SERA 2014b, Section 3.2.2). For backpack applications, worker exposure rates for reference pesticides (i.e., pesticides for which worker exposures in backpack applications are documented) are adjusted for differences in the dermal absorption rates for the reference pesticide and the pesticide under consideration. In Table 14 of SERA (2014b), three reference chemicals with corresponding worker exposure rates are given for backpack applications—i.e., glyphosate (k_a = 0.00041 hour^{-1}), 2,4-D (k_a = 0.00066 hour^{-1}), and triclopyr BEE (k_a = 0.0031 hour^{-1}). As discussed in Section 3.1.3.2, the estimated first-order dermal absorption rate coefficient for boric acid is 0.0000876 hour^{-1} based on the study in humans by Wester et al. (1998). Of the three reference pesticides, glyphosate has the closest k_a and is selected as the reference pesticide. The application of the methodology from SERA (2014b) is detailed in Table 9. Based on this methodology, the worker exposure rates for backpack applications of boric acid are 0.00006 (0.00001-0.0004) mg/kg bw per lb a.i. handled.

The other key parameter for this exposure scenario is the amount of product that a worker might handle in a single day. This amount is calculated as the product of the stump application rate in units of lb B/ft^2 of stump surface and area of stump surface that might be treated in a single day.

As discussed in Section 2.4, the stump application rate is taken as 0.00226 lb B/ft^2 for Sporax® and 0.000525 lb B/ft^2 for Cellu-Treat®.

For the stump surface area that might be treated in a single day, the most recent EPA human health risk assessment estimates that a worker would treat 1000 ft^2 of stump surface per day (U.S. EPA/OPP/HED 2015a, p. 33). As noted in the EPA assessment, this is roughly equivalent to treating 100 tree stumps each with a diameter of 4 feet [100 trees x $\{\pi$ x (4 ft ÷ 2)$^2\}$/tree ≈ 1256 ft^2]. In reviewing this estimate, the Forest Service judges that 1000 ft^2 might be an upper limit for some applications. For other applications in more difficult terrain, the Forest Service estimates the stump surface area treated could be in the range of 200 to 500 ft^2 (Bakke 2016b). As specified in Worksheet A01 of the attachments, the estimates of stump surface treated is taken as 500 (200 to 1000) ft^2/day. The estimate of stump surface area treated per day is an extremely critical parameter in the exposure assessment for workers. For a site-specific application, the values for stump surface treated per day should be adjusted to reflect local conditions.

3.2.2.1.1.2. Deposition-Based Methods

Deposition based exposure methods as implemented by EPA require estimates of dermal and inhalation rates for both absorption (first-order rates) and deposition (fractional value). As discussed in Section 3.1.3.2, the first-order dermal absorption rate coefficient for boric acid (the agent of concern) is taken as 0.0000876 (0.00002-0.000155) hour^{-1} from the study by Wester et al. (1998). The inhalation absorption fraction is taken as 100% (U.S. EPA/OPP/HED 2015a, p. 9). The worker exposure rates (mg per lb handled) are taken from standard values derived by the EPA (U.S. EPA/OPP 2013b). These rates are used for the worker exposure assessments in the most recent EPA human health assessment on borates (U.S. EPA/OPP/HED 2015a).

Two deposition-based exposure assessments are developed. The first scenario (Worksheet C01b) involves backpack applications and is intended to be directly comparable to the absorption-based estimates discussed in Section 3.2.2.1.1.1. The dermal deposition rate is taken as 4.12 mg/lb handled, and the inhalation exposure rate is taken as 0.00258 mg/lb. These are the backpack rates recommended by EPA for forestry applications using double layer gloves for dermal exposure and no respirator for inhalation exposure (U.S. EPA/OPP 2013a, p. 5). The double layer glove value is used to reflect the product label for Cellu-Treat® which indicates that applicators must wear chemical-resistant gloves. The inhalation value for no respirator is used because the product label for Cellu-Treat® indicates that respirators are required only for "*confined spaces*" (Nisus 2010). Forestry applications will be made outdoors and respirators will not be used. The other input value, which affects dermal absorption only, involves the dermal exposure period. The value of 10 hours is used under the assumption that a worker might not effectively wash immediately after an 8-hour work shift.

The second deposition-based scenario (Worksheet C01c) involves stump applications using a backpack sprayer. The absorption-based methods discussed in Section 3.2.2.1.1.1 do not encompass hand-wand applications; however, this application method is considered in the most recent EPA human health risk assessment (U.S. EPA/OPP 2015a, p.37) using an inhalation unit exposure rate of 0.03 mg/lb from U.S. EPA/OPP (2013b, p. 4). The EPA did not use any exposure rates for the dermal route. As noted in U.S. EPA/OPP (2015a, p.33), "*dermal toxicity*

was not identified so dermal risks are not quantified in this section". Other aspects of this exposure assessment are as described above for backpack applications.

As discussed in Section 3.4.2 (Risk Characterization for Workers), the deposition-based and absorption-based methods yield similar HQs, all of which are substantially below the level of concern.

3.2.2.1.2. Dry Stump Applications

The absorption-based worker exposure methods developed for the Forest Service (SERA 2014b) do not accommodate applications of dry dust formulations to stumps. Consequently, only the EPA deposition-based methods are developed. The most recent EPA human health risk assessment (U.S. EPA/OPP 2015a, p.37) develops a worker exposure assessment for shaker can applications of a dust formulation to tree stumps based on inhalation exposure rates from U.S. EPA/OPP (2013b, p. 11). This exposure scenario is detailed in two worksheets: C01d_Ac for acute exposures and C01d_Ch for chronic exposures. These two worksheets are essentially identical except in terms of the duration period of concern. The use of the two worksheets is simply a convenience to facilitate the derivation of separate HQs based on the acute and chronic toxicity values, as discussed further in Section 3.4.2 (risk characterization for workers).

As with the deposition-based exposure assessment for backpack applications and for the same reason (Section 3.2.2.1.1.2), the EPA uses only inhalation exposure factors. Unlike the case with hand wand applications, the EPA uses different exposure rates for differing levels of personal protective equipment—i.e., 17.5 mg/lb with no respirator, 3.5 mg/lb with a PF5 dust filter (i.e., simple nose/mouth mask), and 1.75 mg/lb for a PF10 respirator (i.e., a more efficient and elaborate dust filter that attaches to a full face respirator). All other aspects of the exposure assessment (i.e., stump application rate and stump surface treated per day) are identical to the assessments for wet applications, as discussed in Section 3.2.2.1.1.2.

To be clear, there is a typographical error in the worker exposure rates documented in U.S. EPA/OPP (2015a, p.37) where the rate for no respirator is given as "17,500" µg/lb and the rate for the PF10 is specified as "17500" µg/lb. The additional zero on the rate for PF10 is a simple typographical error. All calculations for PF10 in U.S. EPA/OPP 2015a, p.37) are correct and use the correct PF10 rate of "1750" µg/lb from U.S. EPA/OPP (2013b, p. 11).

All of the exposure rates used by U.S. EPA/OPP (2015a) for shaker can applications of borates are based on dust applications – i.e., the borates are classified as a dust rather than granule. As summarized in U.S. EPA/OPP (2013b, p. 11), the inhalation exposure rates for applications of granules are 12.5 µg/lb for now respirator, 2.51 for a PF5 respirator, and 1.25 for a PF10 respirator. These exposure rates for granules are lower than the corresponding rates for dust by a factors about 1400 – i.e., [17,500 µg/lb ÷ 12.5 µg/lb = 1400] for no respirator, [3,500 µg/lb ÷ 2.51 µg/lb ≈ 1394.2443] for a PF5 respirator, and [1, 750 µg/lb ÷ 1.25 µg/lb ≈ 1400] for a PF10 respirator. Given the substantial differences in exposure rates for dusts and granules, the Forest Service queried Wilbur-Ellis, the registrant for Sporax, on the classification of Sporax as a dust. The registrant confirmed that Sporax is classified as a dust rather than a granule (Bakke 2016c). This determination is consistent with the means of the particle size distributions for borax reported by Culver et al. (1994, p. 134) – i.e., 16.7 to 20.7 microns. As discussed by WHO (1999), 10 microns is generally considered to be the upper bound size for respirable dust – i.e.,

dust that can penetrate into the alveoli of the lungs – but aerodynamic diameters of up to 100 microns are a concern in terms of inhalable dust.

Unlike the case for wet applications, the upper bound of the chronic HQs for dry applications exceeds the level of concern (HQ=1). As detailed in the C01d worksheets, the variability in the HQs is due to two factors: the differences in the worker exposure rates based on no respirator (upper bound), a PF5 filter mask (central estimates), and a PF10 respirator (lower bound) and differences in the stump area treated per day. As detailed in U.S. EPA/OPP (2015a, p.37), the worker exposure rates are applied by EPA to both indoor applications (i.e., greenhouse, warehouse, poultry house) and outdoor applications (i.e., landscaping and tree stumps). The product label for Sporax® does not indicate a requirement for respirators (Wilbur-Ellis 2013). The product label for Cellu-Treat® (which is not labelled for dry applications) notes the following: "*When applying this product in confined spaces, provide ventilation or an exhaust system; or use a NIOSH-approved dust/mist filtering respirator*" (Nisus 2010). The implied distinction on the Cellu-Treat® label between indoor (confined spaces) and outdoor (stump) applications seems sensible. The rationale in U.S. EPA/OPP (2015a, p.37) for using the same exposure rates for indoor and outdoor applications is not apparent.

Intuitively, it seems reasonable to suppose that outdoor applications of Sporax® will typically lead to lower exposures, compared with indoor applications. As summarized in Table 8, Culver et al. (1994) estimated average exposures of U.S. workers involved in indoor handling of borax (packaging and shipping) of up to 24.77 mg B/day (i.e., high exposure group) or about 0.35 mg B/kg bw/day [24.77 mg B/day ÷ 70 kg ≈ 0.3539 mg B/kg bw/day]. Based on the reported standard deviation of 15.35 mg B/day, upper bound (2 SD) exposures would be 55.47 mg B/day or about 0.8 mg B/kg bw/day [55.47 mg B/day ÷ 70 kg ≈ 0.7924mg B/kg bw/day]. Culver et al. (1994) do not indicate that workers used any personal protective equipment to reduce inhalation exposures nor do they describe the ventilation in the workplace. As summarized Worksheet E01 of Attachment 3, the upper bound exposure for workers involved in stump applications of Sporax® is estimated at 0.565 mg B/kg bw/day. Based on this comparison, the EPA method for estimating exposures of workers involved in stump applications appears to be reasonable for indoor applications. This comparison, however, does not address the more import issue of whether the EPA exposure rates are directly applicable to outdoor applications.

In response to a query directed to the U.S. EPA/OPP on the issue of indoor versus outdoor applications, the EPA indicated that separate exposure rates for indoor and outdoor shaker can applications are not available and thus the same rates are used for indoor and outdoor applications …*based on dust/shaker can exposure during applications to pets* (Crowley 2016). In a similar query directed to Wilbur-Ellis, the registrant for Sporax, the company noted that … *if inhalation risk is a concern from the particle dust, Sporax can also be mixed with water* (Rawlins 2016). As noted further in Section 3.4.2 (risk characterization for workers) and detailed in Attachment 2, Worksheet E02, this statement from Rawlins (2016) is correct and risks to workers involved in liquid applications of Sporax are substantially below the level of concern.

The issue of outdoor applications of Sporax® is addressed by the Forest Service in an analysis by Dost et al. (1996). In terms of inhalation exposures, Dost et al. (1996, p. 54) note that:

Inhalation of significant amounts during typical forestry application is highly unlikely; however, data to support this supposition are not included in the analysis.

Given the concordance of the absorption-based and deposition-based exposure assessment for liquid applications (Section 3.2.2.1.1), confidence in the worker exposure assessments for liquid applications is high. Given the uncertainties in the applicability of EPA's exposure rates shaker can applications to workers involved in outdoor dry stump applications in Forest Service programs, confidence in the exposure assessment for dry applications of Sporax® is low.

3.2.2.2. Accidental Exposures

Generally, dermal exposure is the predominant route of exposure for pesticide applicators (Ecobichon 1998; van Hemmen 1992); accordingly, accidental dermal exposures are considered quantitatively in all Forest Service risk assessments.

3.2.2.2.1. Liquid Applications

For liquid applications, two types of dermal exposures are modeled, the emersion of skin in a contaminated solution and accidental spills of the pesticide onto the surface of the skin. Two exposure scenarios are developed for each of the two types of dermal exposure, and the estimated absorbed dose for each scenario is expressed in units of mg chemical/kg body weight. Both sets of exposure scenarios are summarized in Worksheet E01 of the EXCEL workbooks for liquid applications—i.e., Attachments 1 and 2. As well, Worksheet E01 references other worksheets in which the calculations of each exposure assessment are detailed.

Exposure scenarios involving direct contact with borate solutions are characterized either by immersion of the hands in a field solution for 1 minute or wearing pesticide contaminated gloves for 1 hour. The assumption that the hands or any other part of a worker's body will be immersed in a chemical solution for a prolonged period of time may seem unreasonable; however, it is possible that the gloves or other articles of clothing worn by a worker may become contaminated with pesticide. For these exposure scenarios, the key assumption is that wearing gloves grossly contaminated with a chemical solution is equivalent to immersing the hands in the solution. In both cases, the chemical concentration in contact with the skin and the resulting dermal absorption rate are essentially constant. For both scenarios (hand immersion and contaminated gloves), the assumption of zero-order absorption kinetics is appropriate. For these types of exposures, the rate of absorption is estimated based on a zero-order dermal absorption rate (K_p). Details regarding the derivation of the K_p value for boric acid (i.e., the agent of concern) are provided in Section 3.1.3.2. The amount of the pesticide absorbed per unit time depends directly on the concentration of the chemical in solution. The calculation of the concentration of boric acid in the field solution is detailed in Worksheet A01. The details of these accidental exposure scenarios are given in Worksheets C02aW (1-minute exposure) and C02bW (60-minute exposure).

The accidental spill scenarios for workers evaluate spilling a chemical solution on to the lower legs, and spilling a chemical solution on to the hands, with at least some of the solution adhering to the skin. The absorbed dose is then calculated as the product of the amount of chemical on the skin surface (i.e., the amount of liquid per unit surface area multiplied by the surface area of the skin over which the spill occurs and the chemical concentration in the liquid), the first-order absorption rate coefficient, and the duration of exposure. The first-order dermal absorption rate

coefficient (k_a) is derived in Section 3.1.3.2. These exposure scenarios are detailed in Worksheets C03a (spill on to the hand) and C03b (spill onto the lower legs).

3.2.2.2.2. Dry Applications

For dry applications of borates, only the scenarios involving contaminated hands/gloves are used. A reasonable method for estimating spills onto the lower legs for a dust formulation has not been developed.

The only difference between the scenarios involving contaminated hands or gloves for liquid and dry applications involves the concept of field solution. For borates applied as a dry dust, field solution is not a meaningful concept. Consistent with the approach recommended in U.S. EPA/ORD (1992) for neat applications of a compound to the skin, the concentration of boric acid on the surface of the skin is assumed to be equal to the water solubility of boric acid. The water solubility of boric acid is highly variable with temperature. For this exposure scenario, the water solubility is taken as 54.3 mg/mL from Crapse and Kyser (2011) for a boric acid solution at a temperature of 25°C or about 77°F. All other aspects of this exposure scenario are identical to the scenario for wet applications (Section 3.2.2.2.1). These exposure scenarios are detailed in Worksheets C02aD and C02bD. Higher temperatures and thus somewhat higher water solubilities could be applicable in some areas of the United States. As detailed in Worksheet E02 of Attachment 3, the upper bound HQ for this scenario is 0.00006, below the level of concern by a factor of over 16,000 [$1 \div 0.00006 \approx 16{,}666.666\ldots$]. Consequently, explicit considerations of higher temperatures would have no impact on the risk characterization.

3.2.3. General Public

3.2.3.1. General Considerations

3.2.3.1.1. Likelihood and Magnitude of Exposure

Under normal conditions of application, Forest Service activities should not result in members of the general public being exposed to substantial levels of borates. Nonetheless, the Forest Service may apply borates to tree stumps in or near recreational areas like campgrounds, picnic areas, and trails, where, as a result, the general public may be exposed to borates. Conversely, members of the general public are less likely to be exposed to borates in stump applications made in remote areas.

Because of the conservative exposure assumptions used in the current risk assessment, neither the probability of exposure nor the number of individuals who might be exposed has a substantial impact on the characterization of risk presented in Section 3.4. As detailed in SERA (2014a, Section 1.2.2.2), the exposure assessments developed in this risk assessment are based on *Extreme Values* rather than on a single value. Extreme value exposure assessments, as the name implies, bracket the most plausible estimate of exposure (referred to statistically as the central or maximum likelihood estimate and more generally as the typical exposure estimate) with extreme lower and upper bounds of plausible exposures.

This Extreme Value approach is essentially an elaboration on the concept of the *Most Exposed Individual* (MEI), sometime referred to as the *Maximum Exposed Individual* (MEI). As this name also implies, exposure assessments that use the MEI approach are made in an attempt to

characterize the extreme but still plausible upper bound on exposure. This approach is common in exposure assessments made by U. S. EPA, other government agencies, and other organizations. In the current risk assessment and other Forest Service risk assessments, the upper bounds on exposure estimates are all based on the MEI.

In addition to this upper bound MEI value, the Extreme Value approach used in this risk assessment provides a central estimate of exposure as well as a lower bound on exposure. While not germane to the assessment of upper bound risk, it is significant that the use of the central estimate and especially the lower bound estimate is not intended to lessen concern. To the contrary, the central and lower estimates of exposure are used to assess the feasibility of mitigation—e.g., protective measures to limit exposure. If lower bound exposure estimates exceed a level of concern, this is strong indication that the pesticide cannot be used in a manner that will lead to levels of exposure that would typically be classified as acceptable; mitigation should then be considered.

3.2.3.1.2. Summary of Assessments

The exposure scenarios developed for the general public are summarized in Worksheet E03 of the EXCEL workbooks that accompany this risk assessment. As with the worker exposure scenarios, details about the assumptions and calculations used in these assessments are given in the detailed calculation worksheets in the EXCEL workbooks (Worksheets D01–D10).

A standard set of exposure assessments are used in Forest Service risk assessments involving broadcast applications (SERA 2014a, Section 3.2.3.1.2). Because borates are applied only to tree stumps, some of the standard exposure scenarios are not considered. Specifically, borates will not be applied directly to vegetation. Therefore, typical exposures involving spray of a chemical to vegetation—e.g., dermal contact with contaminated vegetation and the consumption of contaminated fruit or vegetation—are not applicable to this risk assessment. As detailed in the following sections, the application of borates to tree stumps could result in increased exposures to boron via contaminated water. Consequently, exposures involving contaminated water, including an accidental spill and exposures from the consumption of contaminated fish, are considered. For liquid stump applications of Cellu-Treat® or Sporax, standard exposure assessments for the accidental direct spray of a young child and a young woman are considered. These scenarios are not relevant to dry stump application of Sporax® only. For dry applications of Sporax, a custom accidental scenario for the direct consumption of Sporax® by a small child is developed.

3.2.3.2. Direct Spray or Direct Consumption

3.2.3.2.1. Direct Spray (Liquid Applications)

Direct spray scenarios for members of the general public are modeled in a manner similar to accidental spills for workers (Section 3.2.2.2.1). In other words, it is assumed that the individual is sprayed with a field solution of the compound and that some amount of the compound remains on the skin and is absorbed by first-order kinetics. Two direct spray scenarios are given, one for a young child (D01a) and the other for a young woman (D01b).

For the young child, it is assumed that a naked child is sprayed directly during a broadcast application and that the child is completely covered with the contaminated solution (i.e., 100% of

the surface area of the body is exposed). This exposure scenario is intentionally extreme. As discussed in Section 3.2.3.1.1, the upper limits of this exposure scenario are intended to represent the *Extreme Value* of exposure for the *Most Exposed Individual* (MEI).

The exposure scenario involving the young woman (Worksheet D01b) is somewhat less extreme, but more plausible, and assumes that the woman is accidentally sprayed over the feet and lower legs. By reason of allometric relationships between body size and dose-scaling, a young woman would typically be subject to a somewhat higher dose than would a man. Consequently, in an effort to ensure a conservative estimate of exposure, a young woman, rather than an adult male, is used in many of the exposure assessments.

For the direct spray scenarios, assumptions are made regarding the surface area of the skin and the body weight of the individual, as detailed in Worksheet A03 of the attachments. The rationale for and sources of the specific values used in these and other exposure scenarios are provided in the documentation for WorksheetMaker (SERA 2011a) and in the methods document for preparing Forest Service risk assessments (SERA 2014a). As with the accidental exposure scenarios for workers (Section 3.2.2.2), different application methods involve different concentrations of boron in field solutions, and details of the calculations for these concentrations are given in Worksheet A01of the attachments to this risk assessment. Thus, these exposure scenarios differ slightly for borax and DOT applications.

3.2.3.2.2. Direct Consumption (Dry Applications)

This accidental exposure scenario assumes that a small child accidentally consumes Sporax® from a treated tree stump. While this exposure scenario is obviously extreme, it is similar to exposure scenarios for the consumption of granular borate formulations used in the most recent EPA human health risk assessment (U.S. EPA/OPP/HED 2015a, p. 49). This exposure scenario is detailed in Worksheet D01c of the attachments to this risk assessment.

There is no information in the available literature from which to predict the amount of Sporax® that a child might consume in 1 day. Accordingly, the current risk assessment estimates the amount of Sporax® that a child might consume in 1 day based on the amount of soil that a child might ingest per day, excluding soil-pica (i.e., an eating disorder). According to the most recent EPA Exposure Factors Handbook (U.S. EPA/NCEA 2011, Table 5-1, p. 5-5), the mean amount of soil that a child consumes per day is estimated to be between 50 and 200 mg soil/day. In developing the exposure assessment for dry applications of borates, the EPA uses an ingestion rate of 300 mg/day (U.S. EPA/OPP/HED 2015a, Table A-5, p. 49).

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 300 mg Sporax/day. A central estimate for Sporax® consumption is taken as 120 mg Sporax/day, the approximate geometric mean of the range. Using the conversion factor for borax to boron-equivalents, the intake is estimated at about 14 (5.6 to 34) mg B/day [$0.113_{B/borax}$ x 120 (50 to 300) mg borax/day]. To yield an estimated dose in units of mg chemical/kg body weight, these exposure numbers are divided by body weight (kg). For the sake of consistency with EPA, a body weight of 11 kg is used (U.S. EPA/OPP/HED 2015a, Table A-5, p. 49).

Details for the calculations involved in this exposure scenario are given in the attachments to this risk assessment in Worksheet D01c. The estimated doses range from about 0.5 mg B/kg bw to about 3.1 mg B/kg bw. As discussed in Section 3.2.1, the reference upper bound background exposure to boron is about 0.04 mg B/kg bw. The exposures estimated for this scenario are higher than the background levels of exposure by factors of about 12 to over 75 [0.5 mg B/kg bw to about 3.1 mg B/kg bw ÷ 0.04 mg B/kg bw = 12.5 to 77.5]. This is the only exposure scenario for the general public developed in this risk assessment that leads to exposure estimates that substantially exceed background levels.

3.2.3.3. Dermal Exposure from Contaminated Vegetation

As discussed in Section 3.2.3.1.2, the borates are applied only to stumps in Forest Service programs. Consequently, as in the previous Forest Service risk assessment on borax (SERA 2006a), exposure assessments involving the consumption of contaminated vegetation are not included in the current risk assessment on borates.

3.2.3.4. Contaminated Water

3.2.3.4.1. Accidental Spill

Most Forest Service risk assessments develop an exposure scenario for spills of a pesticide into a small pond (SERA 2014a, Section 3.2.3.4.1). In previous Forest Service risk assessments, different assumptions were developed for granular and liquid applications using different sets of assumptions that resulted in differing concentrations of the pesticide in water. For the current risk assessment on borates, a different method is developed in which the concentration of the pesticide in the pond is based on the application rate and the amount of pesticide required to treat 5 (1 to 10) acres. Consequently, the concentration of the pesticide in the pond is independent of the type of application—i.e., wet or dry. For the borates, the application rate is expressed in boron equivalents. As discussed in Section 2.4, the anticipated application rate for Sporax® is 1 lb borax/acre, which is equivalent to 0.113 lb B/acre. For Cellu-Treat, the anticipated application rate is 0.5 lb DOT/acre, which is equivalent to 0.105 lb B/acre. These calculations are detailed in Worksheet A01. The estimated concentration of boron in water following an accidental spill is given in Worksheet B04b based on the amount of boron in the formulation that would be required to treat 5 (1 to 10) acres. The size of the pond is taken as 1,000,000 liters, identical to the small pond used in all Forest Service risk assessments. The calculation of the dose for a small child drinking from this pond is detailed in Worksheet D05.

3.2.3.4.2. Accidental Direct Spray/drift for a Pond or Stream

For broadcast applications of pesticides, Forest Service risk assessments will typically estimate concentrations of the pesticide in a small pond and a small stream based on the application rate and estimates of drift for aerial and ground broadcast applications using AgDRIFT (SERA 2014a, Section 3.2.3.4.2). These estimates are typically given in WorksheetMaker attachments in Worksheets B04c and B04d. These types of exposure assessments are not relevant to stump applications. Consistent with the previous Forest Service risk assessment on borax (SERA 2006a), these exposure assessments are not developed for stump applications of borates.

3.2.3.4.3. GLEAMS Modeling

The Forest Service developed a program, Gleams-Driver, to estimate expected peak and longer-term pesticide concentrations in surface water. Gleams-Driver serves as a preprocessor and postprocessor for GLEAMS (Knisel and Davis 2000). GLEAMS is a field scale model developed by the USDA/ARS and has been used for many years in Forest Service and other USDA risk assessments (SERA 2007a, 2011b).

Gleams-Driver offers the option of conducting exposure assessments using site-specific weather files from Cligen, a climate generator program developed and maintained by the USDA Agricultural Research Service (USDA/NSERL 2004). As summarized in Table 10, nine locations are used in the Gleams-Driver modeling. These locations are standard sites used in Forest Service risk assessments for Gleams-Driver simulations and are intended to represent combinations of precipitation (dry, average, and wet) and temperature (hot, temperate, and cool) (SERA 2007a). The characteristics of the fields and bodies of water used in the simulations are summarized in Table 11. For each location, simulations were conducted using clay (high runoff, low leaching potential), loam (moderate runoff and leaching potential), and sand (low runoff, high leaching potential) soil textures. For each combination of location and soil, Gleams-Driver was used to simulate pesticide losses to surface water (a small pond and a small stream) from 100 modeled applications at a unit application rate of 1 lb B/acre, and each of the simulations was followed for a period of about 1½ years post application. Note that an application rate of 1 lb B/acre is used in the GLEAMS-Driver modelling in order to avoid rounding limitations in GLEAMS outputs. Note, however, that the application rates used in the attachments to this risk assessment are adjusted to units of boron—i.e., 0.113 lb B/acre for Sporax® applied at a rate of 1 lb borax/acre and 0.105 lb B/acre for Cellu-Treat® applied at a rate of 0.5 lb DOT/acre.

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. Borates 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). In addition and as discussed in Section 2, the borates 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.

The chemical-specific inputs used in the GLEAMS-Driver simulation are summarized in Table 12. As noted in Section 2.2, boric acid does not undergo standard metabolism—i.e., the degradation rates are essentially zero. GLEAMS, however, requires finite estimates of half-lives. For all half-lives, a value of 9999 days (≈27 years) is used to set the degradation rate to a negligible value. The soil K_{oc} values and sediment K_d values are taken from HERA (2005), which summarizes unpublished studies from TNO, the Netherlands Organization for Applied Scientific Research (https://www.tno.nl/en).

Table 13 summarizes the modeled concentrations of boron in surface water by GLEAMS-Driver and details of the GLEAMS-Driver are given in Appendix 9. The results of EPA modeling of

boron are discussed in Section 3.2.3.4.4, and the concentrations of boron in surface water used in the exposure assessments for the current risk assessment are discussed in Section 3.2.3.4.6.

Table 13 also summarizes monitoring data on the normal background levels of boron in U.S. surface water. This is a subset of the more detailed data on boron levels in surface water and other media from Table 2 of the current risk assessment. These background levels of borates in water are discussed further in Section 3.2.3.4.6.

3.2.3.4.4. Other Modeling Efforts

To estimate concentrations of a pesticide in ambient water as part of a screening level risk assessment, the U.S. EPA typically uses Tier 1 screening models (e.g., GENEEC, FIRST, and SCIGROW). For more refined and extensive risk assessment, the U.S. EPA/OPP typically uses PRZM/EXAMS, a more elaborate Tier 2 modeling system. As part of the EPA's most recent ecological risk assessment, GENEEC was used to model concentrations of boric acid in water for a ground spray using high boom and fine spray input parameters (EPA/OPP/EFED 2015a, Appendix F, p. 77). As in the GLEAMS-Driver modeling (Section 3.2.3.4.3.), the application of GENEEC is based on no wet-in, soil incorporation or spray drift buffer. In addition, the modeling assumed no degradation processes. Based on an application rate of 0.07 lb/acre, the peak and longer-term concentrations projected to occur in ambient water were about 4.10 µg/L. Normalizing for application rates, the estimated water contamination rate is about 58.6 µg/L per lb a.i./acre [4.10 µg/L ÷ 0.07 lb/acre ≈ 58.57143 µg/L]. As summarized in Table 13, this water contamination rate is very close to the central estimates from GLEAMS-Driver for a pond with clay soils (55.2 µg/L per lb/acre) and sandy soils (52.4 µg/L per lb/acre).

3.2.3.4.5. Monitoring Data

As summarized in Table 2 and detailed in the references cited in Table 2, extensive monitoring data are available for boron in surface waters. In terms of evaluating the surface water modeling efforts discussed in the previous sections, the most useful monitoring studies are those that associate monitored concentrations of a pesticide in water with defined applications of the pesticide—e.g., applications at a defined application rate to a well characterized field. When available, such studies can provide a strong indication of the plausibility of modeled concentrations of a pesticide in surface water. For boron, one such study is available (Pratt et al. 1996).

The study by Pratt et al. (1996) involved the stump treatment of conifers with DOT following a clear-cut operation. Stump applications were made using a 6% solution of DOT at a functional application rate in boron equivalents of 2 kg B/ha (≈1.784 lb B/acre). Prior to the DOT application, the concentration of boron in a local stream was assayed at 17 µg B/L. Following the DOT application, the peak concentration of boron in the stream was monitored at 140 µg B/L. Subtracting out the pre-treatment concentration, the peak concentration corresponds with a water contamination rate of about 69 µg B/L per lb/acre [(140 -17) µg B/L ÷ 1.784 lb B/acre ≈ 68.946 µg B/L per lb/acre].

This study was conducted near Glasgow, Scotland (Figure 1 of paper) in a region with predominantly peat soils and an annual rainfall rate of 200-220 cm [≈78.7 to 86.6 inches per year] (Pratt et al. 1996, p. 371, column 2). The paper does not specify local temperatures. Using temperatures for Glasgow Scotland, an average temperature of about 10°C or 50°F

(https://www.yr.no/place/United_Kingdom/Scotland/Glasgow/statistics.html) is a reasonable approximation. Of the soils used in the GLEAMS-Driver runs, peat soil is most similar to clay (SERA 2007a, Table 2, p. 78). As summarized Table 10, an annual rainfall rate of 78.7 to 86.6 inches and a temperature of about 50°F are most similar to the wet/temperate site used in the GLEAMS-Driver simulations. As summarized in Appendix 8, Table A8-5, the WCR for the wet/temperate site with clay soils is 43 (14.4 – 143) µg B/L per lb B/acre. The water contamination rate from the study by Pratt et al. (1996)—i.e., 68.946 µg B/L per lb B/acre—is reasonably close to the midpoint from the GLEAMS-Driver modeling.

The above discussion is not meant to suggest a formal validation or evaluation of the GLEAMS-Driver simulations, which would require a much more detailed consideration of the site-specific characteristics from the study by Pratt et al. (1996). Nonetheless, the reasonable correspondence of the GLEAMS-Driver simulations with the monitoring of a stump application of a borate adds confidence to the use of the results of the GLEAMS-Driver simulations in the exposure assessments involving surface water.

3.2.3.4.6. Concentrations in Water Used for Risk Assessment

The water contamination rates (WCRs) for boron in surface water used in this risk assessment are summarized in Table 14. The concentrations are specified in Table 14 as water contamination rates—i.e., the concentrations in water expected at a normalized application rate of 1 lb/acre, converted to units of ppm or mg/L per lb a.i./acre. In Table 13, the summary of all of the modeling efforts, units of exposure are expressed as ppb or µg/L, as a matter of convenience. In Table 14, however, ppb is converted to mg/L (ppm) because mg/L is the unit of measure used in the EXCEL workbooks for contaminated water exposure scenarios in both the human health and ecological risk assessments. The water contamination rates are entered in Worksheet B04Rt in the attachments to this risk assessment. The values in Worksheet B04Rt are linked to the appropriate scenario-specific worksheets in the EXCEL workbooks and are adjusted to the application rate entered in Worksheet A01—i.e., 0.5 lb Cellu-Treat/acre in Attachments 1 and 1 lb Sporax/acre in Attachments 2 and 3. In all cases, the formulation rates are converted in Worksheet A01 to application rates in units of lb B/acre—i.e., 0.105 lb B/acre for Cellu-Treat® and 0.113 lb B/acre for Sporax.

The water contamination rates are based on the GLEAMS-Driver modeling (Section 3.2.3.4.3). The modeled WCRs from GLEAMS-Driver are reasonably consistent with the modeling from the U.S. EPA (Section 3.2.3.4.4) and remarkably consistent with the monitoring study following stump applications of DOT conducted by Pratt et al. (1996) (Section 3.2.3.4.5). All of the water contamination rates are based on the pond rather than the stream. As summarized in Table 13, the WCRs for the pond are modestly higher than those for the stream. For the sake of clarity, note that the concentrations modelled for a stream in the previous Forest Service risk assessment on borax (SERA 2006a) were much lower than those for the pond. The difference in the current modeling (Table 13) reflects the consideration of sediment binding in the stream scenarios which was introduced in GLEAMS-Driver Version 1.9.3 (SERA 2011a). In previous GLEAMS and GLEAMS-Driver modelling, sediment binding was not considered in the stream scenario.

Note that the central estimate is taken as the arithmetic average of the average for each soil type. The lower bound is taken as the lowest value of the lower bounds across soil types. The upper bound is taken as the highest value of the upper bound across soil types. See Table 13 for a

summary of the values. See Appendix 9 for details by sites and soil types – i.e., Table A9-7 for peak values and Table A9-10 for longer-term averages.

All of the modelled estimates of concentrations from GLEAMS-Driver as well as the EPA modeling (Section 3.2.3.4.4) are based on added levels of boron due to the anticipated uses of borates. As summarized in Table 13 and detailed further in Table 2, typical background levels of boron in U.S. surface waters are about 100 (<10 to 1500) µg/L (U.S. EPA/OPP/EFED 2015a, p. 29). Note that the central estimates and ranges of modelled concentrations of boron as a result of Forest Service uses are below the background levels of boron in surface water from EPA summaries of monitoring data (U.S. EPA/OPP/EFED 2015a, p. 29). For example, the upper bound water contamination rate from Table 14 is 0.43 mg B/L per lb B/acre, which is equivalent to 430 µg B/L per lb B/acre. At an application rate of about 0.1 lb B/acre (the approximate functional application rate used by the Forest Service for both Sporax® and Cellu-Treat® as discussed above), the upper bound expected peak concentration for boron associated with a stump application would be 43 µg B/L [0.1 lb B/acre x 430 µg/L per lb B/ace]. This maximum peak concentration is substantially below the typical background concentration of about 100 µg B/L and far below the upper bound of typical background concentrations of about 1500 µg B/L. In other words, the Forest Service use of Cellu-Treat® or Sporax® will not significantly increase background levels of boron in water, except for in areas with very low background levels of boron. The further discussion of cumulative exposures to boron associated with a combination of the background levels and the contribution from Forest Service uses of borates is given in the risk characterization (Section 3.4.6, Cumulative Effects).

3.2.3.5. Oral Exposure from Contaminated Fish

Many chemicals may be concentrated or partitioned from water into the tissues of aquatic animals including fish. This process is referred to as bioconcentration. Generally, bioconcentration is measured as the ratio of the concentration in the organism to the concentration in the water. For example, if the concentration in the organism is 5 mg/kg and the concentration in the water is 1 mg/L, the bioconcentration factor (BCF) is 5 L/kg [5 mg/kg ÷ 1 mg/L]. As with most absorption processes, bioconcentration depends initially on the duration of exposure but eventually reaches steady state.

Borate compounds do not bioaccumulate in fish (ECETOC 1997; Ohlendorf et al.1986; Klasing and Pilch 1988). While the U.S. EPA/OPP typically requires studies on bioconcentration, no such studies were encountered in the EPA documents on borates. The most recent EPA ecological risk assessment indicates that requests for waivers of bioaccumulation studies in fish were submitted to the EPA (U.S. EPA/OPP/EFED 2015a, p. 67). Neither the status of the request nor comments on the requirement for bioconcentration studies are detailed in the EPA document.

Exposure scenarios for the consumption of contaminated fish are standard in most Forest Service risk assessments. For the sake of completeness, these scenarios are included in the current risk assessment using a bioconcentration factor of 1 L/kg—i.e., no bioconcentration—for both fish muscle and whole fish.

Three sets of exposure scenarios are presented: one set for acute exposures following an accidental spill (Worksheets D08a and D08b), one set for acute exposures based on expected

peak concentrations of boron in water (Worksheets D09c and D09d), and another set for chronic exposures based on estimates of longer-term concentrations in water (Worksheets D09a and D09b). The two worksheets for each set of scenarios are included to account for different consumption rates of caught fish among the general population and subsistence populations. Details of these exposure scenarios are provided in Section 3.2.3.5 of SERA (2014a). The scenarios associated with consumption of contaminated fish are based on the same water concentrations of boron used for the accidental spill scenario (Section 3.2.3.4.1.) and the surface water exposure estimates (Section 3.2.3.4.6).

3.2.3.6. Dermal Exposure from Swimming in Contaminated Water

Some geographical sites maintained by the Forest Service or Forest Service cooperators include surface water in which members of the general public might swim. The extent to which this might apply to areas treated with borates is unclear.

To assess the potential risks associated with swimming in contaminated water, an exposure assessment is developed for a young woman swimming in surface water for 1 hour (Worksheet D10). Conceptually and computationally, this exposure scenario is virtually identical to the contaminated gloves scenario used for workers (Section 3.2.2.2)—i.e., a portion of the body is immersed in an aqueous solution of the compound at a fixed concentration for a fixed period of time.

As in the corresponding worker exposure scenario, the 1-hour period of exposure is intended as a unit exposure estimate. In other words, both the absorbed dose and consequently the risk will increase linearly with the duration of exposure, as indicated in Worksheet D10. Thus, a 2-hour exposure would lead to an HQ that is twice as high as that associated with an exposure period of 1 hour. In cases in which this or other similar exposures approach a level of concern, further consideration is given to the duration of exposure in the risk characterization (Section 3.4). For borates, however, the HQs for this scenario are far below the level of concern.

The scenarios for exposures associated with swimming in contaminated water are based on the peak water concentrations of borates used to estimate acute exposures from drinking water contaminated with boron (Section 3.2.3.4.6).

3.2.3.7. Oral Exposure from Contaminated Vegetation

As discussed in Section 2, borates are applied to tree stumps and the likelihood of human consumption of contaminated vegetation is minimal. As in the previous Forest Service risk assessment on borax (SERA 2006a), exposure scenarios for the consumption of contaminated vegetation are not included in the current risk assessment.

3.3. DOSE-RESPONSE ASSESSMENT

3.3.1. Overview

Table 15 provides an overview of the toxicity values for human health effects used in this risk assessment, and Table 16 provides an overview of these and several other toxicity values derived by different government offices and similar organizations. Following standard practices in Forest Service risk assessments, the toxicity values selected for the current risk assessment are adopted from the most recent human health risk assessment prepared by the U.S. EPA's Office of Pesticide Programs.

For acute exposures, a surrogate acute RfD of 3.5 mg B/kg bw is adopted from EPA based on an acute NOAEL of 350 mg B/kg bw in rats with a recommended uncertainty factor of 100 (U.S. EPA/OPP/HED 2015a). The NOAEL and recommended uncertainty factor is functionally equivalent to an acute RfD of 3.5 mg B/kg bw [350 mg B/kg bw ÷ 100]. Other recommended acute toxicity values include a minimal risk level of 0.2 mg B/kg bw (ATSDR 2010) and a 10-day health advisory of 0.25 mg B/kg bw (U.S. EPA/OW 2008). The surrogate acute RfD from OPP is substantially higher than the other acute toxicity values. Nonetheless, the surrogate acute RfD of 3.5 mg B/kg bw is supported by human experience with borates.

For longer-term exposures, a surrogate chronic RfD of 0.088 mg B/kg bw/day is adopted from U.S. EPA/OPP/HED (2015a). This RfD is based on a chronic NOAEL in dogs of 8.8 mg B/kg bw/day and a recommended MOE of 100 [8.8 mg B/kg bw/day ÷ 100 = 0.088 mg B/kg bw/day]. Furthermore, this surrogate chronic RfD is lower than other chronic values used previously by the EPA as well as chronic toxicity values recommended by other organizations.

Human data on borates suggest that adverse effects, including nausea, vomiting, and skin reactions may be observed in humans exposed to doses greater than 20 mg B/kg bw. Doses greater than 60 mg B/kg bw could cause more severe effects that require medical intervention. Lethality is a concern at doses of about 85 mg B/kg bw.

3.3.2. Acute RfD

As summarized in Table 16, three short-term toxicity values were derived by governmental organizations: an acute short-term minimum risk level (MRL) of 0.2 mg B/kg bw from the Agency for Toxic Substances and Disease Registry (ATSDR 2010), a 10-day health advisory of 0.25 mg B/kg bw from EPA's Office of Water (U.S. EPA/OW 2008), and an acute incidental toxicity value of 3.5 mg B/kg bw from EPA's Office of Pesticide Programs (U.S. EPA/OPP/HED 2015a). In the absence of a compelling reason to do otherwise, Forest Service risk assessments generally adopt the most recent toxicity value from U.S. EPA/OPP.

For boron, there are no compelling reasons to reject EPA's most recent acute toxicity value. The 10-day health advisory is based on the 60-day subchronic study in rats conducted by Lee et al. (1978). As discussed in Section 3.1.3.2, the pharmacokinetics of boron suggests that boron will not accumulate in the body with increasing periods of exposure. Thus, the proximity of this 60-day NOAEL to other shorter-term toxicity values is not remarkable. Nonetheless, subchronic toxicity studies are not commonly used in the dose-response assessment for acute effects. The somewhat lower toxicity value of 0.2 mg B/kg bw from ATSDR (2010) is based on a developmental toxicity study in rats from the open literature (Price et al. 1996b) which was

reviewed and accepted by EPA (U.S. EPA/OPP/ HED 2006a, p. 18, MRID 42164202). Deriving an acute RfD from a developmental study is a common practice, and the acute MRL from ATSDR (2010) has obvious merit.

The most recent EPA human health risk assessment does not explicitly derive an acute RfD but does recommend a NOAEL of 350 mg B/kg bw with an uncertainty factor of 100 (a factor of 10 for species-to-human extrapolation multiplied by a factor of 10 for sensitive individuals). This recommendation is equivalent to an acute RfD of 3.5 mg B/kg bw [350 mg B/kg bw ÷ 100]. This surrogate RfD is somewhat unusual in that it is based on a NOAEL from acute LD_{50} studies in rats (U.S. EPA/OPP/HED 2015a, p. 11). As noted above, the EPA typically derives an acute RfD from developmental studies but does not typically derive an RfD from NOAELs in an acute toxicity study. In the absence of other information, the acute RfD of 3.5 mg B/kg bw would be rejected and the more standard acute MRL of 0.2 mg B/kg bw from ATSDR (2010) would be used. As summarized in Table 5, however, there is substantial human experience with boron, and clinical studies indicating that intravenous doses in the range of 1.4 to 2.08 mg B/kg bw caused no adverse effects in human subjects. These NOAELs in humans are consistent with the surrogate acute RfD of 3.5 mg/kg bw from U.S. EPA/OPP/HED (2015a) but clearly indicate that the acute MRL of 0.2 mg/kg bw from ATSDR (2010) is overly conservative.

A modestly more conservative approach to the acute RfD could be based directly on the human data—i.e., a human acute NOAEL of 2 mg B/kg bw. This approach would avoid the use of the atypical acute RfD based on acute toxicity studies in rats. While this approach has been considered, the relatively modest difference in the alternative acute RfD from that derived by EPA would not justify a divergence from the acute RfD developed by the EPA.

3.3.3. Chronic RfD

As summarized in Table 16, there are an unusually large number of different chronic toxicity values derived for boron—i.e., seven different oral values ranging from 0.088 mg/kg bw/day (U.S. EPA/OPP/HED 2015a, p. 11) to 0.4 mg/kg bw/day (IPCS/WHO 1998) and a chronic inhalation MRL of 0.3 mg/m^3 from ATSDR (2010).

Five of the chronic oral toxicity values are based at least in part on the developmental study by Price et al. (1996a). Two of the five chronic oral toxicity values use the benchmark dose analysis by Allen et al. (1996) of the study conducted by Price et al. (1996a) combined with the developmental study in rats conducted by Heindel et al. (1992). Developmental studies are relatively short-term by definition—i.e., exposures occur only during the gestation period, 11 days in the study by Heindel et al. (1992) and 20 days in the study by Price et al. (1996a). While chronic RfDs may be derived from developmental studies, this approach is appropriate only when the developmental study leads to an estimated chronic RfD that is lower than the chronic toxicity studies—i.e., when developmental toxicity is the most sensitive endpoint. This is not the case for boron.

The other two chronic oral toxicity values are based on the open literature publication by Weir and Fisher (1972). Weir and Fisher (1972) is essentially a review of several studies on borax and boric acid. The EPA's Office of Water derived a chronic health advisory of 0.175 mg B/kg bw/day based on a NOAEL from a standard 2-year chronic study in rats (U.S. EPA/OW 2008, p. 30). The EPA's Office of Pesticide Programs derived a somewhat lower chronic RfD of 0.088

mg B/kg bw/day based on a 2-year dietary NOAEL in dogs, which is cited in U.S. EPA/OPP/HED (2015a) only as MRID 40692310. Based on a more complete citation in U.S. EPA/OPP/HED (2006a, p. 57), the full study in dogs appears to have been submitted and reviewed by EPA. The full studies submitted to EPA in support of pesticide registration contain much more detail than is available in an open literature publication.

Both the chronic rats and chronic dog NOAELs would be common and acceptable in the derivation of a chronic RfD. The lower and more recent value of 0.088 mg B/kg bw/day from U.S. EPA/OPP/HED (2015a) is used in the current Forest Service risk assessment to characterize risks associated with longer-term exposures.

As discussed in Section 3.2.2.1.2, inhalation exposures are a concern for workers involved in dry applications of borax. As summarized in Table 16, ATSDR (2010) proposes a chronic inhalation MRL of 0.3 mg B/m^3. Under the assumption that an 80 kg male breathes 22.8 m^3/day (U.S. EPA/NCEA 2011, p. 6-64) and the assumption of 100% absorption for inhalation exposures (U.S. EPA/OPP/HED 2015a, p. 9), the MRL of 0.3 mg B/m^3 corresponds to a dose of about 0.1 mg B/kg bw [0.3 mg B/m^3 x 22.8 m^3/day ÷ 80 kg ≈ 0.097714 mg B/kg bw]. This dose is modestly higher than the chronic RfD of 0.088 mg/kg bw/day. Consistent with the approach used in U.S. EPA/OPP/HED (2015a, p. 11), the chronic oral RfD is used to characterize risks associated with longer-term inhalation exposures to borates.

3.3.4. Dose-Severity Relationships

As summarized in Table 5, dose-severity relationships in humans are well characterized based on the substantial human experience with borates—i.e., clinical studies, therapeutic uses, and reported poisoning events. Based on estimates of acceptable exposures by WHO (IPCS/WHO 1998), a dose of up to 0.4 mg/kg bw should not be associated with any adverse effects. This estimate is supported by the tolerable upper intake level of 0.3 mg B/kg bw from the National Academies of Science (Institute of Medicine 2001, p.519). Based on intravenous administrations of boric acid to volunteers, doses in the range of 1 to 2 mg B/kg bw should not be associated with overt signs of toxicity. Doses in excess of about 20 mg B/kg bw have resulted in signs of toxicity including nausea, vomiting, and skin reactions. Dose above 60 mg B/kg bw may result in severe signs of toxicity requiring medical attention. Lethal doses for boric acid are reported to range from 85 to 112 mg B/kg bw (Table 5).

3.4. RISK CHARACTERIZATION

3.4.1. Overview

In both the human health and ecological risk assessments, the quantitative expression of the risk characterization is the hazard quotient (HQ), the ratio of the anticipated dose or exposure to the RfD (human health) or no-observed-adverse-effect level or concentration (ecological effects) using 1 as the level of concern—i.e., an HQ of < 1 is below the level of concern. For the human health risk assessments the toxicity values are a surrogate acute RfD of 3.5 mg B/kg bw/day and a chronic RfD of 0.088 mg B/kg bw/day (Table 15). The HQs for workers (Worksheet E02) and members of the general public (Worksheet E04) are summarized in the attachments to this risk assessment—i.e., Attachment 1 for liquid applications of Cellu-Treat, Attachment 2 for liquid applications of Sporax, and Attachment 3 for dry applications of Sporax.

Exposure levels for workers involved in dry application of Sporax® over a prolonged period is the only exposure scenario in the human health risk assessment for which the HQs exceed the level of concern. For this scenario, the HQs are 0.6 (0.1 to 6) with only the upper bound of the HQ exceeding the level of concern. This exposure scenario involves a deposition-based exposure assessment developed by EPA which is based on inhalation exposures. A major reservation with this exposure scenario is that the EPA applied the same exposure rates for both indoor (confined spaces) and outdoor dust applications. The extent to which the use of the same exposure rates for indoor and outdoor dust applications may overestimate exposures for forestry workers involved in stump applications is unclear. While the upper bound HQ of 6 indicates that upper bound exposure levels would be viewed as generally unacceptable, it is not clear that these exposure levels would lead to overt toxic effects.

The only other exposure scenario that approaches the level of concern is the upper bound HQ of 0.9 for the direct consumption of Sporax® by a small child following a dry stump application. The dose associated with the upper bound HQ is 3.1 mg B/kg bw. This dose is below the anticipated adverse effect level by a factor of over 6.

As noted in Section 2.2, the registration for stump applications of Sporax® is no longer being supported. While the Forest Service may continue to use existing stocks of Sporax, stump treatments will be limited to liquid applications of Cellu-Treat® once the existing stocks of Sporax® have been exhausted. For liquid applications of Cellu-Treat, non-accidental HQs are below the level of concern by a factor of over 300 for workers and over 100 for members of the general public. The highest accidental HQ (i.e., consumption of contaminated water by a small child) is below the level of concern by a factor of 100.

3.4.2. Workers

The HQs associated with liquid exposures of borates are far below the level of concern (HQ=1). As summarized in Worksheet E02 of Attachments 1 and 2, the HQs based on standard absorption based methods used by the Forest Service for worker exposure estimates (i.e., as detailed in Section 3.2.2.1.1.1) are concordant with the HQs based on EPA deposition-based methods (Section 3.2.2.1.1.2). For liquid applications of Cellu-Treat® (Attachment 1), the upper bound HQs for general exposures range from 0.0008 to 0.003, which are below the level of concern by factors of about 333 to 1250. For liquid applications of Sporax® (Attachment 2), the upper bound HQs range from 0.003 to 0.01—i.e., below the level of concern by factors of 100 to about

333. The differences in the HQs for the two formulations are due solely to the higher stump application rate for Sporax® (0.00226 lb B/ft^2) relative to Cellu-Treat® (0.000525 lb B/ft^2), as discussed in Section 2.4. Under the assumption that workers will treat the same stump area with applications of the two formulations—i.e., 500 (200 to 1000) ft^2/day as discussed in Section 3.2.2.1.1—workers applying Sporax® will handle a greater amount of boron per day than workers applying Cellu-Treat®.

For dry applications of Sporax, the upper bound of the HQ for workers does exceed the level of concern for chronic exposures—i.e., HQs of 0.6 (0.1 to 6) based on the chronic surrogate RfD 0.088 mg/kg bw/day. For acute exposures, the HQs are below the level of concern—i.e., acute HQs of 0.02 (0.002 to 0.2) based on the acute surrogate RfD of 3.5 mg/kg bw. The chronic HQs for workers is concordant with the Margin of Exposure (MOE) of 18 derived in U.S. EPA/OPP/HED (2015a, Table 8.1.1, p. 37) for stump applications made without the use of a respirator or dust filter. As discussed in Section 3.2.2.1.2, the exposure assessment for workers involved in dry applications of Sporax® is based on the exposure methods from U.S. EPA/OPP (2013a, p. 5). As also discussed in Section 3.2.2.1.2, the EPA applied the same exposure rates for both indoor (confined spaces) and outdoor dust applications. The extent to which the use of the same exposure rates for indoor and outdoor dust applications may overestimate exposures for forestry workers involved in stump applications is unclear.

The longer-term upper bound HQ of 6 for workers involved in dry applications of Sporax® is based on an estimated daily dose of about 0.565 mg B/kg bw/day (Attachment 3, Worksheet E01). As summarized in Table 16 and discussed in Section 3.3, this dose is only modestly higher than the Tolerable Daily Intake of 0.4 mg/kg bw/day derived by IPCS/WHO (2001) and the Tolerable Upper Intake Level of 0.3 mg B/kg bw/day derived by the NAS Institute of Medicine (2001). In addition, dose-severity considerations (Section 3.3.4) suggest that daily doses in the range of 1 to 2 mg B/kg bw should not lead to adverse effects in humans, at least for short periods of exposure. Thus, while the upper bound HQ of 6 indicates exposures that would be viewed as generally unacceptable, it is not clear that these exposures would lead to overt toxic effects or reproductive effects.

All of the accidental worker exposure scenarios for workers involve dermal exposure. Given the poor dermal absorption of boric acid, the HQs for all of the accidental exposure scenarios are far below the level of concern. The highest accidental HQ is 0.0001 (the upper bound of the HQ for workers following a spill on to the lower legs with an exposure period of 1 hour during liquid applications of Cellu-Treat). This HQ is below the level of concern (HQ=1) by a factor of 10,000.

3.4.3. General Public

The risk characterization for members of the general public is simple and unequivocal. None of the exposure scenarios, accidental or otherwise, results in HQs that exceed the level of concern. The highest HQ for any non-accidental exposure scenario is 0.01—i.e., the upper bound of the longer-term HQ for the consumption of contaminated water following applications of Sporax® at an application rate of 0.113 lb B/acre.

Some but not all of the HQs for non-accidental exposures associated with Sporax® applications are modestly higher than those associated with Cellu-Treat® applications. This difference is due

solely to the somewhat higher application rate in terms of boron equivalents for Sporax® (i.e., 1 lb Sporax/acre x $0.113_{B/Borax} \approx 0.113$ lb B/acre) relative to Cellu-Treat® (i.e., 0.5 lb Cellu-Treat/acre x $0.210_{B/DOT} \approx 0.105$ lb B/acre). Many of the HQs for Cellu-Treat® and Sporax® are identical, because most HQs, by convention, are rounded to one significant place (SERA 2011a). The underlying values of the non-accidental HQs for Sporax® are higher than the corresponding HQs for Cellu-Treat® by a factor of about 1.08 [0.113 lb B/acre ÷ 0.105 lb B/acre ≈ 1.0761]. Consequently, some of the HQs for Sporax® are rounded one integer higher than those for Cellu-Treat®.

All of the HQs for accidental exposures associated with liquid applications of either Cellu-Treat® or Sporax® are also below the level of concern. The highest accidental HQ for a liquid application is 0.02—i.e., the upper bound of HQ associated with the consumption of contaminated water by a child following an accidental spill. This HQ is below the level of concern by a factor of 50.

The only HQ for an accidental exposure that approaches the level of concern is the upper bound HQ of 0.9 for the direct consumption of Sporax® by a small child following a dry stump application. As detailed in Worksheet D01c of Attachment 3, this HQ is associated with a dose of 3.1 mg B/kg bw which is below the surrogate acute RfD of 3.5 mg/kg bw. As discussed in Section 3.2.3.2.2, the exposure estimate is based on soil consumption rather than any direct estimate or case report of the consumption of borax by a child. The upper bound estimate of 300 mg/day is adopted directly from U.S. EPA/OPP/HED (2015a, Table A-5, p. 49) and may be considered extreme. As discussed in Section 3.3.4, doses of about 20 mg B/kg bw may be associated with overt signs of toxicity including nausea, vomiting, and skin reactions. The dose of 3.1 mg B/kg bw is below this adverse effect level by a factor of over 6 [20 mg B/kg bw ÷ 3.1 mg B/kg bw ≈ 6.4516].

3.4.4. Sensitive Subgroups

The more recent assessment of boron in ATSDR (2010) does not identify subgroups likely to be particularly more sensitive to borates:

> *No data were located identifying a population that is unusually susceptible to boron toxicity. Case reports in humans suggest that large variability exists with the human population to the lethal effect of boron. However, there are no data to suggest which segment of the population is more susceptible to boron.*
>
> ATSDR, 2010, p. 103

As discussed in Section 3.1, the major concern with exposure to borates involves reproductive effects including testicular atrophy. As summarized in Table 15, the longer-term surrogate RfD is based on testicular atrophy. As summarized in Table 16, the NOAEL for this endpoint is below other NOAELs for reproductive effects. Thus, the current risk assessment should be protective of reproductive effects. As noted in the previous Forest Service risk assessment, *males with underlying testicular dysfunction could be at increased risk for boron-induced testicular toxicity* (SERA 2005a, p. 3-27). While this may be the case, the uncertainty factors used by U.S. EPA (U.S. EPA/OPP/HED 2015a, p. 11) and incorporated into the current risk assessment are intended to accommodate sensitive individuals in the human population.

3.4.5. Connected Actions

The Council on Environmental Quality (CEQ), which provides the framework for implementing NEPA, defines connected actions (40 CFR 1508.25) as actions which occur in close association with the action of concern; in this case, the use of a pesticide. Actions are considered to be connected if they: (i) Automatically trigger other actions which may require environmental impact statements; (ii) Cannot or will not proceed unless other actions are taken previously or simultaneously; and (iii) Are interdependent parts of a larger action and depend on the larger action for their justification. Within the context of this assessment of borates, "connected actions" include other management or silvicultural actions or the use of other chemicals necessary to achieve management objectives which occur in close association with the use of the borates.

As discussed in detail in Sections 3.1.14, the borate formulations considered in the current risk assessment do not contain inert components. In addition, the borates are not applied in combination with other products or additives.

3.4.6. Cumulative Effects

Cumulative effects may involve either repeated exposures to an individual agent or simultaneous exposures to the agent of concern (in this case boric acid) and other agents that may cause the same effect or effects by the same or a similar mode of action.

The most recent EPA human health risk assessment does not make a determination of whether other pesticides may have cumulative effects with borates:

> *Unlike other pesticides for which EPA has followed a cumulative risk approach based on a common mechanism of toxicity, EPA has not made a common mechanism of toxicity finding as to boric acid and its sodium salts and any other substances and boric acid/sodium salts do not appear to produce a toxic metabolite produced by other substances. For the purposes of this tolerance action, therefore, EPA has not assumed that boric acid/sodium salts have a common mechanism of toxicity with other substances.*
>
> U.S. EPA/OPP/HED 2015a, p. 54

As discussed in both Section 2 and Section 3.2, boron is a naturally occurring element. At least conceptually, cumulative effects associated with the contribution of the Forest Service uses of borates to normal background levels of borates are a consideration. As detailed in Section 3.2, however, the uses of borates in Forest Service programs will not contribute substantially to normal background levels of exposure, as reflected in the extraordinarily lower HQs for most exposure scenarios as discussed above. The only exceptions involve workers involved in dry applications of Sporax® and the accidental exposure scenario for the consumption of borax by a child. In both of these cases, background exposures to borax are much lower than estimated exposures for the worker or the child. Thus, a specific consideration of background levels of exposure would not affect the risk characterization. For the sake of clarity, it should be noted that the explicit doses reported in all of the toxicity studies as well as human incidents also involve implicit and unquantified background exposures to boron.

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 physiological pH and in most surface waters, most organisms are exposed primarily to boric acid. Therefore, information on boric acid is reviewed as appropriate and used as surrogate data in this risk assessment for borax and DOT. In order to facilitate any comparisons between borax, DOT, 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).

Adverse reproductive effects, including skeletal defects, the inhibition of normal spermatogenesis, and testicular pathologies are characteristic of over-exposure to boron in several groups of organisms including mammals, birds, and aquatic phase amphibians. While the mechanism of action of borates is not fully characterized, these reproductive and developmental effects could be related to the suppression of normal cell proliferation by boron. Although boron appears to reduce oxidative stress in mammals, sublethal exposure to borates appears to increase oxidative stress in some insects. At least in plants, boron is an essential trace element, and biphasic dose-response curves (e.g., Figure 2) are common in terrestrial plants. Boron has not been shown to be clearly essential in other groups of organisms; yet, biphasic dose-response curves (i.e., beneficial effects at low doses) have been noted in mammals, birds, and aquatic phase amphibians.

Boron is a naturally occurring element, and like most naturally occurring elements can be toxic at high levels of exposure. There is, however, little indication that boron is toxic to most organisms at normal (i.e., background) levels of exposure.

4.1.2. Terrestrial Organisms

4.1.2.1. Mammals

The toxicity studies used to assess the risk of human exposure to borates (Section 3.1 and Appendix 1) are equally applicable to the risk assessment for mammalian wildlife. As summarized in Section 3.1, boric acid is the agent of concern for both borax and DOT, which are considered toxicologically equivalent to boric acid in terms of boron content. Borax and DOT, as well as many other borate compounds, are converted to undissociated boric acid at physiological pH. The primary endpoints of concern involve reproductive effects, including skeletal defects, the inhibition of normal spermatogenesis, and testicular pathologies. While the mechanism of action of borates is not fully characterized, these reproductive and developmental effects could be related to the suppression of normal cell proliferation by boron.

The ecological risk assessment attempts to identify subgroups of mammals that may display greater or lesser sensitivity to a particular pesticide. These differences may be based on allometric scaling (e.g., Sample and Arenal 1999) or differences in physiology. The standard acute oral lethality studies conducted on dogs and rats (Appendix 1, Table A1-1) are not useful in assessing species differences between rats and dogs because vomiting occurs in dogs but not

rats after administration of potentially lethal doses of borates. Thus, only indefinite LD_{50} values are available in dogs (>166 mg B/kg bw), and these are not comparable to the definitive LD_{50} values in rats (≈500 mg B/kg bw). An intraperitoneal LD_{50} for mice is reported as 376 mg B/kg bw (Soriano-Ursua et al. 2014), which is not remarkably different from the oral LD_{50} in rats. As summarized in Table 5 and discussed in Section 3.1.4.2, the lower range of lethal oral doses in humans ranges from about 85 to 100 mg B/kg bw. These lethal doses are consistent with the oral LD_{50} values in experimental mammals—i.e., for an oral LD_{50} of about 400 mg B/kg bw (the approximate value for rats and mice), mortality in some animals would not be unusual at doses in the range of 100 mg B/kg bw. Thus, the acute lethality data do not clearly indicate a systematic relationship in sensitivity among species. Similarly, as discussed in Section 3.1.5, no systematic differences are apparent in the subchronic toxicity of borates to mice, rats, and dogs. Furthermore, as discussed in Section 3.1.9, rats appear to be somewhat more sensitive than mice and rabbits to borates, in terms of developmental effects. On the other hand, this apparent difference could be an artifact of the greater number of studies available on rats, relative to mice and rabbits. Given the lack of differences in species sensitivity based on acute and longer-term toxicity studies and the equivocal nature of the data from developmental studies, there are no clearly significant and substantial sensitivity differences among mammals exposed to borates.

Field observations and field studies also may be useful in assessing risks to mammalian wildlife. The most recent EPA ecological risk assessment briefly summarizes incident reports involving borates (U.S. EPA/OPP/EFED 2015a, pp. 44-45). While no incidents are reported for stump applications, the EPA expresses concern that …*animals may be attracted and exposed to baits and traps if used outdoors* (U.S. EPA/OPP/EFED 2015a, p. 45).

The Forest Service conducted a study in 1994 (Campbell et al., no date) to determine whether deer are attracted to borax following stump applications. The results of the unpublished study are inconclusive, indicating that although some deer were observed licking treated stumps, there was no statistically significant evidence that deer were either attracted to or repelled by treated stumps.

Dost (1994) describes an incident in which a dead cow was found in an area of borax treated stumps. No clinical observations or clinical chemistry data were available for the cow. Dost (1994, p. 13) estimated that a cow (360 kg) consuming all borax from a 14-inch stump would receive a dose of about 25 mg borax/kg bw or about 3 mg B/kg bw [25 mg borax/kg bw x $0.113_{B/Borax}$ = 2.825 mg B/kg bw]. Dost (1994, p. 18) concluded that it is …*highly unlikely that this animal was poisoned by borax acquired from cut stump surfaces*. Given that the dose estimate of about 3 mg B/kg bw is below the acute RfD of 3.5 mg B/kg bw (Section 3.3), the current risk assessment concurs with the conclusion of Dost (1994). Without apparent differences in species sensitivity to borates, the approximate lethal dose of about 100 mg B/kg (Section 3.1.4.2) for humans might be applied to larger mammals, like a cow. If so, the cow would have to consume all of the borax from about 35 stumps to achieve the lethal dose [100 mg B/kg ÷ 2.825 mg B/kg bw ≈ 35.398].

4.1.2.2. Birds

Typically, the EPA requires three types of avian toxicity studies for pesticide registration: single gavage dose LD_{50} studies, 5-day dietary toxicity studies, and chronic (≈30-week) dietary reproduction studies. The required studies are usually conducted with mallard ducks and

bobwhite quail. Three oral gavage studies are available, two in quail and one in mallards (Appendix 2, Table A2-1). One standard acute dietary study in quail is available as well as two atypical studies in chickens and turkeys (Appendix 2, Table A2-2). Standard reproduction studies are available on quail and mallards along with several additional longer-term exposure studies from the open literature (Appendix 2, Table A2-3).

4.1.2.2.1. Acute Toxicity

Single dose gavage toxicity studies are available in quail for both borax and DOT. The single gavage study in quail exposed to borax yielded an indefinite LD_{50} of >284 mg B/kg bw (Fink et al. 1982a, MRID 00100657). Based on the full study reviewed in the previous Forest Service risk assessment (SERA 2006a), the dose of 284 mg B/kg bw resulted in one mortality. No mortality was observed at the lower doses (45, 72, 113, and 180 mg B/kg bw), and the only adverse effect was a slight loss of body weight in the 180 mg B/kg bw dose group over the first 3 days after dosing. The apparent NOAEL for mortality and weight loss from this study is 113 mg B/kg bw. The gavage study in quail exposed to DOT (MRID 00107904) is summarized in U.S. EPA/OPP/EFED (2015a) and not otherwise available. The reported LD_{50} is >284 mg B/kg bw, identical to the indefinite LD_{50} for borax. The gavage study in mallards reports a somewhat higher LD_{50} of >376 mg B/kg bw (ACC 254367 also summarized in U.S. EPA/OPP/EFED 2015a).

A full copy of the one standard 5-day dietary study in quail (Reinart and Fletcher 1977, MRID 00149195) was available for the previous Forest Service risk assessment (SERA 2006a) and is summarized in Appendix 2, Table A2-2. No increase in mortality or other adverse effects were noted at a dietary concentration of up to 5000 ppm borax. Based on reported body weights and food consumption, this NOAEL corresponds to a dose of about 136 mg B/kg bw/day.

U.S. EPA/OPP/EFED (2015a) briefly summarizes two acute studies with boric acid, one in chickens and the other in turkeys. Both studies report the LC_{50} value as >1.27 kg B/ft^2. In the absence of information on consumption, doses in units of mg B/kg bw cannot be estimated, and comparisons to the more standard studies cannot be made.

The indefinite gavage LD_{50} values in birds are somewhat higher than the indefinite LD_{50} values in dogs—i.e., >110 and >166 mg B/kg bw, as summarized in Appendix 1, Table A1-1. This comparison is not particularly meaningful, however, because of the strong vomiting response in dogs and the nature of indefinite LD_{50} values. The acute dietary NOAEL of 136 mg B/kg bw/day in quail is somewhat below the acute NOAEL of 350 mg B/kg bw for rats—i.e., MRID 40692303 from Appendix 1, Table A1-1. In the absence of a dietary LOAEL in quail, this comparison cannot be used to suggest relative sensitivities. The acute gavage LOAEL of 180 mg B/kg bw in quail (Fink et al. 1982a, MRID 00100657) is below the NOAEL of 350 mg B/kg bw in rats. While the acute toxicity data are limited, this comparison suggests that some birds might be somewhat more sensitive than some mammals on an acute basis. As discussed below, this supposition is supported by long-term studies.

4.1.2.2.2. Longer-term Toxicity

The two available standard reproduction studies in birds are reviewed in U.S. EPA/OPP/EFED (2015a). The reproduction study in quail reports an NOAEL of about 6 mg B/kg bw/day with a corresponding LOAEL (based on percent hatchlings/live embryos and male weight gain) of 12

mg B/kg bw/day (MRID 49185901). The toxicity values for mallards are somewhat lower—i.e., a NOAEL of 3.7 mg B/kg bw/day and LOAEL of 11 mg B/kg bw/day based on the percent hatchlings and live embryos (MRID 49009801). There is high confidence in the mallard toxicity values in that dose estimates in units of mg B/kg bw/day are reported in U.S. EPA/OPP/EFED (2015a) presumably based on monitored food consumption and body weights. As summarized in Table 7 and discussed in Section 3.1.9, there are many available developmental and reproductive toxicity studies in mammals. The lowest mammalian toxicity values are a NOAEL of 9.6 mg B/kg bw/day with a corresponding LOAEL of 13.7 mg B/kg bw/day. This comparison strongly supports the assessment that some birds appear to be somewhat more sensitive than mammals to borate toxicity.

Somewhat higher toxicity values for reproductive effects are reported in the open literature—i.e., a NOAEL of 20 and a LOAEL of 70 mg B/kg bw/day in mallards by Smith and Anders (1989) and a LOAEL of 17.5 mg/kg bw/day in chickens by Rossi et al. (1993), as summarized in Appendix 2, Table A2-3. As with mammals (Table 7), this level of variability is unremarkable. Also, as with mammals, the chickens in the study by Rossi et al. (1993) had impaired sperm development, although the damage was only marginally significant ($p<0.051$).

The open literature on borates includes several other subchronic toxicity studies in birds (mallards in the study by Hoffman et al. 1990 and hens in the studies by Eren et al. 2004; Olgun et al. 2012; Yeslibag and Eren 2008), as summarized in Appendix 2, Table A2-3. Based on changes in clinical chemistries (i.e., increased serum triglycerides), Hoffman et al. (1990) report a LOAEL of 8.4 mg B/kg bw/day in a 70-day study in mallards. This LOAEL is consistent with the LOAEL in mallards of 11 mg B/kg bw/day and does not contradict the NOAEL of 3.7 mg B/kg bw/day in the standard reproduction study (MRID 49009801). Eren et al. (2004) report a NOAEL of 6.7 mg B/kg bw/day with a corresponding LOAEL of 13 mg B/kg bw/day in hens. These data are consistent with, albeit somewhat higher than, the reproductive NOAELs in mallards (MRID 49009801).

At lower doses (i.e., up to about 3 mg B/kg bw/day), no clear signs of toxicity are apparent in hens (Olgun et al. 2012; Yeslibag and Eren 2008). At doses of up to about 1.2 mg B/kg bw/day, Yeslibag and Eren (2008) noted beneficial effects in birds (e.g., egg shell quality).

Both the standard reproduction study reviewed in U.S. EPA/OPP/EFED (2015a, MRID 49009801) and the open literature study by Hoffman et al. (1990) suggest that mallards may be somewhat more sensitive than either quail or chickens to borate toxicity.

4.1.2.3. Reptiles and Amphibians (Terrestrial Phase)

Information is available on the toxicity of borates to aquatic phase amphibians (Section 4.1.3.2); data concerning the toxicity of borates to reptiles or terrestrial phase amphibians are not included in the most recent EPA ecological risk assessment (U.S. EPA/OPP/EFED 2015a) or in the review of amphibian toxicity studies by Pauli et al. (2000). No other information on the toxicity of borates to reptiles or terrestrial phase amphibians was identified in the open literature. As noted in the EPA risk assessment, the EPA recommends the use of birds as surrogates for reptiles and terrestrial phase amphibians (U.S. EPA/OPP/EFED 2015a, p. 39).

A concern with the use of birds as a surrogate for amphibians involves the permeability of amphibian skin to pesticides and other chemicals. Quaranta et al. (2009) indicate that the skin of the frog *Rana esculenta* is much more permeable than pig skin to several pesticides and that these differences in permeability are consistent with differences in the structure and function of amphibian skin, relative to mammalian skin.

4.1.2.4. Terrestrial Invertebrates

Borates are registered as both insecticides and acaricides (U.S. EPA/OPP/EFED 2015a). In addition, boric acid is registered by Nisus for the control of snails and slugs (EPA Reg. No. 64405-2). Given the use of borates as insecticides, acaricides, and molluscicides, there is a robust open literature on the toxicity of borates to terrestrial invertebrates. Some of the earlier literature on the toxicity of borates to terrestrial invertebrates was reviewed by the U.S. Fish and Wildlife Service (Eisler 1990); however, reviews of the more recent literature were not identified. Hence, many studies, primarily from the open literature, are summarized in Appendix 3. These summaries include toxicity studies in bees (Table A3-1), toxicity and efficacy studies in other insects [Tables A3-2 (toxicity) and A3-3 (efficacy)], toxicity studies in soil arthropods, (Tables A3-4), and toxicity studies in earthworms and other non-arthropods (Table A3-6).

Based on a standard acute contact LD_{50} of 63 µg B/bee in the honeybee (Atkins 1987, MRID 40269201), U.S. EPA/OPP/EFED (2015a, p. 35) classifies boric acid as *Practically Nontoxic* to the honey bee. Typical body weights for worker bees range from 81 to 151 mg (Winston 1987, p. 54). Taking 116 mg as an average body weight, the LD_{50} of 63 µg B/bee corresponds to a dose of about 540 mg B/kg bw [63 µg ÷ 0.116 g ≈ 543.10 µg B/g bw or mg B/kg bw].

Studies on the oral toxicity of boric acid to bees are summarized in Appendix 3, Table A3-1,. The study by Ferreira et al. (2013) in a stingless bee (*Scaptotrigona postica*) notes substantial mortality from Day 5 (≈20%) to Day 10 (100%) in bees fed a diet of containing boric acid at a concentration of 0.75% (7500 mg BA/kg diet) for a period of 10 days. This exposure corresponds to a dose of about 0.75 µg BA/bee/day (Ferreira et al. 2013, p. 58) or about 0.13 µg B/bee/day [$0.175_{B/BA}$ x 0.75 µg BA = 0.13125 µg B]. The 10-day exposure period used by Ferreira et al. (2013) would be classified as a subchronic rather than acute exposure. Nonetheless, the lethal dose of 0.13 µg B/bee/day is substantially lower than the <2 µg/bee criteria used by EPA for classifying a pesticide as highly toxic to bees (i.e., SERA 2014a, Table 16). Ferreira et al. (2013) do not specify the weight of the bees. Taking a body weight of 30 mg for this species from Thompson (2015, Table 1), the dose of 0.13 µg B/bee/day corresponds to a dose of about 4.3 mg B/kg bw [130 ng B/bee/day ÷ 30 mg bw ≈ 4.3 ng/mg or mg/kg bw]. While the oral lethal dose from Ferreira et al. (2013) is not directly comparable to the contact LD_{50} in the honeybee, the much lower lethal dose for the stingless bee suggests that honeybees may not be the species of bee most sensitive to borates.

As summarized in Appendix 3 (Table A3-2), the toxicity of borates has been assayed in several other groups of insects—i.e., cockroaches (Blattodea), beetles (Coleoptera), flies (Diptera), and moths (Lepidoptera). With the exception of one study in fruit flies submitted to EPA (MRID 45356601), these studies are not standardized bioassays, and the results of these studies are difficult to compare quantitatively. Nonetheless, striking differences in sensitivity among different groups of insects are not generally apparent, with most dietary toxicity values ranging from 1000 to over 10,000 mg/kg diet. One exception is the study by Buyukguzel et al. (2013),

which reports an atypically low LC_{50} of 160 mg BA/kg diet for the greater wax moth (*Galleria mellonella*). This level of sensitivity, however, is not corroborated in an assay of the same species by Hyrsl et al. (2007), in which improved survival was observed in both larvae and adults at a dietary concentration of 156 mg BA/kg diet. As discussed in Section 3.2, borates appear to reduce oxidative stress in mammals. At least in the Lepidoptera, sublethal doses of borates have been associated with increased oxidative stress (Buyukguzel et al. 2013; Hyrsl et al. 2007). Many of the efficacy studies in insects involve the use of borates in baits (Appendix 3, Table A3-3). For the most part, these studies suggest that borates can be effective in the control of cockroaches, beetles, flies, ants, and mosquitoes. One notable exception is the study by Nondillo et al. (2014) which found that boric acid at liquid bait concentrations of up to 12% was ineffective in the control of Argentine ants (*Linepithema micans*). Conversely, another study on the same species notes efficacy at somewhat lower concentrations of 8% boric acid (Mathieson et al. 2012). Again, these inconsistencies are not remarkable given the variability in the designs of the different studies conducted by different groups of investigators.

As discussed further in Section 4.2.3 (exposure assessments for terrestrial invertebrates), stump treatments with borates are not amenable to meaningful exposure assessments for most groups of terrestrial insects. Given the nature and variability in the numerous available toxicity studies on terrestrial insects, standard dose-response assessments in units comparable to exposure assessments cannot be developed readily. Given these limitations, the position taken in the most recent EPA risk assessment seems reasonable—i.e., risk to terrestrial invertebrates …*is assumed rather than calculated* (U.S. EPA/OPP/EFED (2015a, p. 9).

One notable exception, however, involves soil invertebrates. Studies in soil arthropods (Table A3-4) and worms (Table A3-5) suggest that toxic levels of borates in soil range from 100 to over 1000 mg/kg soil. As summarized in Table 2, typical levels of boron in soil range from about 10 to 100 mg B/kg soil. As discussed further in Section 4.2.3, GLEAMS-Driver modeling suggests that stump treatments will add less than 0.05 mg B/kg soil. Thus, as in many exposure scenarios in the human health risk assessment (Section 3.2), stump treatments with borates will not contribute substantially to background levels of boron in soil. While the toxicity data in soil invertebrates is noted for the sake of completeness, soil invertebrates are not identified as a group of concern in the assessment of stump treatments with borates.

4.1.2.5. Terrestrial Plants (Macrophytes)

Studies on the toxicity of borates to terrestrial plants are summarized in Appendix 4. For herbicides, the EPA generally requires relatively sophisticated Tier II bioassays on plants. For other pesticides that may be applied to plants, much simpler Tier 1 studies are generally required. For the borates, only relatively simple Tier 1 assays were conducted for vegetative vigor (Appendix 4, Table A4-1) and seedling emergence (Appendix 4, Table A4-2) in support of the registration review for borates (U.S. EPA/OPP/EFED 2015a). No effects were noted in the standard study on vegetative vigor (NOAEL of >0.03 lb B/acre). This indefinite NOAEL is substantially below the functional application rates of about 0.1 lb B/acre used in Forest Service programs (Section 2). In the assays on seedling emergence, dicots (NOAEL of 0.11 lb B/acre) were more sensitive than monocots (>0.87 lb B/acre). The ‘greater than’ (>) designation for the NOAELs indicates that no effects were noted at the highest concentration assayed.

Boron is an essential trace element for terrestrial plants. As reviewed by Butterwick et al. (1989, Figure 3 of paper), dose-response relationships for plants expressed in soil levels of boron are biphasic, similar to Figure 2 in the current risk assessment. Too little boron will impair growth due to deficiency and too much boron will impair growth due to toxicity. The concentrations of boron required to produce optimal growth and development vary tremendously between species and even between strains of the same species (ECETOC 1997, Jamjod and Rerkasem 1999, Moore 1997, Tanji 1990, IPCS/WHO 1998). Symptoms of boron deficiency include cessation of root and leaf growth, leaf, stem and root tip necrosis, reduced germination, and death (IPCS/WHO 1998). At sub-toxic levels, the use of fertilizers containing boron can improve plant vigor and increase crop yield for plants grown in boron-deficient soils (ECETOC 1997). On the other hand, excess boron can lead to adverse effects in plants, including chlorosis of leaves, leaf necrosis, and decreased germination (ECETOC 1997, IPCS/WHO 1998). In some 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, IPCS/WHO 1998).

Despite the many phytotoxicity studies on borates in the open literature, there are few studies that provide useful data for quantifying risk to terrestrial plant, and they are summarized in Appendix 4, Table A4-3. The study by Apostol and Zwiazek (2004) in jack pine is somewhat unusual in that it focuses on liquid exposures—i.e., pine seedlings in nutrient solutions with levels of boron ranging from about 5 to 21.4 mg B/L. Although the highest boron concentration caused leaf necrosis, which is a common sign of toxicity, there were no effects on pine seedling growth. This study is noted because it involves a species with obvious relevance to forestry. The route of exposure, however, is marginally relevant to the assessment of risks associated with stump applications.

All of the other studies summarized in Appendix 4, Table A4-3, involve soil exposures, which are relevant to this risk assessment. Boron concentrations as low as 13 mg B/kg soil may be toxic to sensitive species (i.e., turnip in the study by Stanley and Tapp 1982). No adverse effects are reported at soil concentrations below 8 mg B/kg soil (i.e., poppies in the study by Sopova et al. 1981). While these studies are cited for the sake of completeness, they do not have a practical impact on the current risk assessment. As noted in Section 4.1.2.4 in the discussion of soil invertebrates and discussed further in Section 4.2.3, stump treatments with borates will not contribute substantially to background levels of boron in soil—i.e., about 10 to 100 mg B/kg soil.

4.1.2.6. Terrestrial Microorganisms

As noted in Section 2.2, borax and DOT are effective in the control of fungal disease in conifers caused by the fungi *Heterobasidion irregulare* or *Heterobasidion occidentale*. The borates are also effective for the control of species of fungi and bacteria (U.S. EPA/OPP/EFED 2015a). Given these uses, it seems reasonable to identify soil microorganisms as organisms of potential concern in the application of borates.

Notwithstanding the above statements, many fungi and bacteria are less sensitive than plants to boron toxicity (Butterwick et al. 1981). More recently, Becker et al. (2011) demonstrated that boric acid concentrations of up to 2400 mg/kg soil dry weight (≈ 420 mg B/kg soil) did not decrease soil nitrate levels. In studies involving bacteria grown in culture media, no effects were observed in *Bacillus firmus* at concentrations of up to about 10,000 mg B/L [1000 mM] (Verce et

al. 2012) or in *Rhodococcus baikonurensi* at concentrations of up to about 1000 mg B/L [100 mM] (Yoon et al. 2010).

A more sensitive species of bacteria in growth media assays is *Escherichia coli*. Yu et al. (2013) report an EC_{50} of 570 mg borax/L (≈64.4 mg B/L) for the inhibition of respiration. While *E. coli* may survive in soil as naturalized strains, this species exists most commonly as coliform bacteria in the digestive tract, with some strains being pathogenic (VanderZaag et al. 2010).

As with soil invertebrates and terrestrial plants, the toxicity data on soil microorganisms is noted only for the sake of completeness. As discussed in Section 4.2.3, stump treatments with borates will not contribute substantially to background levels of boron in soil—i.e., about 10 to 100 mg B/kg soil.

4.1.3. Aquatic Organisms

4.1.3.1. Fish

Boron toxicity data on fish are summarized in Appendix 5. All of the available toxicity studies summarized in Appendix 5 involve either borax or boric acid; none of the studies were conducted with DOT (disodium octaborate tetrahydrate). The lack of toxicity studies on DOT does not have a substantial impact on the current risk assessment. As discussed in Section 2.2, both borax and DOT are converted to boric acid, and boric acid is the agent of toxicological concern. Based on an 96-hour LC_{50} of 404 mg BA/L in fathead minnow (equivalent to 70.6 mg B/L), U.S. EPA/OPP/EFED (2015a, Table 5.2, p. 39) classifies boron as slightly toxic to fish and boric acid as practically nontoxic to fish. As noted in SERA (2015a, Table 16), the EPA toxicity categories for aquatic organisms are based on mass concentrations in which LC_{50} values of 10 to 100 mg/L are classified as slightly toxic and LC_{50} values of >100 mg/L are classified as practically nontoxic. Since exposure assessments used in the EPA risk assessment as well as the current risk assessment are based on boron equivalents, the categorization of boron as slightly toxic is most germane to the current risk assessment.

Based on the acute LC_{50} values summarized in Appendix 5, Table A5-1, the fathead minnow appears to be the most sensitive species with an LC_{50} of 70.6 mg B/L, as summarized in U.S. EPA/OPP/EFED (2015a). The least sensitive species appears to be rainbow trout. For this species, indefinite LC_{50} values are reported to range from >140 mg B/L (U.S. EPA/OPP/EFED 2015a) to >192 mg B/L (U.S. EPA/OPP 1992a). In a review, Hovatter and Ross (1995) cite a definitive 48-hour LC_{50} of 387 mg B/L attributed to Alabaster (1969). As indicated in Appendix 5, Table A5-1, this toxicity value cannot be located in the paper by Alabaster (1969). While differences in species sensitivities are typically a major focus in the Forest Service risk assessments, these differences do not have a substantial impact on the current Forest Service risk assessment. As discussed further in Section 4.4.3 (risk characterization for aquatic species), exposure levels of borates associated with stump applications are far below the level of concern for fish and other aquatic organisms.

Several early life-stage studies were conducted with boric acid or borax, as summarized in Appendix 5, Table A5-2. For characterizing chronic risks to fish, U.S. EPA/OPP/EFED (2015a, Table 5.2, p. 39) uses a NOAEC of 7.4 mg B/L in fathead minnow with a corresponding LOAEL of 13 mg B/L, based on a decrease in post-hatch survival (MRID 48914601). The open literature

study by Padilla et al. (2012) reports a much lower developmental EC_{50} of 60.685 µM for boric acid in zebrafish (*Danio rerio*). Taking a molecular weight of 10.811 g/mole for boron, this EC_{50} corresponds to about 0.656 mg B/L [0.060685 mM x 10.811 mg/mM ≈ 0.65607 mg B/L]. U.S. EPA/OPP/EFED (2015a, Table 16, p. 101) appears to convert a concentration of 0.656 mg a.e./L to 3.75 mg B/L. The basis for this conversion is unclear. In any event, the results reported by Padilla et al. (2012) are not consistent with another bioassay in zebrafish which reports an NOAEC of 13 mg B/L (U.S. EPA/OPP/EFED 2015a, ECOTOX ID: E105984) as well as much higher LC_{50} values for zebrafish embryos—i.e., about 60 mg B/L (Selderslaghs et al. 2012) and 197 mg B/L (Teixido et al. 2013).

Despite the lack of available information demonstrating that boron is an essential element for fish, the study by Rowe et al. (1998, Figure 3 of paper) does note a classic U-shaped dose-response curve for both rainbow trout and zebrafish (as illustrated in Figure 2 of the current risk assessment).

4.1.3.2. Amphibians (Aquatic Phase)

Information on the toxicity of borates to aquatic phase amphibians is summarized in Appendix 6. In terms of acute toxicity, the reported LC_{50} values for amphibians range from about 47 mg B/L (the leopard frog in the study by Birge and Black 1977) to over 239 mg B/L (the African clawed frog, as summarized in U.S. EPA/OPP/EFED 2015a). This range of acute LC_{50} values is similar to the range for fish—i.e., about 70 mg B/L to >192 mg B/L, as discussed in Section 4.1.3.1.

The similarities in the sensitivity of amphibians and fish to boron are evident in the early life-stage studies by Birge and Black (1977). As summarized in Appendix 6, Table A6-2, LC_{50} values for two species of frogs range from 47 to 145 mg B/L. As summarized in Appendix 5, Table A5-2, this study cites a similar range of LC_{50} values in three species of fish—i.e., about 22 to 155 mg B/L.

In addition to the early life-stage studies by Birge and Black (1977), several studies in amphibians involved exposure periods of about 30 days (Fort et al. 1998, 2001; Lapsota and Dunson 1998). As with the acute toxicity studies, Fort et al. (1998, 2001) noted malformations at both low and high, but not intermediate, levels of exposure. As discussed in Section 3.1.4.1, the testes and sperm are target organs for boron in mammals. Testicular toxicity and abnormal sperm development were also observed in the African clawed frog in the study conducted by Fort et al. (2001). Lapsota and Dunson (1998) did not assay for potential boron deficiency but did observe fetotoxic and developmental abnormalities at concentrations of about 50 mg B/L and higher in four species of amphibians.

As discussed in Section 3.1.2 and illustrated in Figure 2, dose-response curves for boron are sometimes biphasic with adverse effects occurring at low and high concentrations. The study by Fort et al. (1998) notes that boron concentrations of less than 3 µg B/L over a 4-day period increased mortality in African clawed frog embryos; whereas, concentrations of up to 5 mg B/L did not cause adverse effects. In a longer-term (30-day) study in this species, adverse effects were observed only at concentrations of 50 mg B/L and higher (Fort et al. 2001).

4.1.3.3. Aquatic Invertebrates

As summarized in Appendix 7, there is a robust literature on the effects of borates to aquatic invertebrates. Based on acute toxicity studies (Appendix 7, Table A7-1), the most sensitive species appears to be *Ceriodaphnia dubia* with EC_{50} values ranging from about 45.5 mg B/L (ECOTOX ID E118810 as summarized in U.S. EPA/OPP/EFED 2015a) to 180.6 mg B/L (Hickey 1989). A related cladoceran, *Daphnia magna*, appears to be almost as sensitive with EC50 values ranging from about 73 mg B/L (Bringmann and Kuhn 1977) to 319.8 mg B/L (Hickey 1989). The somewhat higher EC_{50} values reported by Hickey (1989) are probably attributable at least in part to the 24-hour duration of the Hickey (1989) bioassays. All other EC_{50} values for the daphnids are based on 48 hour exposures.

Dipterans and ostracods appear to be relatively tolerant to boron with 48-hour LC_{50} values of 1376 mg B/L (the dipteran *Chironomus decorus* from the study by Maier and Knight 1991) and 645 mg B/L (the ostracod *Cypris subglobosa* from the study by Khangarot and Das 2009). These comparisons, however, are limited because the observations are based only a single assay and a single species for each order.

The saltwater shrimp, *Litopenaeus vannamei*, appears to be somewhat less sensitive to boron with 48-hour LC_{50} values of 153.35 mg B/L in water with 3% salinity and 219.52 mg B/L in water with 20% salinity (Li et al. 2008). As detailed in Appendix 7, Table A7-1, the study by Li et al. (2008) provides 24, 48, 72, and 96 hour LC_{50} values and a strong temporal effect is apparent. For example, the 96-hour LC_{50} is below the 24-hour LC_{50} by a factor of over 20 in water with 3% salinity [552.55 mg B/L ÷ 25.05 mg B/L ≈ 22.058]. Other studies do not provide EC_{50} or LC_{50} values over a similar range of durations.

Reported acute EC_{50} values in bivalves are somewhat variable. The most sensitive species is the black sandshell mussel with an 96-hour EC_{50} of 147 mg B/L and the least sensitive species is washboard mussel with an indefinite 96-hour EC_{50} of >554 mg B/L (U.S. EPA/OPP/EFED 2015a). Despite this range of toxicity, boron is classified as *practically non-toxic* to all three of these species (U.S. EPA/OPP/EFED 2015a, p. 90).

As summarized in Appendix 7, Table A7-2, differences in chronic toxicity among aquatic invertebrates are not remarkable. The most sensitive NOAECs for daphnids are in the range of about 6 to 10 mg B/L for both *Ceriodaphnia dubia* (Hickey 1989) and *Daphnia magna* (Lewis and Valentine 1981; Gerisch 1984). For benthic organisms, similar NOAECs based on pore water concentrations have been reported in the study by Hall et al. (2014) for clams (i.e., a 21-day NOAEC for growth of 10 mg B/L) and blackworms (an NOAEC of 12.5 mg B/L in pore water). As with other groups of aquatic invertebrates, these NOAECs are substantially above concentrations that could be associated with stump applications (i.e., about 0.043 mg B/L) as well as maximum background concentrations of boron in surface water (i.e., about 1.5 mg B/L).

4.1.3.4. Aquatic Plants

4.1.3.4.1. Algae

Studies on the toxicity of borates to algae are summarized in Appendix 8, Table A8-1. The studies include standard bioassays submitted to EPA in support of the registration of borates. Summaries of these studies are taken from U.S. EPA/OPP/EFED (2015a). Additional studies on algae are available in the open literature. The EPA summaries are more detailed than the open literature publications and include EC_{50} values as well as NOAECs and LOAECs.

Boric acid and some borate salts are registered as algicides (U.S. EPA/OPP/EFED 2015a, p. 48). Some species of algae are modestly more sensitive than either fish or aquatic invertebrates to boron exposure. The most sensitive species of algae appears to be *Anabaena flosaquae* with a 96-hour EC_{50} of 14.2 mg B/L (MRID 48820801). Based on EC_{50} values, the most tolerant species of algae appears to be *Navicula pelliculosa* with a 96-hour EC_{50} of 102 mg B/L. As discussed further in the dose-response assessment (Section 4.3.3.4.1), the most tolerant species based on NOAECs appears to be *Skeletonema costatum* with an NOAEC of 47.1 mg B/L.

In several of the studies summarized in U.S. EPA/OPP/EFED (2015a, Table I12, p. 103), the EPA notes that boric acid appears to be algistatic rather algicidal. These studies are not described in detail but appear to have involved taking algae subject to high concentrations of boric acid (≈1000 mg a.e./L or 175 mg B/L), transferring the algae to lower concentrations (10 to 66 mg a.e./L or 1.75 to ≈12 mg B/L), and observing substantial increases in algal growth.

4.1.3.4.2. Aquatic Macrophytes

Information on the toxicity of borates to aquatic macrophytes is summarized in Appendix 8, Table A8-2. For many pesticides, including many herbicides, toxicity data on aquatic macrophytes are limited to relatively standardized bioassays on duckweed, either *Lemna gibba* or *Lemna minor*. One bioassay on *Lemna gibba* is summarized in U.S. EPA/OPP/EFED (2015a). The bioassay reports a 7-day EC_{50} of 28.5 mg B/L for reduced biomass with an NOAEC of 11 mg B/L and a LOAEC of 22 mg B/L (MRID 48820802). This registrant-submitted study is supported by an open literature study conducted by Brick (1985) in which exposure of *Lemna minor* resulted in a NOAEC of 20 mg B/L and a LOAEC of 100 mg B/L, based on growth inhibition, with mortality at 200 mg B/L for a 6-day exposure. As with the aquatic algae discussed in the previous section, the growth inhibition observed in the Brick (1985) study was reversible when the duckweed was transferred to control media.

Based on the findings of other studies in the open literature, duckweed does not appear to be the most sensitive species; however, these comparisons are compromised by differences in study duration. The lowest EC_{50} value is 5 mg B/L in both species of *Elodea* and *Myriophyllum* (watermilfoil) based on 21-day exposures (Nobel 1981). Based on the study by Bergmann et al. (1995) as summarized in ECETOC (1997) and IPCS/WHO (1998), the most tolerant species of aquatic macrophyte appears to be *Phragmites australis*, a perennial aquatic grass, with a 3-month NOAEC of 8 mg B/L and a 2-year NOAEC of 4 mg B/L.

4.1.3.5. Other Aquatic Microorganisms

Aquatic microorganisms are not a group of organisms typically considered in EPA risk assessments. As reviewed by IPCS/WHO (1998, pp. 108-111), data are available primarily from

the German literature indicating that the toxicity of boron to aquatic microorganisms is similar to that of algae with minimal response toxicity values (i.e., NOAEC, EC_3, and EC_{10}) in the range of 0.3 to nearly 300 mg B/L (IPCS/WHO 1998, Table 18, p. 109). The lower end of this range is based on a study by Bringmann and Kuhn (1980) which reports an EC_3 value (presumably a 3% inhibition of growth) of 0.3 mg B/L for *Entosiphon sulcatum*, a protozoan flagellate. This toxicity value is not supported by the Guhl (1996) study in the same species, which reports an NOEC of >10 mg B/L. With the exception of the low EC_3 by Bringmann and Kuhn (1980), other minimal response toxicity values for aquatic microorganisms are in the range of 7.6 to 340 mg B/L, somewhat higher than those generally noted for algae (Section 4.1.3.4.1). Consequently, aquatic microorganisms do not appear to be more sensitive than aquatic algae. Consistent with the approach used in the most recent EPA ecological risk assessment (U.S. EPA/OPP/EFED 2015a), aquatic microorganisms other than algae are not considered as a separate subgroup.

4.2. EXPOSURE ASSESSMENT

4.2.1. Overview

As discussed in Section 3.2, Cellu-Treat® and Sporax® are applied directly to the surfaces of freshly cut tree stumps. These borates are not applied using broadcast spray methods and not applied directly to vegetation. Therefore, many of the standard exposure scenarios 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 likely to result in potentially significant exposures considering the atypical application method for these borates.

The exposure assessments for terrestrial vertebrates are summarized in Worksheet G01 of the attachments to this risk assessment. The highest levels of potential exposure are associated with the consumption of borates from treated stumps. This is an atypical exposure scenario not used in other Forest Service risk assessments. Adopting and modifying the EPA approach for estimating risks from exposures in units of LD_{50}/ft^2, the estimated exposure levels of boron for mammals and birds following Cellu-Treat® applications are about 3.5 (1.7 to 7) mg B/kg bw. For Sporax, the estimated doses are substantially higher—i.e., about 15 (7 to 30) mg B/kg bw. The differences between the exposures for Cellu-Treat® and Sporax® are due to differences in the stump application rates for Cellu-Treat® and Sporax, as discussed in Section 2.3. The other exposure scenarios are analogous to those used for members of the general public (Section 3.2.3) and include the consumption of contaminated water and the consumption of contaminated fish. For these scenarios, the highest estimated exposure is about 0.13 mg/kg bw—i.e., the upper bound for a small bird consuming contaminated water following an accidental spill.

There is no basis for asserting that stump applications of borates will lead to significant increases in the concentration of boron in soils. Consequently, a formal exposure assessment for soil contamination is not developed for either terrestrial invertebrates or plants. The potential for exposures of terrestrial plants from spray drift also seems low. Nonetheless, estimates of drift are developed for terrestrial plants for stump applications of liquid solutions of borates. These estimates are based on standard drift values used for backpack foliar applications of herbicides. Consequently, the estimates are likely to overestimate exposures and perhaps grossly so.

Exposure levels for aquatic organisms are based on the same estimates of boron concentrations in water used to assess the exposure to human and other terrestrial species from contaminated water. While soil organisms may be exposed to boron following stump applications of either Cellu-Treat® or Sporax, these applications will not significantly increase the concentration of boron in soil.

4.2.2. Mammals and Birds

4.2.2.1. Oral Exposure to Sporax® Applied to Tree Stumps

One obvious route of exposure for mammals and birds involves the direct consumption of boron from tree stumps. 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.

Very little information, however, is available to estimate objectively the amount of boron that deer, other mammals, or birds might consume. For exposure assessments involving broadcast applications of borates as a liquid, the U.S. EPA/OPP/EFED (2015a, Table 5.4, p. 40) uses standard residue rates commonly used in Forest Service risk assessments (SERA 2014a, p. 66). For granular applications of borates, the EPA uses the LD_{50}/ft^2 method (U.S. EPA/OPP/EFED 2015a, Table 5.5, p. 40). As discussed in U.S. EPA/OPPTS (2004, p. 40), this method involves comparing the amount of pesticide applied per square foot to an acute LD_{50} value.

For large mammals, such as a deer, it seems plausible that a deer might consume all of the borates applied to a tree stump within a 1 square foot surface area. As detailed in Worksheet F01 of the attachments to this risk assessment, this assumption is elaborated to consider a deer (70 kg) consuming borates from a 1 (0.5 to 2) square foot area which could involve one or several tree stumps. As discussed in Section 2.4, the stump application rate for Cellu-Treat® is 0.000525 lb B/ft^2 and the corresponding rate for Sporax® is 0.00226 lb B/ft^2. Based on these assumptions, the amount of boron consumed by the deer and the dose to the deer may be readily calculated. Note that this exposure assessment should be viewed as a unit estimate, similar to the LD_{50}/ft^2 method used by EPA. As discussed further in the risk characterization (Section 4.4.2), the estimated HQs for this exposure scenario are interpreted in terms of the surface area of a treated stump that a deer must consume to approach a level of concern (HQ=1).

Modifications of the above exposure scenario for the deer are developed for a large bird (4 kg) in Worksheet F02, small mammal (20 g) in Worksheet F03, and small bird (10 g) in Worksheet F04. The characteristics of these receptors are detailed in Table 17. It is, of course, not reasonable to assume that small animals will consume as much as 70 kg deer will consume. Consequently, the estimates of the stump surface areas consumed by these small organisms are approximately scaled to body weights. As with the deer scenario, the resulting HQs are based on the amount of borate on the treated stump (in units of mg B/ft^2) multiplied by the scaled estimate of the surface area (ft^2) of the treated stump that the small mammal might clear.

Note that the LD_{50}/ft^2 method is typically used by EPA for granular applications. For liquid applications, it seems reasonable to suppose that mammals and birds would consume lesser amounts of borate than would be the case for granular applications. In other words, a liquid application would probably lead to more rapid absorption of borates into the treated stump, leaving lesser amounts of borates available for consumption by a mammal or bird. While this difference is acknowledged, the available data do not permit a quantitative estimate of the difference, as discussed further in the risk characterization (Section 4.4.2).

4.2.2.2. Ingestion of Contaminated Water

The methods for estimating boron concentrations in water are identical to those used in the human health risk assessment (Section 3.2.3.4) using the water contamination rates (mg B/L of water per lb B/acre), as summarized in Table 14. In the attachments to this risk assessment, the water contamination rates are entered into Worksheet B04Rt and adjusted to expected concentrations in water in Worksheet B04a. As with the human health risk assessment (Section

3.2.3.4.1), exposure scenarios are also developed for an accidental spill, as detailed in Worksheet B04b.

Exposure scenarios for birds and mammals are developed for a small mammal and a small bird in Worksheets F05a/F06a (accidental spill), F05b/F06b (peak expected exposures), and F05c/F06c (longer-term exposures). Body weight and water consumption rates are the major differences in the exposure estimates for birds and mammals, relative to humans. The water consumption rates, which are well characterized in terrestrial vertebrates, are based on allometric relationships in mammals and birds, as summarized in Table 17.

Like food consumption, water consumption in birds and mammals varies substantially with diet, season, and many other factors. Quantitative estimates regarding the variability of water consumption by birds and mammals are not well documented in the available literature and are not considered in the exposure assessments. As discussed further in Section 4.4.2.1 (risk characterization for mammals) and Section 4.4.2.2 (risk characterization for birds), exposures associated with the consumption of contaminated surface water are far below the level of concern (HQ=1). Consequently, extreme variations in the estimated consumption of contaminated water by mammals and birds would have no impact on the risk characterization for mammals and birds.

4.2.2.3. Ingestion of Contaminated Fish

As with the consumption of contaminated water, the consumption of contaminated fish by piscivorous species is a potential route of exposure to boron. Exposure scenarios are developed for the consumption of contaminated fish by a 4 kg carnivorous mammal and a 2.4 kg piscivorous bird for an accidental spill (Worksheets B07a/B08a), peak expected exposures (Worksheets B07b/B08b), and longer-term exposures (Worksheets B07c/B08c). As summarized in Table 17, the 5 kg mammal is representative of a fox, and the 2.4 kg bird is representative of a heron. As with the contaminated fish scenario in the human health risk assessment (Section 3.2.3.5), the corresponding exposure assessments for wildlife use a bioconcentration factor of 1 L/kg—i.e., no bioconcentration.

4.2.2.4. Direct Spray

The unintentional direct spray of a small mammal during broadcast applications of a pesticide is a standard exposure scenario in Forest Service risk assessments and is a credible exposure scenario, similar to the accidental exposure scenarios for the general public discussed in Section 3.2.3.2. For directed applications of borates to stumps, however, this exposure scenario seems less likely than standard directed foliar applications. While this exposure scenario cannot be ruled out, the direct spray of a small mammal is included in the current risk assessment. This exposure scenario is used only for liquid applications of Cellu-Treat (Attachment 1) and Sporax (Attachment 2). In this exposure scenario, the amount of pesticide absorbed depends on the application rate, the surface area of the organism, and the rate of absorption.

For this risk assessment, two direct spray or broadcast exposure assessments are conducted. The first spray scenario (Worksheet F09a) concerns the direct spray of half of the body surface of a 20 g mammal during a pesticide application. This exposure assessment assumes first-order dermal absorption using the first-order dermal absorption rate coefficient (k_a) discussed in Section 3.1.3.2. The second exposure assessment (Worksheet F09b) assumes complete

absorption over Day 1 of exposure. This assessment is included in an effort to encompass increased exposures due to grooming.

Exposure assessments for the direct spray of a large mammal are not developed. As discussed further in Section 4.4.2.1, the direct spray scenarios lead to HQs far below the level of concern, and an elaboration for body size would have no impact on the risk assessment.

4.2.3. Terrestrial Invertebrates and Other Soil Invertebrates

Forest Service risk assessments typically include formal exposure assessments for direct spray and the consumption of contaminated vegetation or prey. These exposure scenarios are not relevant to stump applications. As discussed in Section 4.1.2.4, toxicity data are available for terrestrial insects, and incidental exposures to insects on or near a tree stump could occur during applications of borates. An objective method for estimating these exposures is not apparent. As discussed further in the risk characterization (Section 4.4.2.4), these exposures might adversely affect individual organisms exposed during stump applications of borates but are not likely to affect insect populations.

As summarized in Appendix 9, Table A9-1, the maximum impact of stump applications on the concentration of boron in soil at an application rate of 1 lb B/acre would be about 0.5 mg B/kg soil. As discussed in Section 2.3, the maximum application rate for the borates is about 0.1 lb B/acre, and the maximum contribution of stump applications to soil concentrations of boron would be about 0.05 mg B/kg soil. Normal background concentrations of boron in soil range from about 1.5 mg/kg soil to 300 mg B/kg soil. Thus, at the lower range of the background concentrations, stump applications of borates would increase soil concentrations of boron by a factor of about 0.3% [0.05 mg B/kg soil ÷ 1.5 mg/kg soil = 0.00333…]. This increase is insubstantial; therefore, formal exposure assessments are not developed for soil invertebrates. This assessment is supported by detailed monitoring data from Dost et al. (1996, Appendix A, Tables 1-4) indicating modest but inconsistent increases in soil boron near some treated stumps but no substantial or consistent increases of boron concentrations in soil away from treated stumps. Increases in soil boron near (i.e., within 5 cm) treated stumps is noted also by Lloyd and Pratt (1997, Table 3 of paper, p. 137). Thus, while soil boron levels may be increased in areas immediately adjacent to treated stumps, general increases of soil boron are not expected to extend beyond the treated area.

4.2.4. Terrestrial Plants

Forest Service risk assessments typically include exposure scenarios associated with runoff (i.e., contamination of soil) and spray drift (foliar exposures). As with terrestrial invertebrates (Section 2.4.3), there is no basis for asserting that stump applications of borates will lead to significant increases in the concentration of boron in soils. Consequently, a formal exposure assessment for soil contamination is not developed.

The potential for exposures of terrestrial plants from spray drift seems low. Standard backpack applications of herbicides may involve treatment of vegetation up to or possibly above the chest height of the applicator. In the case of stump applications, the borate solution will be applied essentially at ground level (i.e., the height of the treated stump); hence. offsite drift should be minimal. Nonetheless, at the request of the Forest Service, a standard backpack drift scenario is

developed as detailed in Worksheet G04 of Attachment 1 (liquid applications of Cellu-Treat) and Attachment 2 (liquid applications of Sporax).

Drift associated with backpack applications (directed foliar applications) is likely to be much less than drift from ground broadcast applications. Few studies, however, are available for quantitatively assessing drift after backpack applications. For the current Forest Service risk assessment, estimates of drift from backpack applications are based on an AgDRIFT Tier 1 run of a low boom ground application using Fine to Medium/Coarse drop size distributions (rather than very fine to fine) as well as 50th percentile estimates of drift (rather than the 90th percentile used for ground broadcast applications). Thus, the drift estimates should be regarded as little more than generic estimates similar to the water concentrations modeled using GLEAMS (Section 3.2.3.4.3). Actual drift will vary according to a number of conditions—e.g., the topography, soils, weather, and the pesticide formulation. All of these factors cannot be considered in this general risk assessment.

Notwithstanding the above reservations, it seems reasonable to suggest that the general drift estimates used in the current risk assessment, which are generally used for herbicide applications, will overestimate drift of borates during stump applications. As discussed further in Section 4.4.2.5 (risk characterization for terrestrial plants), the exposure scenarios for drift lead to HQs that are substantially below the level of concern (HQ=1).

4.2.5. Aquatic Organisms

Exposure assessments for aquatic organisms are based on estimated boron concentrations in water, identical to those used in the human health risk assessment (Section 3.2.3.4.6) and the risk assessment for terrestrial vertebrates (Section 4.2.2.2). The water contamination rates are summarized in Table 14 and the application of these rates to estimating expected concentrations of boron in water are discussed in Section 3.2.3.4.6.

4.3. DOSE-RESPONSE ASSESSMENT

4.3.1. Overview

The specific toxicity values used in this risk assessment are summarized in Table 18, and the derivation of each of these values is discussed in the various subsections of this dose-response assessment. The available toxicity data support separate dose-response assessments in four groups of terrestrial organisms (i.e., mammals, birds, invertebrates and plants) as well as five groups of aquatic organisms (fish, aquatic phase amphibians, aquatic invertebrates, aquatic macrophytes, and algae). 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.

Borates are relatively nontoxic to mammals and birds. Based on both acute and chronic NOAELs, birds appear to be modestly more sensitive than mammals to borates—i.e., a factor of about 3 based on acute NOAELs [350 mg/kg bw/day ÷ 113 mg/kg bw/day ≈ 3.1] and a factor of about 2 based on chronic NOAELs [8.8 mg/kg bw/day ÷ 3.7 mg/kg bw/day ≈ 2.3]. Given that NOAELs reflect experimental doses rather than statistical estimates of a threshold, these differences are insubstantial. While the data on terrestrial invertebrates is limited, there is no indication that invertebrates are more sensitive than mammals and birds to borates.

The borates are not remarkably toxic to aquatic organisms. The estimated acute NOAELs for sensitive species of amphibians, fish, aquatic invertebrates, aquatic invertebrates, and aquatic macrophytes span a narrow range—i.e., from about 0.7 to 5 mg B/L for acute exposures and 0.7 to 4 mg B/L for longer-term exposures. The estimated NOAELs for tolerant groups of aquatic organisms are more variable; however, this variability has little impact on the risk characterization. The dose-response assessment for aquatic invertebrates is somewhat atypical, because of limitations in the available data and because estimates of acute NOAECs are used for both acute and longer-term exposures.

4.3.2. Toxicity to Terrestrial Organisms

4.3.2.1. Mammals

In characterizing risk to mammalian wildlife, Forest Service risk assessments generally use the NOAELs which serve as the basis for the acute and chronic RfDs from the human health risk assessment.

As discussed in Section 3.3.2 and summarized in Table 16, several acute toxicity values for boron have been derived by offices within the EPA as well as the Agency for Toxic Substances and Disease Registry (ATSDR). As also discussed in Section 3.3.2 and summarized in Table 15, the current Forest Service risk assessment adopts the acute RfD of 3.5 mg/kg bw/day based on the NOAEL in rats of 350 mg/kg bw/day. This is the most recent acute RfD derived by EPA. It should be noted that the most recent EPA ecological risk assessment uses an LD_{50} of 450 mg boric acid/kg bw (79 mg B/kg bw) for risk characterization (U.S. EPA/OPP/EFED 2015a, p. 35) referenced to Weir and Fisher (1972). The paper by Weir and Fisher (1972, p. 354) notes several LD_{50} values for boric acid in the range of 3.16 to 4.08 g/kg bw for boric acid, but an LD_{50} of 450 mg boric acid/kg bw was not identified in the paper.

As also summarized in Table 15, the chronic NOAEL is taken as 8.8 mg/kg bw/day. This NOAEL is also taken from Weir and Fisher (1972) and is used by U.S. EPA/OPP/HED (2015) as the basis for the chronic RfD.

As discussed in Section 4.1.2.1, there are no apparent or substantial differences in sensitivities to borates among different groups of mammals. Consequently, the acute and chronic NOAELs discussed above are applied to all groups of mammals considered in the current risk assessment.

4.3.2.2. Birds

As with mammals, Forest Service risk assessments generally defer to the U.S. EPA/OPP on study selection, unless there is a compelling reason to do otherwise. Unlike the EPA, however, Forest Service risk assessments use acute NOAELs or NOAECs rather than acute LD_{50} or LC_{50} values (SERA 2009, Section 5.2.1). For characterizing acute risks to birds, the most recent EPA ecological risk assessment uses scaled indefinite gavage LD_{50} values ranging from >1170 to >2100 a.e./kg bw (≈ 200 to 370 mg B/kg bw) and an acute dietary LC_{50} of >5620 mg a.e./kg bw (≈980 mg B/kg diet) (U.S. EPA/OPP/EFED 2015a, p. 39). As noted in Appendix 2, Tables A2-1 and A2-2, the lowest NOAEL is 113 mg B/kg bw in quail from the gavage study by Fink et al. (1982a, MRID 00100657). This NOAEL is supported by an acute dietary NOAEL of 136 mg B/kg bw in quail with the dose estimate based on reported food consumption and body weights (Reinart and Fletcher 1977, MRID 00149195). The somewhat lower (i.e., more conservative) NOAEL of 113 mg B/kg bw is used to characterize acute risks to birds in the current Forest Service risk assessment.

For chronic exposures, the U.S. EPA/OPP/EFED (2015a, Table 5.4, p. 39) uses a chronic NOAEL of 249 mg a.e./kg diet in mallards (MRID 49009801). As summarized in Appendix 2, Table A2-3, this NOAEL is the lowest reported NOAEL in birds and is equivalent to a dose of 3.7 mg B/kg bw/day based on EPA dose estimates which are presumably based on reported food consumption and body weights. This NOAEL is supported by a somewhat higher reproductive NOAEL of 6 mg B/kg bw/day in quail (MRID 49185901). While these two NOAELs are not substantially different, the current Forest Service risk assessment, consistent with the approach used by EPA, uses the lower NOAEL of 3.7 mg B/kg bw/day in mallards as the NOAEL for the most sensitive species.

As discussed further in the risk characterization for birds (Section 4.4.2.2), all of the acute and chronic HQs are substantially below the level of concern (HQ=1); thus, an elaboration of the dose-severity relationships is unnecessary.

4.3.2.3. Reptiles and Amphibians (Terrestrial Phase)

The toxicity of borates to terrestrial phase amphibians is not addressed in the available literature, as discussed in Section 4.1.2.3. Consequently, no dose-response assessment for this group of organisms is developed. Also, as noted in Section 4.1.2.3, U.S. EPA/OPP/EFED (2015a, p. 39) uses birds as a surrogate for reptiles and terrestrial-phase amphibians, as discussed further in the risk characterization for terrestrial phase amphibians (Section 4.4.2.3).

4.3.2.4. Terrestrial Invertebrates

As discussed in Section 4.1.2.4, borates are registered as insecticides, acaricides, and molluscicides, and the available literature on the toxicity of borates to terrestrial invertebrates is

substantial. Even though, as discussed in Section 4.2.3, stump applications of borates may result in incidental and possibly substantial exposures to individual insects, there is not an objective method to estimate the magnitude of these incidental exposures. Accordingly, no exposure assessments for terrestrial invertebrates involving stump applications are derived in the most recent EPA ecological risk assessment (U.S. EPA/OPP/EFED 2015a). As noted in Section 4.2.3, exposure assessments could be developed for soil invertebrates; however, because boron is naturally occurring in soils and stump applications will not substantially increase boron levels in soils, dose-response assessments for fossorial invertebrates are not warranted.

For the sake of completeness, it is noted that the NOAEL for honeybees (i.e., a standard test species used by EPA) is 63 µg B/bee. This toxicity value reported in Atkins (1987), as summarized in Appendix 3, Table A3-1, is cited in the recent EPA ecological risk assessment and used to classify boric acid as Practically Nontoxic to the honeybee (U.S. EPA/OPP/EFED 2015a). Taking a body weight of 116 mg for this species (Winston 1987, p. 54), the toxicity value is equivalent to about 0.543 µg/mg bw or 540 mg B/kg bw. This NOAEL is included in Table 18 for comparison to NOAELs in birds and mammals but is not otherwise used in the current risk assessment.

4.3.2.5. Terrestrial Plants and Microorganisms

Also, as noted in Section 4.1.2.5, the NOAEL for seedling emergence in plants is >0.87 lb B/acre, which is substantially higher than the functional application rates of about 0.1 lb B/acre used in Forest Service programs (Section 2). In addition, the exposure assessment (Section 4.2.3) for plants indicates that stump applications will not lead to substantial and wide-spread increases in boron levels in soil. Consequently, formal dose-response assessments for terrestrial plants and microorganisms associated with soil exposures are not derived.

As also discussed in Section 4.2.4, drift during liquid stump applications of borates should be less than drift during standard foliar applications of herbicides. Nonetheless, exposures of terrestrial plants to borate associated with drift during stump applications are considered in the current risk assessment. For characterizing risks associated with foliar exposures due to drift, the current Forest Service risk assessment uses the NOAEL of ≥ 0.03 lb B/acre from MRID 48885401. This is identical to the approach taken in the most recent ecological risk assessment from U.S. EPA/OPP/EFED (2015a, Table 4.3, p. 36). Note that ≥ 0.03 lb B/acre is a free-standing NOAEL—i.e., exposure levels associated with signs of toxicity were not identified. As discussed further in Section 4.4.2.5 (risk characterization in terrestrial plants), this is not a serious limitation in the current risk assessment because all HQs associated with drift are substantially below the level of concern (HQ=1).

4.3.3. Aquatic Organisms

Stump applications of borates could increase general background levels of exposure to boron in surface waters in areas with low levels of naturally occurring boron. Unlike the case with soil exposures, these increases would not necessarily be limited to areas directly adjacent to treated stumps. As summarized in Table 2, reported background levels of boron in U.S. waters are variable but generally cover a range of about 0.04 to >1 mg B/L. Based on the Water Contamination Rates (WCRs in units of mg B/L per lb B/acre) from the GLEAMS-Driver modeling (Table 14) and the estimated application rates in Forest Service programs (i.e., about 0.1 lb B/acre as discussed in Section 2), upper bound estimates of expected additions of boron

concentrations in surface water attributable to stump applications are less than 0.05 mg B/L. These calculations are detailed in Worksheet B04a of the EXCEL workbooks that accompany this risk assessment. Thus, under extreme conditions (i.e., low levels of naturally occurring boron and high levels of boron loss to surface water from stump applications, stump applications could increase boron concentrations in surface water by a factor of 2 or more (i.e., ≈0.04 mg B/L background plus up to 0.05 mg B/L attributable to stump applications). Thus, a standard set of dose-response assessments for aquatic organisms is warranted.

4.3.3.1. Fish

4.3.3.1.1. Sensitive Species

As with other groups of organisms, Forest Service risk assessments typically base dose-response assessments on studies identified by EPA as most appropriate for risk characterization of sensitive species. For acute exposures of fish to borates, U.S. EPA/OPP/EFED (2015a, Table 5.2, p. 39) uses the LC_{50} of 404 mg a.e. (≈70.6 mg B/L) as the lowest LC_{50} for fish. Forest Service risk assessments use NOAECs rather than LC_{50} values for characterizing risk (SERA 2009, Section 5.2.1). In the absence of a reported NOAEC for an aquatic organism, Forest Service risk assessments adopt the variable level of concern method from the EPA and divide the LC_{50} by a factor of 20 (SERA 20014a, Section 4.4). As summarized in Appendix 5, Table A5-1, the study selected by EPA appears to be the most sensitive (i.e., the lowest available LD_{50}). This LC_{50} is supported by an LC_{50} of 97 from Furuta et al. (2007). In the absence of a reported NOAEC, the LC_{50} is divided by 20 to estimate an acute NOAEC of 3.53 mg B/L [70.6 mg B/L ÷ 20 = 3.53 mg B/L].

The chronic toxicity value for sensitive species of fish is more problematic. U.S. EPA/OPP/EFED (2015a, Table 5.2, p. 39) uses the NOAEC of 42 mg a.e./L (7.4 mg B/L) from the 32-day early life-stage study in fathead minnow (MRID 48914601). As summarized in Appendix 5, Table A5-2, Birge and Black (1977) conducted shorter-term early life-stage studies in three other species of fish and report 9-day LC_{50} values in the range of 22 to 155 mg B/L. The lowest EC_{50} is 22 mg B/L with a corresponding LC_1 of 0.2 mg B/L—i.e., the 9-day LC_{50} in channel catfish conducted in hard water. It seems overly conservative to use the 0.2 mg B/L as a functional NOAEC. Dividing the EC_{50} of 22 mg B/L leads to an estimated NOAEC of 1.1 mg B/L [22 mg B/L ÷ 20 = 1.1 mg B/L]. While perhaps a conservative approach, the current Forest Service risk assessment uses the lower estimated chronic NOAEC of 1.1 mg B/L to characterize longer-term risks in sensitive species of fish. As discussed further in Section 4.4.3.1 (risk characterization for fish), this somewhat more conservative approach has no impact on the risk characterization, because all longer-term exposures are below the level of concern. As also discussed in Section 4.4.3.1 this lower estimated NOAEC does affect the interpretation of the potential impact of background levels of boron for sensitive species of fish.

4.3.3.1.2. Tolerant Species

Based on acute toxicity studies (Appendix 5, Table A5-1), the most tolerant species of fish appears to be rainbow trout. Two registrant studies report indefinite LC_{50} values of >192 mg B/L (MRID 40594601, no mortality) and >140 mg B/L (TN 2751/TN 2860). Hovatter and Ross (1995) cite a 48-hour definitive LC_{50} of 387 mg B/L for rainbow trout and attribute this LC50 to the study by Alabaster (1969). This definitive LC_{50} cannot be verified in the Alabaster (1969)

publication. The concentration of 192 mg B/L is taken as a NOAEC for mortality and is used to characterize risks in tolerant species of fish following acute exposures.

For tolerant species of fish, the NOAEC of 7.4 mg B/L—i.e., the chronic NOAEC used by EPA, as discussed in the previous section—is used to characterize risks of longer-term exposures in fish. A somewhat higher NOAEC for zebrafish is available (Rowe et al. 1998); however, this NOAEC, while classified as an early life-stage study, involved only a 96-hour exposure.

4.3.3.2. Amphibians

As summarized in Appendix 6, acute toxicity data for aquatic phase amphibians are available only for the African clawed frog (Table A6-1), but early life-stage studies are available on several species (Table A6-2). Based on the early life-stage studies, the African clawed frog appears to be the most sensitive species with a NOAEC of 1.75 mg B/L in the reproduction study by Fort et al. (2001). Based on the early life-stage study by Birge and Black (1977), the Fowler's toad appears to be the most tolerant species with an LC_{50} of 145 mg B/L and a corresponding LC_1 of 25 mg B/L. Unlike the case with sensitive species of fish (Section 4.3.3.1.1), the LC_1 is not substantially below the LC_{50}—i.e., a factor of about 6. Moreover, it seems reasonable to use the LC_1 directly as an estimate of a functional longer-term NOAEC in tolerant species rather than dividing the early life-stage LC_{50} by a factor of 20 to approximate an NOAEC.

Given the apparent greater sensitivity of the African clawed frog, relative to other species based on longer-term exposures, the African clawed frog is taken as a sensitive species for acute exposures. Based on a 96-hour NOAEC of 5 mg B/L for the African clawed frog cited in the early life-stage study conducted by Fort et al. (1998), 5 mg B/L is taken as a NOAEC for sensitive species. As discussed in Section 4.1.3.2 and summarized in Appendix 6, Table A6-1, Fort et al. (1998) notes adverse effects in frog embryos at concentrations of less than 3 µg B/L. As summarized in Table 2, there is no indication that boron concentrations of less than 3 µg B/L will occur naturally. Thus, the potential issue of boron deficiency in at least some species of amphibians is not addressed further.

In the absence of information on the acute toxicity of boron to tolerant species of amphibians, the longer-term functional NOAEC of 25 mg B/L for Fowler's toad from the study by Birge and Black (1977), as discussed above, is used to characterize risks associated with acute exposures. As discussed further in Section 4.4.3.2 (risk characterization for amphibians), this approach has no impact on the risk characterization because all HQs for amphibians are substantially below the level of concern (HQ=1).

No comparisons with EPA toxicity values are warranted for aquatic phase amphibians. While the most recent EPA ecological risk assessment discusses toxicity studies on aquatic phase amphibians, fish are used as surrogates for aquatic phase amphibians for the purpose of risk characterization (U.S. EPA/OPP/EFED 2015a, p. 38). As summarized in Table 18, the EPA approach is clearly reasonable in that the sensitivities of fish and aquatic phase amphibians are not remarkably different. In addition, as noted above, amphibians do not appear to be a group of organisms at risk (Section 4.4.3.2).

4.3.3.3. Aquatic Invertebrates

4.3.3.3.1. Sensitive Species

For risk characterization of aquatic invertebrates, the most recent EPA ecological risk assessment uses LC_{50} values of 260 mg a.e./L (45.4 mg B/L) for *Ceriodaphnia dubia* for freshwater species and 80.1 mg a.e./L (≈14 mg B/L) for a saltwater shrimp for marine/estuarine species (U.S. EPA/OPP/EFED 2015a, Table 5.1, p. 38). As summarized in Appendix 7, Table A7-1, the lower LC_{50} of about 14 mg B/L is from the open literature study by Li et al. (2008) in *Litopenaeus vannamei*, a species of saltwater shrimp. The higher LC_{50} of about 45.4 mg B/L is from the open literature study by Dethloff et al. (2009) which reports several acute LC_{50} values for *Ceriodaphnia dubia* in both natural waters and reconstituted waters. For risk characterization, the EPA selected the lowest LC_{50} from reconstituted water with a pH of 8.1 and hardness of 96 mg $CaCO_3$/L. While this conservative approach seems appropriate, it is worth noting that all LC_{50} values from natural waters are higher than the toxicity value selected by EPA—i.e., 82.7 to 160.9 mg B/L, as detailed in Appendix A7-1 and Table 3 in the paper by Dethloff et al. (2009).

While the EPA typically derives separate acute toxicity values for freshwater and saltwater species, Forest Service risk assessments typically use the lowest toxicity value for either group of organisms. This approach is taken because of the large number of freshwater invertebrate species relative to the number of species on which data are generally available. In the absence of a reported NOAEC for sensitive species, the LC_{50} of about 14 mg B/L is divided by a factor of 20 to estimate an acute NOAEC of 0.7 mg B/L [14 mg B/L ÷ 20].

For longer-term exposures, U.S. EPA/OPP/EFED (2015a, Table 5.1, p. 38) uses a chronic NOAEC of 8.9 mg B/L. This toxicity value is specified by EPA (U.S. EPA/OPP/EFED 2015a, Table 4.1, p. 33) as an NOAEC in *Ceriodaphnia dubia* which is attributed to Lewis and Valentine (1981) and Gersich (1992). As summarized in Appendix A7-2, these papers involved *Daphnia magna*, and the NOAEC of 8.9 mg a.e./L cannot be identified in the original papers. The paper by Lewis and Valentine (1981) is correctly summarized in the EFED risk assessment on p. 92 (Table 13), and the paper by Gersich (1984) is correctly summarized in the EFED risk assessment on p. 93 (Table 13). In any event, the lowest available longer-term NOAEC for an aquatic invertebrate is the NOAEC of 6 mg B/L from the study by Lewis and Valentine (1981). Typically, this NOAEC would be used directly for risk characterization for longer-term exposures in aquatic invertebrates. As discussed above, however, the acute toxicity studies indicate that *Ceriodaphnia dubia* is less sensitive than *Litopenaeus vannamei* by a factor of about 3.25 based on acute LC_{50} values [45.5 mg B/L ÷ 14 mg B/L = 3.25]. Adjusting the longer-term NOAEC of 8.9 mg a.e./L by this ratio of relative acute toxicity, the estimated NOAEC for *Litopenaeus vannamei* would be about 1.8 mg B/L [6 mg B/L ÷ 3.25 ≈ 1.84 mg B/L]. This estimated chronic NOAEC, however, is above the estimated acute NOAEC (discussed above) of 0.7 mg B/L.

The above manipulations of toxicity values are obviously uncertain and unappealing. For boron, however, the lack of an unambiguous data set and the uncertainties in data manipulation do not have a substantial impact on the risk assessment. As discussed further in Section 4.4.3 (risk characterization for aquatic organisms), the use of the lower estimated NOAEC of 0.7 mg B/L leads to HQs that are consistently and substantially below the level of concern (HQ=1). Thus,

while the use of an acute NOAEC for the assessment of chronic risk is atypical, this approach is used in the current risk assessment.

4.3.3.3.2. Tolerant Species

As discussed above, sensitive species of aquatic invertebrates do not appear to be at risk. Thus, the dose-response for tolerant species is not a critical factor in the current risk assessment. Nonetheless, for the sake of completeness, a dose-response assessment can be developed readily. For acute exposures, the most tolerant species appears to be midge larvae (*Chironomus decorus*) with a 96-hour NOAEC for reduced growth of 10 mg B/L from the study by Maier and Knight (1991). For longer-term exposures, the highest reported longer-term NOAEC is 12.5 mg B/L from the 28-day study in *Lumbriculus variegatus*, a species of aquatic worm, from the open literature publication by Hall et al. (2014).

The acute NOAEC of 10 mg B/L in midge larvae is somewhat below the longer-term NOAEC of 12.5 mg/L in the aquatic worm. This difference may simply reflect differences in species sensitivity that cannot be documented for both acute and longer-term exposures. Nonetheless, it is not sensible to propose an acute NOAEC that is below the longer-term NOAEC for aquatic invertebrates. Consequently, the acute NOAEC is used to characterize risk for both acute and chronic exposures. As noted above, this selection of the NOAEC for tolerant species has no impact on the risk characterization.

4.3.3.4. Aquatic Plants

4.3.3.4.1. Algae

Relative to aquatic invertebrates, the dose-response assessment for algae is straightforward. For sensitive species of algae, U.S. EPA/OPP/EFED (2015a, Table 5.3, p. 39) uses an NOAEC of 9.2 mg a.e./L (≈1.6 mg B/L) for *Anabaena flosaquae*, a species of blue-green algae (MRID 48820801). As detailed in Appendix 8, Table A8-1, this is the lowest of the NOAECs reported for several species of algae. The EPA applies this NOAEC to *listed species* of algae, not otherwise specified, and uses an LC_{50} for other species. Threatened or endangered species of algae were not identified at the U.S. Fish and Wildlife Service web site for endangered species (https://www.fws.gov/endangered/); nevertheless, endangered species of algae are discussed and listed in the open literature (Brodie et al. 2009). As noted previously and discussed in SERA (2009), the Forest Service uses NOAECs rather than LC_{50} values for all species, regardless of the listed status of the species. Thus, the NOAEC of 1.6 mg B/L is used for sensitive species of algae in the current risk assessment.

Based on the available toxicity studies in algae, the most tolerant species appears to be *Skeletonema costatum*, a marine diatom, with an NOAEC of 47.1 mg B/L (MRID 48820803, as summarized in Appendix 8, Table 8-2). This study was reviewed by EPA and is classified as Supplemental/Quantitative (U.S. EPA/OPP/EFED 2015a, p. 104). As discussed in Section 4.1.3.4.1, this is one of the studies cited by EPA indicating that high concentrations of boron may be algistatic rather than algicidal. This NOAEC of 47.1 mg B/L is used to characaterize risks in tolerant species of algae.

4.3.3.4.2. Aquatic Macrophytes

For aquatic macrophytes, the most recent ecological EPA risk assessment uses a 7-day EC_{50} for growth inhibition of 163 mg a.e./L (28.5 mg B/L) and an NOAEC of 130 mg a.e./L (11 mg B/L) in *Lemna gibba* to characterize risks to non-listed and listed species of aquatic macrophytes (U.S. EPA/OPP/EFED (2015a, Table 5.3, p.39). The review by IPCS/WHO (1998), however, summarizes a study from the German literature (Bergmann et al. 1995) that reports a somewhat substantially lower NOAEC of 4 mg B/L in an aquatic grass, *Phragmites australis*. This study involved a 2-year period of exposure, which is highly atypical for a study in aquatic plants. Nonetheless, the NOAEC 4 mg B/L is supported by EC_{50} values of 5 mg B/L for decreased photosynthesis in two other species of aquatic macrophytes (Nobel 1981, as summarized in IPCS/WHO 1998). For the current Forest Service risk assessment, the NOAEC of 4 mg B/L is used for sensitive species of aquatic macrophytes. The higher NOAEC of 11 mg B/L in *Lemna gibba* is used to characterize risks in more tolerant species of aquatic macrophytes.

4.4. RISK CHARACTERIZATION

4.4.1. Overview

As with the human health risk assessment, the quantitative risk characterization in the ecological risk assessment is given as the hazard quotient (HQ), the level of exposure divided by a NOAEC or approximated NOAEC. The level of concern is an HQ of greater than 1—i.e., the exposure exceeds the NOAEC. The HQs for terrestrial organisms are given in Worksheet G02, and the HQs for aquatic organisms are given in Worksheet G03 of the attachments to this risk assessment.

As discussed in Section 4.2 (exposure assessments for ecological receptors), most of the exposure assessments involve concentrations of boron in surface water which are directly proportional to the application rate. As discussed in Section 2, the application rates in units of lb B/acre are virtually identical for both Cellu-Treat® (0.105 lb B/acre) and Sporax® (0.113 lb B/acre). Thus, for exposures involving surface water, there are no remarkable differences in HQs for Cellu-Treat® and Sporax®. The only exposure scenarios not dependent on application rates in units of lb B/acre are the exposure assessments for terrestrial organisms consuming borates from treated stumps. These exposure assessments are dependent on the stump application rate—i.e., 0.000525 lb B/ft^2 for Cellu-Treat® and 0.00226 lb B/ft^2 for Sporax®. Thus, the HQs for Sporax® involving the consumption of borates from tree stumps are a factor of about 4 greater than the corresponding HQs for Cellu-Treat®. Qualitatively, these differences are insignificant in that none of the HQs exceed the level of concern.

For aquatic organisms, the highest non-accidental HQ is 0.07, the upper bound HQ for acute exposures in sensitive species of aquatic invertebrates following applications of Sporax®. This HQ is below the level of concern by a factor of about 14 [$1 \div 0.07 \approx 14.2857$]. The corresponding HQ for Cellu-Treat® is only marginally lower than the HQ for Sporax—i.e., 0.06 which is below the level of concern by a factor of about 17 [$1 \div 0.06 \approx 16.666\ldots$]. This benign risk characterization is consistent with the recent EPA ecological risk assessment, which describes risks to aquatic organisms as *Predominant Evidence of Negligible Risk* (U.S. EPA/OPP/EFED 2015a, p. 9).

The risk characterization for mammals and birds involving exposures to boron in surface water is similarly benign. The highest HQ is 0.002, the longer-term HQ for small birds consuming contaminated water as well as piscivorous birds consuming fish over a longer-term period. This HQ is below the level of concern by a factor of 500 [$1 \div 0.002$].

The risk characterization for mammals and birds consuming borates from treated stumps is somewhat more nuanced in that the exposure assessments have a high degree of uncertainty. As described in Section 4.1.2.1, the exposure assessment for the 70 kg mammal (deer) consuming borates from a treated stump is the only exposure scenario supported by direct observations—i.e., that deer may lick treated stumps. For this exposure assessment, the central estimate of the HQ for Sporax® is 0.04, and the central estimate of the HQ for Cellu-Treat® is 0.01. As detailed in Section 4.2.2.1, these central estimates are based on the assumption that a deer will consume all of the borate from a 1 ft^2 treated stump. Thus, to reach the level of concern, a deer must consume all of the borates applied to 25 ft^2 of stumps treated with Sporax® or 100 ft^2 of

stumps treated with Cellu-Treat®. In the absence of information indicating that deer or other terrestrial vertebrates are attracted to stumps treated with borates, the clearance of 25 ft^2 or more of treated stumps seems implausible.

Stump applications of borates will not substantially increase concentrations of boron in soil, with the exception of areas immediately adjacent to treated stumps. Consequently, there is no basis for asserting that stump applications of borates would cause adverse effects in terrestrial plants, invertebrates, or microorganisms through soil exposures. The potential for adverse effects associated with foliar exposures also appears to be remote. Liquid stump applications are likely to lead to lower levels of foliar exposure relative to standard backpack foliar applications of herbicides because the borate solution will be applied essentially at ground level (i.e., the height of the treated stump); hence off-site drift should be minimal. Nonetheless, HQs for terrestrial plants based on estimates of drift lead to HQs that are substantially below the level of concern. An HQ of 4 is estimated for direct spray of a terrestrial plant. This HQ, however, is based on a study in which an adverse effect level was not defined. Thus, the HQ of 4 should not be interpreted as an indication that adverse effects in plants would be anticipated, because the levels of exposure causing adverse effects following foliar exposures have not been defined.

Although the EPA considers risks to terrestrial insects because borates are registered as insecticides, Forest Service applications to stumps will limit any exposures of insects to incidental events that should not have a substantial impact on insect populations.

4.4.2. Terrestrial Organisms

4.4.2.1. Mammals

As discussed in Section 4.2.2, the exposure scenarios considered in this risk assessment are the direct consumption of borates applied to tree stumps (acute exposure), consumption of water contaminated by an accidental spill (acute exposure), and acute and longer-term exposure from contaminated surface water.

As summarized in Worksheet G02 of the attachments to this risk assessment, all of the exposures associated with the consumption of contaminated water lead to HQs that are far below the level of concern (HQ=1). The highest HQ is 0.0004, which is below the level of concern by a factor of 2500. This HQ is associated with the upper bound of the longer-term consumption of contaminated water by a small mammal. This HQ is higher than the accidental spill HQs, because the chronic HQ is based on the longer-term NOAEL (8.8 mg B/kg bw/day) which is substantially below the acute NOAEL (350 mg B/kg bw). Because of allometric considerations—i.e., small mammals will consume more water per unit of body weight than larger mammals will consume—exposure assessments and risk characterizations are not explicitly developed for larger mammals.

For exposures associated with the consumption of borates from a tree stump, exposure scenarios are developed for both a large mammal (i.e., a 70 kg deer) and a small mammal (i.e., a 20 g mouse). The large mammal is used to accommodate information discussed in Section 4.2.2.1 indicating that deer may lick stumps treated with borates, although there is no evidence that deer are attracted to treated stumps. For this exposure scenario, a unit exposure of 1 ft^2 of stump surface is used (Section 4.2.2.1). This exposure scenario is adapted from the LD_{50}/ft^2 method

used by EPA (e.g., U.S. EPA/OPP/EFED 2015a, Table 5.5, p. 40). Under the assumption that a deer clears (i.e., completely consumes all of the borates from a treated stump) a 1 ft^2 stump, the HQ is 0.02 following applications of Cellu-Treat® and 0.08 following treatments of Sporax®. The higher HQ for Sporax® reflects the higher stump application rate for Sporax, as detailed in Section 2 (Program Description). Based on these HQs, a deer must consume all of the borate on stump surfaces equivalent to 50 ft^2 following applications of Cellu-Treat® or 12.5 ft^2 following applications of Sporax®. These types of exposures seem unlikely, particularly for liquid applications. As noted in Section 4.1.2.1, no credible incidents involving poisonings to mammals were identified in the available literature. The exposure assessments in the current Forest Service risk assessment, albeit crude, clearly suggest that the risk of exposure for a large mammal consuming borates applied to tree stumps is low.

As discussed in Section 4.2.2, exposures for a small mammal are scaled by body weight in terms of the amount of borates consumed from a treated stump. Hence, the risk characterization for a small mammal is essentially identical to that of a large mammal. As also discussed in Section 4.2.2, the exposure assessment method used for mammals as well as birds is clearly more relevant to granular than to liquid applications. Consequently, risks associated with liquid applications (e.g., Cellu-Treat) are probably over estimated and perhaps substantially so. While this probable bias is acknowledged, it has no qualitative impact on the risk characterization for liquid applications, because all of the HQs are far below the level of concern.

As discussed in Section 4.2.2.4, exposure scenarios are developed for the direct spray of a small mammal. These exposure scenarios are relevant only to liquid applications of Cellu-Treat (Attachment 1) and Sporax (Attachment 2). For both of these formulations, the upper bound HQs are far below the level of concern – i.e., HQs of 0.00003 based on first-order absorption and HQs of 0.01 based on 100% absorption.

4.4.2.2. Birds

As with mammals, risks to birds associated with the consumption of contaminated water appear to be low. The highest HQ for the consumption of contaminated surface water is 0.002, which is below the level of concern (HQ=1) by a factor of 500 [1 ÷ 0.002]. As with mammals, the highest HQs are associated with longer-term exposures, because the longer-term NOAEL (i.e., 3.7 mg B/kg bw for birds) is substantially lower than the acute NOAEL (i.e., 113 mg B/kg bw for birds).

For exposure scenarios associated with the consumption of borates from a treated stump, the risk characterization for birds is qualitatively similar to that for mammals in that none of the HQs exceed the level of concern (HQ=1). Quantitatively, the acute NOAEL for birds (113 mg B/kg bw) is about a factor of 3 below the NOAEL for mammals (350 mg B/kg bw); thus, HQs for birds are higher than those for mammals by about a factor of 3. For birds, the upper bound HQ for Sporax® applications is 0.3, which approaches the level of concern. For Cellu-Treat® applications, however, the upper bound HQ is only 0.1, below the level of concern by a factor of about 10. The differences in the HQs for Sporax® and Cellu-Treat® reflect the differences in the stump application rates—i.e., 0.00226 lb B/ft^2 for Sporax® and 0.000525 lb B/ft^2 for Cellu-Treat®.

As discussed in Section 4.1.2.2.1, U.S. EPA/OPP/EFED (2015a) briefly summarizes acute toxicity studies with boric acid in chickens and turkeys in which the LD_{50} is expressed as >1.27

kg B/ft^2. These studies appear to have involved exposures of the birds to a granular form of boric acid at surface application rates of up to >1.27 kg B/ft^2. As discussed in Section 2, the highest stump application rate for the borates is 0.00226 lb B/ft^2 (i.e., the stump application rate for Sporax® in units of boron) or about 0.001 kg B/ ft^2. This application rate is below the indefinite LD_{50} for a chicken and turkey by a factor of 1270 [1.27 kg B/ft^2 ÷ 0.001 kg B/ft^2]. While this comparison cannot be viewed as a standard HQ [e.g., 1 ÷ 1270 ≈ 0.000787], it does support the assessment discussed above that risks of exposure to birds consuming borates from treated stumps is low.

Also as with mammals (Section 4.4.2.1) and for the same reasons, it is likely that the HQs for liquid applications of borates (e.g., Cellu-Treat) are overestimated and perhaps substantially so. Given that all of the HQs for birds are below the level of concern, the probable overestimate of potential risk does not have a qualitative impact on the risk characterization.

4.4.2.3. Reptiles and Amphibians (Terrestrial Phase)

No risk characterization is developed for reptiles or terrestrial phase amphibians, because the available toxicity data do not support a dose-response assessment (Section 4.3.2.3).

4.4.2.4. Terrestrial Invertebrates

The only quantitative risk characterization for terrestrial insects in the EPA risk assessment is a risk quotient (RQ) for honeybees of <0.01 based on spray applications of boric acid in agriculture (U.S. EPA/OPP/EFED 2015a, p. 42). Much greater incidental exposures might occur during stump applications. For example, Forest Service risk assessments typically develop HQs for honeybees based on application rates and the planar surface area of the honeybee (1.42 cm^2) using algorithms suggested by Humphrey and Dykes (2008) for a bee with a body length of 1.44 cm. As discussed in Section 4.3.2.4, the toxicity value used by EPA for the honeybee is a NOAEL 63 µg B/bee. Normalized for surface area, this NOAEL is equivalent to about 44 µg/cm^2 [63 µg B/bee ÷ 1.42 cm^2 ≈ 44.3661 µg B/cm^2]. As discussed in Section 2, the maximum stump application rate for Sporax® is 0.00226 lb B/ft^2, which is equivalent to about 1.1 mg B/cm^2 or 1100 µg B/cm^2 [(0.00226 lb B x 453592 mg/lb) /(ft^2 x (929.03 cm^2/ft^2) ≈ 1.1034 mg B/cm^2]. Thus, in a stump application of Sporax, an HQ for a bee could be calculated as about 25 [1100 µg B/cm^2 ÷ 44 µg B/cm^2 = 25]. This HQ is not developed as a formal quantitative risk characterization, however, because a bee being exposed to borates during a stump application would be an incidental and probably rare event.

The most likely exposures for terrestrial invertebrates would involve soil invertebrates exposed by contamination of soil due to runoff or other incidental loss from stumps. As discussed in Section 4.2.3, stump applications of borates are not likely to lead to substantial wide-spread soil contamination, relative to normal background levels of boron in soil. Consequently, there is no basis for asserting that soil organisms would be at risk due to stump applications of borates. Nonetheless, increases in soil boron could be evident in the immediate area of treated stumps, particularly in areas with low levels of naturally occurring soil boron. As with the direct exposure of a honeybee, exposures in the direct area of treated stumps could impact relatively small and discrete populations of soil invertebrates.

4.4.2.5. Terrestrial Plants

As discussed above (Section 4.4.2.4), stump applications of borates will not substantially increase concentrations of boron in soil, with the exception of areas immediately adjacent to treated stumps. As discussed in Section 4.1.2.5, boron is an essential element for plants, and the seedling emergence NOAEC for soil applications is 0.11 lb B/acre. As discussed in Section 2, the application rate in terms of boron for both Cellu-Treat® and Sporax® is about 0.11 lb B/acre. Consequently, there is no basis for asserting that stump applications of borates would cause adverse effects in terrestrial plants through soil exposures.

The potential for adverse effects associated with foliar exposures also appears to be remote. As discussed in Section 4.2.4, liquid stump applications are likely to lead to lower levels of foliar exposure relative to standard backpack foliar applications of herbicides because the borate solution will be applied essentially at ground level (i.e., the height of the treated stump); hence offsite drift should be minimal. As detailed in Worksheet G04 of Attachments 1 and 2, standard estimates of drift used for backpack applications of herbicides lead to HQs from 0.03 at 25 feet downwind to 0.001 at 900 feet downwind. Because these HQs are based on standard estimates of drift for foliar applications of herbicides, they are probably overestimates and probably substantial overestimates of potential risks to terrestrial plants.

As also indicated in Worksheet G04 of Attachments 1 and 2, the HQ for direct spray is 4. As discussed in Section 4.3.2.5, this HQ is based on a NOAEL of ≥ 0.03 lb B/acre from a study (MRID 48885401) in which adverse effects were not noted. Thus, while the HQ is given in the Worksheet G04 at 4, the HQ should be interpreted as <4. In other words, the HQ of 4 should not be interpreted as an indication that adverse effects in plants would be anticipated, because the levels of exposure causing adverse effects following foliar exposures have not been defined.

An important reservation with this risk characterization for terrestrial plants is noted by EPA:

> *For terrestrial plants, the maximum single application rate did not cause LOC* [level of concern] *exceedances from runoff and spray drift. … Since woody plants are not represented in the terrestrial plant toxicity tests, this is an uncertainty. Therefore, sensitive plants in the immediate application area may be affected. Incident reports helped substantiate that plant damage may occur if plants come in direct contact with products, though these were mostly from swimming pool algicides, rather than broadcast uses.*
>
> U.S. EPA/OPP/EFED 2015a, p. 49.

While this reservation is noteworthy, this type of reservation (i.e., associated with data limitations in terms of the number and types of species on which data are available) is common in many ecological risk assessments for many groups of organisms.

4.4.2.6. Terrestrial Microorganisms

Borates are effective microbicides, and effective applications of borates to tree stumps would be detrimental to microorganisms (target and nontarget) on the treated stumps and possibly to microorganisms in soil near treated stumps. There is, however, no evidence that the adverse effects would extend substantially beyond the area of treated stumps.

4.4.3. Aquatic Organisms

The HQs for aquatic organisms are summarized in Worksheet G03 of the attachments to this risk assessment. The concentrations of boron in surface water and consequently the HQs for aquatic organisms are dependent on the application rate in units of lb B/acre. As discussed in Section 2, the application rates in units of active ingredient are 1 lb a.i./acre for Sporax® and 0.5 a.i./acre for Cellu-Treat®. In terms of lb B/acre, however, the application rates for the two formulations are virtually identical—i.e., 0.113 lb B/acre for Sporax® and 0.105 lb B/acre for Cellu-Treat®. Consequently, the HQs are virtually identical for applications of both Sporax® and Cellu-Treat®. The following discussion of the HQs is based on the HQs for Sporax.

As summarized at the start of Section 4.3.3 and detailed further in Section 3.2.3.4, in areas with low levels of naturally occurring boron in surface water, stump applications of borates could increase boron concentrations in surface water by a factor of up to about 2 at sites distant from treated stumps. This difference, however, has no impact on the risk characterization. The upper bound HQs for non-accidental peak and longer-term concentration of boron in surface water are substantially below the level of concern. The highest HQ is 0.07, the upper bound HQ for a sensitive aquatic invertebrate. This HQ is below the level of concern by a factor of about 14 [$1 \div 0.07 \approx 14.2857$].

The highest accidental HQ is 0.7 and is also associated with a sensitive aquatic invertebrate. As discussed in Section 3.2.3.4.1, the accidental scenario is associated with a spill, based on the application rate and the amount of pesticide required to treat 5 (1 to 10) acres. A somewhat more severe accidental scenario (i.e., the amount of pesticide required to treat about 14 acres) would lead to concentrations in surface water that would reach the level of concern for a sensitive species of aquatic invertebrates. The most reasonable characterization of the accidental scenarios is that adverse effects to some sensitive species of aquatic organisms could not be ruled-out in the event of a serious accidental spill. The level of risk would be highly dependent on site-specific circumstances, including the magnitude of the spill and the size and possibly flow characteristics of the water body.

The benign risk characterization for aquatic organisms given above is consistent with the risk characterization from EPA's most recent ecological risk assessment—i.e., there is predominant evidence of *negligible risk* to aquatic organisms from the use of borates (U.S. EPA/OPP/EFED 2015a, p. 9).

5. REFERENCES

NOTE: The initial entry for each reference in braces {} simply specifies how the reference is cited in the text. The final entry for each reference in brackets [] indicates the source for identifying the reference.

DOCKET01	**Documents from Docket ID EPA-HQ-OPP-2009-0306: Boric Acid and Sodium Borate Salts Registration Review.**
DOCKET02	**Documents from Docket ID EPA-HQ-OPP-2005-0062: Boric Acid Group. Focus on TRED.**
ECOTOX	**Taken from ECOTOX (http://cfpub.epa.gov/ecotox/).**
FS	**Inputs/reviews from the Forest Service.**
Nisus	**Materials received form Nisus Corporation.**
RA2006	**References from previous Forest Service risk assessment on Borax**
[Sec]	**Information from a secondary source.**
SET00	**Papers from preliminary scoping.**
SET01	**Initial literature search.**
SET02-05	**Supplemental searches and other communications.**
Sec	**Summary of citation from a secondary source.**
Std	**Standard references used in most Forest Service risk assessments.**

{Abou-Shakra et al. 1989} Abou-Shakra FR; Havercroft JM; Ward NI. Lithium and boron in biological tissues and fluids. Trace Elements in Medicine. 6:142-146. [Set05]

{Acerbo and Miller 2009} Acerbo AS; Miller LM. 2009. Assessment of the Chemical Changes Induced in Human Melanoma Cells by Boric Acid Treatment Using Infrared Imaging. Analyst. 134(8):1669-74. [Set01]

{ACGIH 2006} ACGIH (American Conference of Governmental Industrial Hygienists). 2006. Boron. Threshold limit values for chemical substances and physical agents and biological exposure indices. Cincinnati, OH: American Conference of Governmental Industrial Hygienists, 14-15. As summarized in ATSDR 2010. [Sec]

{Acs et al. 2006} Acs N; Banhidy F; Puho E; Czeizel AE. 2006. Teratogenic Effects of Vaginal Boric Acid Treatment During Pregnancy. International Journal of Gynecology and Obstetrics. 93(1):55-6. [Set01]

{Aho et al. 1983}Aho PE; Fiddler G; Srago M. 1983. Logging damage in thinned, young-growth true fir stands in California and recommendations for prevention. USDA Forest Service, Pacific Northwest Forest and Range Experiment Station. PNW-304, January 1983. 9 pages. Available at: http://www.fs.fed.us/pnw/pubs/pnw_rp304.pdf. [FS]

{Alabaster 1969} Alabaster JS. 1969. Survival of fish in 164 herbicides, insecticides, fungicides, wetting agents, and miscellaneous substances. International Pest Control. 11(2):29-35. [RA2006]

{Alabaster 1969} Alabaster JS. 1969. Survival of fish in 164 herbicides, insecticides, fungicides, wetting agents, and miscellaneous substances. International Pest Control. Vol 11(2):29-35. As cited in Hovatter and Ross 1995. [RA2006]

{Ali et al. 2014} Ali SE; Thoen E; Evensen Oslash; Wiik-Nielsen J; Gamil AA; Skaar I. 2014. Mitochondrial Dysfunction Is Involved in the Toxic Activity of Boric Acid Against Saprolegnia. PLOS One. 9(10):e110343. [Set01 - Toxline]

{Allen et al. 1996} Allen BC; Strong PL; Price CJ; Huubard SA; Daston GP. 1996. Benchmark Dose Analysis of Developmental Toxicity in Rat Exposed to Boric Acid. Fundam. Appl. Toxicol. 32:194-204. [RA2006]

{Amorim et al. 2008} Amorim MJ; Novais S; R”mbke J; Soares AM. 2008. *Enchytraeus albidus* (Enchytraeidae): A Test Organism in a Standardised Avoidance Test? Effects of Different Chemical Substances. Environment International. 34(3):363-71. [Set01]

{Anaka et al. 2008} Anaka A; Wickstrom M; Siciliano SD. 2008. Increased Sensitivity and Variability of Phytotoxicity Responses in Arctic Soils to a Reference Toxicant, Boric Acid. Environmental Toxicology and Chemistry. 27(3):720-6. [Set01/ ECOTOX - 105883]

{Anderson et al. 1994} Anderson DL; Cunningham WC; Lindstrom TR. 1994. Concentrations and intakes of H, B, S, K, Na, Cl, and NaCl in foods. Journal of Food Composition and Analysis. 7: 59-82. [Set02]

{Anon 1970} Anon. 1970. Deadly diapers. British Medical Journal. 2(5705):314. [RA2006]

{Anon 1992} Anon. 1992. Initial submission: developmental toxicity of boric acid in New Zealand white rabbits (Final report) with attachments and cover letter dated 010692. EPA/OTS; Doc #88-920000648. [RA2006]

{Apostol and Zwiazek 2004} Apostol KG; Zwiazek JJ. 2004. Boron and Water Uptake in Jack Pine (*Pinus banksiana*) Seedlings. Environmental and Experimental Botany. 51(2): 145-153. [ECOTOX - 166780]

{Aquea et al. 2012} Aquea F; Federici F; Moscoso C; Vega A; Jullian P; Haseloff J; Arce-Johnson P. 2012. A Molecular Framework for the Inhibition of Arabidopsis Root Growth in Response to Boron Toxicity. Plant, Cell and Environment. 35(4):719-34. [Set01]

{Ardic et al. 2009} Ardic M; Sekmen AH; Tokur S; Ozdemir F; Turkan I. 2009. Antioxidant Responses of Chickpea Plants Subjected to Boron Toxicity. Plant Biology. 11(3): 328-338 [ECOTOX - 119264]

{Ardic et al. 2009} Ardic M; Sekmen AH; Tokur S; Ozdemir F; Turkan I. 2009. Antioxidant Responses of Chickpea Plants Subjected to Boron Toxicity. Plant Biology (Stuttgart). 11(3):328-38. [Set01]

{Artman et al. 1969} Artman JD; Frazier DH; Morris CL. 1969. Fomes annosus and chemical stump treatment in Virginia a three-year study. Plant Disease Reporter. 53(2):108-110. [RA2006]

{Atkins 1987} Atkins EL. 1987. Laboratory Bee Adult Toxicity Tests (BATDT) for boric acid, powdered, 100% technical. MRID 40269201. Summarize in SERA 2006a. [RA2006]

{ATSDR (Agency for Toxic Substances and Disease 1992} ATSDR (Agency for Toxic Substances and Disease Registry). 1992. Toxicological Profile for Boron and Compounds. Availble at: http://www.atsdr.cdc.gov/toxprofiles/tp26.html . [RA2006]

{ATSDR (Agency for Toxic Substances and Disease 2010} ATSDR (Agency for Toxic Substances and Disease Registry). 2010. Toxicological Profile for Boron. Availble at: http://www.atsdr.cdc.gov/ToxProfiles/tp26.pdf . [Set00]

{Ayaki and Iwasawa 2011} Ayaki M; Iwasawa A. 2011. Cell Viability of Four Corneoconjunctival Cell Lines Exposed to Five Preservatives and a Surfactant Used for Infection Control in Eyedrops. Biocontrol Science. 16(3):117-21. [Set01]

{Bakke 2003} Bakke D. 2003. David Bakke, Pesticide-Use Specialist, Invasive Plants Program Manager, Forest Service , State and Private Forestry, Pacific Southwest Region. Personal communication via email to Patrick Durkin. November 25, 2003. [RA2006]

{Bakke 2005} Bakke D. 2005. David Bakke, Pesticide-Use Specialist, Invasive Plants Program Manager, Forest Service , State and Private Forestry, Pacific Southwest Region. Attachment to R5 Pesticide-Use Advisory Memorandum 06-01, Responding to Issues Raised by CATs Concerning Borax (Sporax). Report dated November 2005. [Set00]

{Bakke 2016a} Bakke D. 2016a. David Bakke, Pesticide-Use Specialist, Invasive Plants Program Manager, Forest Service , State and Private Forestry, Pacific Southwest Region. Comments on Preliminary Program Description – Borax and Cellu-Treat®. Comments dated January 13, 2016. [FS]

{Bakke 2016b} Bakke D. 2016b. David Bakke, Pesticide-Use Specialist, Invasive Plants Program Manager, Forest Service , State and Private Forestry, Pacific Southwest Region. Comments on stump applications. Email from Dave Bakke to Patrick Durkin (SERA) dated June 15, 2016. [FS]

{Bakke 2016c} Bakke D. 2016c. David Bakke, Pesticide-Use Specialist, Invasive Plants Program Manager, Forest Service , State and Private Forestry, Pacific Southwest Region. Sporax Question – Dust vs Granule. Email from Dave Bakke to Patrick Durkin (SERA) dated October 4, 2016. [FS]

{Bantel et al. 1999} Bantle JA; Finch RA; Fort DJ; et al. 1999. Phase III Interlaboratory Study of FETAX Part 3. FETAX Validation Using 12 Compounds with and Without an Exogenous Metabolic Activation System. Journal of Applied Toxicology. 19(6): 447-472. [ECOTOX - 62058]

{Barranco and Eckhert 2004} Barranco WT; Eckhert CD. 2004. Boric Acid Inhibits Human Prostate Cancer Cell Proliferation. Cancer Letters. 216(1):21-9. [Set01]

{Barranco and Eckhert 2006a} Barranco WT; Eckhert CD. 2006a. Molecular Manifestations of Boric Acid Induced Toxicity in Du-145 Prostate Cancer Cells. Toxicological Sciences. 90(1-S):288. [Set01]

{Barranco and Eckhert 2006b} Barranco WT; Eckhert CD. 2006b. Cellular Changes in Boric Acid-Treated Du-145 Prostate Cancer Cells. British Journal of Cancer. 94(6):884-90. [Set01]

{Barranco et al. 2007} Barranco WT; Hudak PF; Eckhert CD. 2007. Evaluation of Ecological and *in vitro* Effects of Boron on Prostate Cancer Risk (United States). Cancer Causes and Control. 18(1):71-7. [Set01]

{Barranco et al. 2009} Barranco WT; Kim DH; Stella Sl Jr; Eckhert CD. 2009. Boric Acid Inhibits Stored $Ca2^{+}$ Release in Du-145 Prostate Cancer Cells. Cell Biology and Toxicology. 25(4):309-20. [Set01]

{Barres 1967} Barres M. 1967. Contribution a l'etude de l'isopoly-condensation des berates alcalins par electrometrie et partages. Rev Chem Miner, 4: 803-838. [Set02]

{Basaran et al. 2012} Basaran N; Duydu Y; Bolt HM. 2012. Reproductive Toxicity in Boron Exposed Workers in Bandirma, Turkey. Journal of Trace Elements in Medicine and Biology. 26(2-3):165-7. [Set01]

{Becker et al. 2011} Becker L; Scheffczyk A; Forster B; et al. 2011. Effects of Boric Acid on Various Microbes, Plants, and Soil Invertebrates. Journal of Soils and Sediments. 11(2): 238-248. [ECOTOX -166393]

{Beckett et al. 2001} Beckett WS; Oskvig R; Gaynor ME; Goldgeier MH. 2001. Association of reversible alopecia with occupational topical exposure to common borax-containing solutions. J Am Acad Dermatol 2001 Apr;44(4):599-602. [RA2006]

{Benson et al. 1984} Benson WH; Birge WJ; Dorough HW. 1984. Absence of mutagenic activity of sodium borate (Borax) and boric acid in the salmonella typhimurium preincubation test. ENVIRON TOXICOL CHEM; 3 (2). 1984. 209-214. [RA2006]

{Bergmann et al. 1995} Bergmann W; Bruchlos P; Marks G. 1995. Ein Beitrag zur Frage des toxixchen Bor-Grenzwertes in Gewassern fur Phragmites australis-Schilfrohr. Tenside Detergents, 32, 229-237. As cited in ECETOC Working Group 1997. [RA2006]

{Berry and Bretz 1964} Berry FH; Bretz TW. 1964. Urea and other chemicals effective against colonization of shortleaf pine stumps by Fomes annosus in Missouri. Plant Disease Reporter. 48(11): 886-887. [RA2006]

{Beyer et al. 1983} Beyer KH; Bergfeld WF; Berndt WO; Boutwell RK; Carlton WW; Hoffmann DK; Schroeter AL. 1983. Final report on the safety assessment of sodium borate and boric acid. J Am College Toxicol. 2(7): 87-125. [RA2006]

{Beyond Pesticides 2006} Beyond Pesticides. 2006(?). Boric Acid: chemical WATCH Factsheet. Not clearly dated. Available at: http://www.beyondpesticides.org/assets/media/documents/pesticides/factsheets/Boric%20Acid.pdf. [Set00]

{Bhami and Das 2015} Bhami LC; Das SS. 2015. Boric Acid Ovicidal Trap for the Management of *Aedes* Species. Journal of Vector Borne Diseases. 52(2):147-52. [Set01]

{Bhunya and Behura 1986} Bhunya SP; Behura T. 1986. Evaluation of clastogenicity of three pesticides in the grasshopper test system. J Zool Soc India. 38(1-2): 73-82. [RA2006]

{Bicho et al. 2015} Bicho RC; Gomes SI; Soares AM; Amorim MJ. 2015. Non-Avoidance Behaviour in Enchytraeids to Boric Acid Is Related to the GABAergic Mechanism. Environmental Science and Pollution Research International. 22(9):6898-903. [Set01]

{Bintein and Devillers 1994} Bintein S; Devillers J. 1994. QSAR for organic chemical sorption in soils and sediments. Chemosphere. 28(6): 1171-1188. [RA2006]

{Biondi et al. 2013} Biondi A; Zappala L; Stark JD; Desneux N. 2013. Do Biopesticides Affect the Demographic Traits of a Parasitoid Wasp and its Biocontrol Services Through Sublethal Effects? PloS one. 8(9):e76548. [Set01]

{Birge et al. 1983} BirgeWJ; Black JA; Westerman AG; Ramey BA. 1983. Fish and Amphibian Embryos - a Model System for Evaluating Teratogenicity. Fundamental and Applied Toxicology. 3:237-242. [ECOTOX - 19124]

{Birge WJ and Black 1977} Birge WJ and Black JA. 1977. Sensitivity of Vertebrate Embryos to boron compounds. EPA-560/1-76-008, prepared by University of Kentucky, Lexington KY, under contract No. 68-01-3920, Office of Toxic Substances, US EPA, Washington, DC. [RA2006]

{Black et al. 1993} Black JA; Barnum JB; Birge WJ. 1993. An integrated assessment of the biological effects of boron in rainbow trout. Chemosphere 26(7): 399-371. [RA2006]

{Bodek et al. 1988} Bodek I; Lyman WJ; Reehl WF; Rosenblatt DH. 1988. Environmental Inorganic Chemistry: Properties, Processes, and Estimation Methods. SETAC Special Publication Series. Pergamon Press, New York. [RA2006]

{Bolt et al. 2012} Bolt HM; Ba#351aran N; Duydu Y. 2012. Human Environmental and Occupational Exposures to Boric Acid: Reconciliation with Experimental Reproductive Toxicity Data. Journal of Toxicology Environmental Health, Part A: Current Issues. 75(8-10):508-14. [Set01]

{Boncukcuoglu et al. 1998} Boncukcuoglu R; Kocakkerim MM; Alkan M. 1998. Borax production from borax slime, an industrial waste. Water Air and Soil Pollution. 104(1-2): 103-112. [RA2006]

{Bringmann and Kuhn 1977} Bringmann G; Kuhn R. 1977. Befunde der Schadwirkung wassergefahrdender Stoffe gegen Daphnia magna. Z.f. Wasser- und Abwasser-forcsh. 10: 161-166. As cited in Hovatter and Ross 1995. [RA2006]

{Brockman et al. 1985} Brockman RP; Audette RJ; Gray M. 1985. Borax toxicity. Can Vet J Rev Vet Can. 26: 147. [RA2006]

{Brodie et al. 2009} Brodie J; Andersen RA; Kawachi M; Millar JK. 2009. Endangered algal species and how to protect them. Phycologia. 48 (5): 423-438. [Std]

{Brown et al. 2013} Brown JS; Gordon T; Price O; Asgharian B. 2013. Thoracic and respirable particle definitions for human health risk assessment. Particulate and Fibre Toxicology. 10:12. DOI: 10.1186/1743-8977-10-12. Available at: http://particleandfibretoxicology.biomedcentral.com/articles/10.1186/1743-8977-10-12. [Set05]

{Buist et al. 2005} Buist HE; Van De Sandt JJ; Van Burgsteden JA; De Heer C. 2005. Effects of Single and Repeated Exposure to Biocidal Active Substances on the Barrier Function of the Skin *In Vitro*. Regulatory Toxicology and Pharmacology. 43(1):76-84. [Set01]

{Bundschuh 1992} Bundschuh J. 1992. Boron contamination of the ground- and surface waters of Lerma valley, Argentina. Aqua: journal of water supply research and technology (Oxford); 41 (1): 13-17. [RA2006]

{Bundschuh 1992} Bundschuh J. 1992. Boron contamination of the ground- and surface waters of Lerma valley, Argentina. Aqua: journal of water supply research and technology (Oxford); 41 (1): 13-17. [RA2006]

{Butterwick et al. 1989} Butterwick L; De Qude N; Raymond K. 1989. Safety Assessment of Boron in Aquatic and Terrestrial Environments. Ecotoxicology and Environmental Safety. 17: 339-371. [RA2006]

{Buyukguzel et al. 2013} Buyukguzel E; Suyukguzel K; Snela M. et al. 2013. Effect of boric acid on antioxidant enzyme activity, lipid peroxidation, and ultrastructure of midgut and fat body of *Galleria mellonella*. Cell Biology and Toxicology. 29:117-129. [Set01-Have]

{Cain et al. 2004} Cain WS; Jalowayski AA; Kleinman M; et al. 2004. Sensory and associated reactions to mineral dusts: Sodium borate, calcium oxide, and calcium sulfate. Journal of Occupuational and Environmental Hygiene. 1:222-236. [Set02]

{Cain et al. 2008} Cain WS; Jalowayski AA; Schmidt R,; et al. 2008. Chemesthetic responses to airborne mineral dusts: Boric acid compared to alkaline materials. International Archives of Occupational and Environmental Health. 81(3):337-345. [Set02]

{Calabrese 2010} Calabrese EJ. 2010. Hormesis is central to toxicology, pharmacology and risk assessment. Human and Experimental Toxicology. 29(4): 249-261. [Std]

{Calabrese 2013} Calabrese EJ. 2013. Hormetic mechanisms. Critical Reviews in Toxicology. 43(7): 580-606. [Std]

{CalEPA 2013} CalEPA (California Environmental Protection Agency). 2013. Summary of Toxicology Data Boric Acid and Related Inorganic Borates. Department of Pesticide Regulation, Medical Toxicology Branch. Original Date: 8/26/1989. Updated 8/26/2013. [Set00]

{Campbell et al. No Date} Campbell DL; Engeman RM; Nolte DL. No Date. An evaluation of the attraction of black-tailed deer to borax fungicide. Internal Report conducted for USDA/FS. [RA2006]

{Capinera 2013} Capinera JL. 2013. Cuban Brown Snail, *Zachrysia provisoria* (Gastropoda): Damage Potential and Control. Crop Protection. 52(0): 57-63. [ECOTOX - 166381]

{CDPR 2015} CDPR (California Department of Pesticide Regulation). 2015. Summary of Pesticide Use Report Data 2013, Indexed by Chemical. Report dated May 2015. Available at: www.cdpr.ca.gov/docs/pur/pur13rep/13sum.htm. [Std]

{Cervilla et al. 2007} Cervilla LM; Blasco B; Rios JJ; Romero L; Ruiz JM. 2007. Oxidative Stress and Antioxidants in Tomato (*Solanum lycopersicum*) Plants Subjected to Boron Toxicity. Ann. Bot.100(4): 747-756 [ECOTOX - 151401]

{Cervilla et al. 2008} Cervilla LM; Blasco B; Rios JJ; et al. 2008. Response of Nitrogen Metabolism to Boron Toxicity in Tomato Plants. Plant Biology. 11(5): 671-677. [ECOTOX - 152311]

{Cervilla et al. 2009} Cervilla LM; Rosales MA; Rubio-Wilhelmi MM; et al. 2009. Involvement of Lignification and Membrane Permeability in the Tomato Root Response to Boron Toxicity. Plant Science.176(4): 545-552. [ECOTOX - 166604]

{Chamberlain et al. 1996} Chamberlain K; Evans AA; Bromilow RH. 1996. 1-Octanol/water partition coefficient (Kow) and pKa for ionizable pesticides measured by a pH-metric method. Pesticide Science. 47(3): 265-271. [RA2006]

{ChemIDplus 2014} ChemIDplus. 2014. United States National Library of Medicine. Available at: http://chem.sis.nlm.nih.gov/chemidplus/. [Std]

{Chernobrovkina et al. 2012} Chernobrovkina NP; Titov AF; Robonen EV; Morozov AK. 2012. Effect of Boric Acid on the Ability of Plants to Accumulate Heavy Metals. Russian Journal of Ecology. 43(1): 29-32. [ECOTOX - 159071]

{Clark et al. 1987} Clark WB; Koekebakker M; Barr RD; Dowining RG; Fleming RF. 1987. Analysis of ultratrace lithium and boron by neutron activation and mass-spectrometric measurement of ^{3}He and ^{4}He. Applied Radiation and Isotopes. 38: 735–734. [Set05]

{Col and Col 2003} Col M; Col C. 2003. Environmental boron contamination in waters of Hisarcik area in the Kutahya Province of Turkey. Food and Chemical Toxicology. 41: 1417-1420. [RA2006]

{Colak et al. 2011} Colak S; Geyikoglu F; Keles ON; Turkez H; Topal A; Unal B. 2011. The Neuroprotective Role of Boric Acid on Aluminum Chloride-Induced Neurotoxicity. Toxicology and Industrial Health. 27(8):700-10. [Set01]

{Colwell and Baker 1939} Colwell WE; Baker GO. 1939. Studies of boron deficiency in Idaho soils. Am Soc Agron. 31: 503-512. [RA2006]

{Corradi et al. 2010} Corradi F; Brusasco C; Palermo S; Belvederi G. 2010. A Case Report of Massive Acute Boric Acid Poisoning. European Journal of Emergency Medicine. 17(1):48-51. [Set01]

{Cotton et al. 2007} Cotton FA; Wilkinson G; Murillo CA; Bochman M. 2007. Advanced Inorganic Chemistry, Sixth Edition. Wiley. [Std]

{Coughlin 1996} Coughlin JR. 1996. Inorganic borates: Chemistry, human exposure, and health and regulatory guidelines. Journal of Trace Elements in Experimental Medicine. 9(4): 137-151. [RA2006]

{Cox 1940} Cox TR. 1940. Relation of boron to heart rot in the sugar beet. Am Soc Agron. 32: 354-370. [RA2006]

{Cram 2005} Cram M. 2005. Summary of: Borax Applicator for Feller-bunchers. Michelle M. Cram, USDA Forest Service, Region 8, Forest Heath Protection, Athens, GA 30602. Email to Henry Appleton dated August 11, 2004. As summarized in SERA 2006a. [RA2006]

{Crapse and Kyser 2011} Crapse KP; Kyser EA. 2011. Literature Review of Boric Acid Solubility Data. SRNL-STI-2011-00578. Savannah River National Laboratory. Prepared for the U.S. Department of Energy under contract number DE-AC09-08SR22470. Available at: http://sti.srs.gov/fulltext/SRNL-STI-2011-00578.pdf. [Set00]

{Crowley 2016} Crowley M. 2016. Response to query on shaker can applications. E-mail dated September 27, 2016 to Patrick Durkin (SERA Inc.) via Moana Appleyard, U.S. EPA/OPP, Risk Management and Implementation Branch V. [Set06]

{Cui et al. 2004} Cui Y; Winton MI; Zhang Z-F; et al. 2004. Dietary boron intake and prostate cancer risk. Oncology Reports. 11: 887-892. [Set05]

{Culver and Hubbard 1996} Culver BD; Hubbard SA. 1996. Inorganic boron health effects in humans: an aid to risk assessment and clinical judgment. Journal of Trace Elements in Experimental Medicine. 9(4): 175-184. [RA2006]

{Culver et al. 1994} Culver BD; Shen PT; Taylor TH; Lee-Feldstein A; Anton-Culver H; Strong PL. 1994. The relationship of blood and urine-boron to boron exposure in borax-workers and the usefulness of urine-boron as an exposure marker. Environmental Health Perspectives. 102 (Supplement 7): 133-137. [RA2006]

{Cureton and Torrens 1976} Cureton GL; Torrens WW. 1976. Dissolving abradant cleanser for acne. Drug Cosmet Ind. 118:38-41; 101-104. [RA2006]

{da Silva Cruz et al. 2010} da Silva Cruz A; da Silva-Zacarin EC; Bueno OC; Malaspina. 2010. Morphological Alterations Induced by Boric Acid and Fipronil in the Midgut of Worker Honeybee (*Apis mellifera* L.) Larvae: Morphological Alterations in the Midgut of *A. mellifera*. Cell Biology and Toxicology. 26(2):165-76. [Set01]

{Dani et al. 1971} Dani HM; Saini HS; Allag IS; Singh B; Sareen K. 1971. Effect of boron toxicity on protein and nucleic acid contents of rat tissues. Res Bull Panjab Univ Sci. 22(1-2): 229-235. [RA2006]

{Das and Mohanty 1985} Das SR; Mohanty NN. 1985. Studies on the chemical control of stem-rot disease of jute. Indian J Plant Pathol. 3(2): 210-212. [RA2006]

{Davis 1974} Davis AC. 1974. Ninety-six Hour LC50 of Grotan HD II in Rainbow Trout and Bluegill Sunfish: Laboratory No. 4E-3069. (Unpublished study received Feb 20, 1975 under 10000-3; prepared by Cannon Laboratories, Inc., submitted by Hallemite Lehn & Fink, Montvale, N.J.; CDL:232140-D). MRID 00067967. As summarized in SERA 2006a. [RA2006]

{Dethloff et al. 2009} Dethloff GM; Stubblefield WA; Schlekat CE. 2009. Effects of Water Quality Parameters on Boron Toxicity to *Ceriodaphnia dubia*. Archives of Environmental Contamination and Toxicology. .57(1): 60-67. [ECOTOX - 118810]

{De Vette et al. 2000} De Vette HQM; van Asten JG; Hanstveit AO. 2000. A study on the adsorption/desorption of Boric acid Manufacturing Grade to soil particulates in four soil types. TNO Nutrition and Food Research, Delft, The Netherlands. TNO study no. IMW-99-9047-02. Unpublished study as summarized in HERA 2005. [Sec]

{Devirian and Volpe 2003} Berivian TA; Volpe SL. 2003. The physiological effects of dietary boron. Critical Reviews in Food Science and Nutrition. 43(2): 219-231. [Set 02]

{Di Renzo et al. 2006} Di Renzo F; Luisa Broccia ML; Menegola E; Giavini E. 2006. HDAC Inhibition and Axial Malformations. Reproductive Toxicology. 22(2):269-70 [Set01]

{Di Renzo et al. 2007} Di Renzo F; Cappelletti G; Broccia ML; Giavini E; Menegola E. 2007. Boric Acid Inhibits Embryonic Histone Deacetylases: A Suggested Mechanism to Explain Boric Acid-Related Teratogenicity. Toxicology and Applied Pharmacology. 220(2):178-85. [Set01]

{Dierickx 1989} Dierickx PJ. 1989. Cytotoxicity testing of 114 compounds by the determination of the protein content in HEP G2 cell cultures. Toxicol In Vitro. 3(3): 189-194. [RA2006]

{Dieter et al. 1991} Dieter M; Bishop J; Eustis S et al. 1991. Toxicology and Carcinogenesis Studies of Boric Acid in B6C3F1 Mice: Lab Project Number: NTP/TR 324. Available at: https://ntp.niehs.nih.gov/ntp/htdocs/lt_rpts/tr324.pdf. Cited in U.S. EPA/OPP/HED 2006a as MRID 40692309 [Set00]

{Dinca and Score 2013} Dinca L; Scorei R. 2013. Boron in Human Nutrition and its Regulations Use. Journal of Nutritional Therapeutics., 2: 22-29. [Set02]

{Dixon et al. 1976} Dixon RL; Lee IP; Sherins RJ. 1976. Methods to assess reproductive effects of environmental chemicals: studies of cadmium and boron administered orally. Environmental Health Perspectives. 13:59-67. [RA2006]

{Dixon et al. 1979} Dixon RL; Sherins RJ; Lee IP. 1979. Assessment of environmental factors affecting male fertility. Environmental Health Perspectives. 30:53-68. [RA2006]

{Dost 1994} Dost FN. 1994. Safety of cattle grazing in areas where borax is applied to cut stumps for control of root fungus. USDA Forest Service. Internal memorandum from Max M. Ollieu, Director of Forest Pest Managment, dated March 16, 1994 to Forest Supervisor, Fremont NF. [RA2006]

{Dost et al. 1996} Dost FN; Norris L; Glassman C. 1996. Assessment of Human Health and Environmental Risks Associated with Use of Borax for Cut Stump Treatment. 1996. Prepared for USDA-Forest Service, Regions 5 and 6. July 1, 1996. [RA2006]

{Doyle 1988a} Doyle R. 1988a. 20 Mule Team Tim-Bor: Acute Oral Toxicity Study in Rats--Median Lethal Dosage Determination: Lab Project Number: 88-3195-21. Unpublished study prepared by Hill Top Biolabs, Inc. 22 p. MRID 43500101. As summarized in SERA 2006a. [RA2006]

{Doyle 1989b} Doyle R. 1989b. Primary Eye Irritation with Disodium Octaborate Tetrahydrate: Lab Project Number: 88-3442-211(C). Unpublished study prepared by Hill Top Biolabs, Inc. 34 p. MRID 42521000. As summarized in SERA 2006a. [RA2006]

{Doyle 1989c} Doyle R. 1989c. Primary Skin Irritation with Disodium Octaborate Tetrahydrate: Lab Project Number: 88-3442-211(B). Unpublished study prepared by Hill Top Biolabs, Inc. 28 p. MRID 42521001. As summarized in SERA 2006a. [RA2006]

{Doyle 1989d} Doyle R. 1989d. (Primary) Eye Irritation Study without Rinsing in Rabbits: Disodium Octaborate Tetrahydrate: Lab Project Number: 89-3708-21. Unpublished study prepared by Hill Top Biolabs, Inc. 30 p. MRID 42521002. As summarized in SERA 2006a. [RA2006]

{Doyle 1989e} Doyle R. 1989e. Disodium Octaborate Tetrahydrate: Acute Dermal Toxicity Study in Rabbits: Lab Project Number: 88-3442-21(A). Unpublished study prepared by Hill Top Biolabs, Inc. 14 p. MRID 43500102. As summarized in SERA 2006a. [RA2006]

{Draize and Kelley 1959} Draize JH; Kelley EA. 1959. The urinary excretion of boric acid preparations following oral administration and topical applications to intact and damaged skin of rabbits. Toxicology and Applied Pharmacology. 1(3): 267-276. [Set05]

{Dregne and Powers 1942} Dregne HE; Powers WL. 1942. Boron fertilization of alfalfa and other legumes in oregon. Am Soc Agron. 34: 902-912. [RA2006]

{Driver 1963a} Driver CH. 1963a. Effect of certain chemical treatments on colonization of slash pine stumps by Fomes annosus. Plant Disease Reporter. 47(6):569-571. [RA2006]

{Driver 1963b} Driver CH. 1963b. Further data on borax as a control of surface infection of slash pine stumps by Fomes annosus. Plant Disease Reporter. 47(11):1006-1009. [RA2006]

{Dunn 1996a} Dunn J. 1996a. Primary Dermal Irritation of 20 Mule Team Sodium Tetraborate Decahydrate in New Zealand White Rabbits: Addendum to MRID No. 43553203: Lab Project Number: 8403A. Unpublished study prepared by U. S. Borax Inc. 11 p. MRID 44084600. As summarized in SERA 2006a. [RA2006]

{Dunn 1996b} Dunn J. 1996b. Primary Eye Irritation with Disodium Octaborate Tetrahydrate: Addendum to MRID Nos. 42521001 and 42521003. Unpublished study prepared by U. S. Borax Inc. 5 p. MRID 44084600. As summarized in SERA 2006a. [RA2006]

{Dunn 1996c} Dunn J. 1996c. Primary Skin Irritation with Disodium Octaborate Tetrahydrate: Addendum to MRID No. 42521002. Unpublished study prepared by U. S. Borax Inc. 5 p. MRID 44084603. As summarized in SERA 2006a. [RA2006]

{Dunn 1996d} Dunn J. 1996d. Disodium Octaborate Tetrahydrate Dermal Sensitization Study: Addendum to MRID No. 43500105: Lab Project Number: 3312. Unpublished study prepared by U. S. Borax Inc. 7 p. MRID 44084604. As summarized in SERA 2006a. [RA2006]

{Dunn 1996e} Dunn J. 1996e. Acute Oral Toxicity in Rats--Median Lethal Dosage Determination of 20 Mule Team Tim-bor: Addendum to MRID 43500102. Unpublished study prepared by Hill Top Research. 5 p. MRID 44113800. As summarized in SERA 2006a. [RA2006]

{Dunn 1996f} Dunn J. 1996f. Corrosion Characteristics Information for Disodium Octaborate Tetrahydrate. Unpublished study prepared by U. S. Borax Inc. 6 p. MRID 44084605. As summarized in SERA 2006a. [RA2006]

{Durkin et al. 1995} Durkin PR; Rubin L; Withey J; Meylan W. 1995. Methods of assessing dermal absorption with emphasis on uptake from contaminated vegetation. Toxicology and Industrial Health. 11(1): 63-79.[Std]

{Durmus and Buyukguzel 2008} Durmus Y; Buyukguzel K. 2008. Biological and Immune Response of *Galleria mellonella* (Lepidoptera: Pyralidae) to Sodium Tetraborate. Journal of Economic Entomology. 101(3):777-83. [Set01]

{Duydu et al. 2011} Duydu Y; Basaran N; Ustundag A; et al.. 2011. Reproductive Toxicity Parameters and Biological Monitoring in Occupationally and Environmentally Boron-Exposed Persons in Bandirma, Turkey. Archives of Toxicology. 85(6):589-600. [Set01]

{Duydu et al. 2012a} Duydu Y; Basaran N; Ustundaq A; et al. 2012a. Assessment of DNA Integrity (Comet Assay) in Sperm Cells of Boron-Exposed Workers. Archives of Toxicology. 86(1):27-35. [Set01]

{Duydu et al. 2012b} Duydu Y; Basran N; Bolt HM. 2012b. Exposure Assessment of Boron in Bandirma Boric Acid Production Plant. Journal of Trace Elements in Medicine and Biology. 26(2-3):161-4. [Set01]

{Dye et al. 1983} Dye MH; Buchanan L; Dorofaeff FD; Beecroft FG. 1983. Dieback of apricot trees following soil application of boron. N Z J Exp Agric. 11(4): 331-342. [RA2006]

{ECETOC 1995} ECETOC Working Group. 1995. Reproductive and general toxicology of some inorganic borates and risk assessment for human beings. ECETOC Technical Report Vol:63. 91 p. [RA2006]

{ECETOC 1997} ECETOC Working Group. 1997. Ecotoxicology of some inorganic borates. ECETOC Special Report Vol. 11 97 pp. [RA2006]

{ECHA 2010} ECHA (European Chemical Agency 2013). 2010. Draft Support Document for Identification of Boric Acid as a Substance of Very High Concern Because of Its CMR Properties. Document dated June 9, 2010. Available at: http://echa.europa.eu/documents/10162/13638/svhc_supdoc_boric_acid_publication_en.pdf. [Set00]

{ECHA 2013} ECHA (European Chemical Agency 2013). 2013. CLH report, Proposal for Harmonised Classification and Labelling, Substance Name: Boric Acid. Version Number 2. Document dated 4/23/2013. Available at: http://echa.europa.eu/documents/10162/13626/clh_report_boric_acid_en.pdf. [Set00]

{Ecobichon 1998} Ecobichon DJ. 1998. Occupational Hazards of Pesticide Exposure – Sampling, Monitoring, Measuring. Taylor & Francis, Philadelphia, PA. 251 pp.[Std]

{Edmonds et al. 1989} Edmonds, R.L., D.C. Shaw, T. Hsiang and C.H. Driver. 1989. Impact of precommercial thinning on development of Heterobasidion annosum in western hemlock. pg. 85-94 in Proceedings of the Symposium on Research and Management of Annosus Root Disease in Western North America. GTR-PSW-116. USDA Forest Service. Pacific Southwest Forest and Range Experiment Station. Available at: http://www.treesearch.fs.fed.us/pubs/28318. [Set 00]

{EFSA 2009} EFSA (European Food Safety Authority). 2009. Scientific Opinion on the substantiation of health claims related to boron and maintenance of bone (ID 218, 219) and maintenance of joints (ID 219, 220) pursuant to Article 13(1) of Regulation (EC) No 1924/20061. EFSA Journal. 7(9): 1261. 16 pp. Available at: http://www.efsa.europa.eu/sites/default/files/scientific_output/files/main_documents/1261.pdf. [Set00]

{EFSA 2013} EFSA (European Food Safety Authority). 2013. Scientific Opinion on the re-evaluation of boric acid (E 284) and sodium tetraborate (borax) (E 285) as food additives. EFSA Journal. 11(10): 3407. 95 pp. Available at: http://www.efsa.europa.eu/sites/default/files/scientific_output/files/main_documents/3407.pdf. [Set00]

{Eisen et al. 1991} Eisen EA; Wegman DH; Kriebel D; Woskie SR; Hu X. 1991. An epidemiologic approach to the study of acute reversible health effects in the workplace. Epidemiology. 2(4):263-270. [RA2006]

{Eisler 1990} Boron Hazards to Fish, Wildlife, and Invertebrates: A Synoptic Review. U.S. Fish and Wildlife Service, Biological Report 85(1.20), Contaminant Hazard Reviews, Report 20. Document dated April 1990. [Set02]

{El-Dakdoky and Abd El-Wahab 2013} El-Dakdoky MH; Abd El-Wahab HM. 2013. Impact of Boric Acid Exposure at Different Concentrations on Testicular DNA and Male Rats Fertility. Toxicology Mechanisms and Methods. 23(5):360-7. [Set01]

{Ellison 1994} Ellison F. 1994. Tim-bor Insecticide Preliminary Analysis and Precision and Accuracy of Analytical Method Used to Validate Certified Limits: Final Report: Lab Project Number: 970-04. Unpublished study prepared by Case Consulting Lab., Inc. 15 p. MRID 43500100. As summarized in SERA 2006a. [RA2006]

{Epsky et al. 1994} Epsky ND; Heath RR; Holler TC; Harris DL; Mullins T. 1994. Corn steepwater as protein bait for anastrepha suspensa (Diptera: tephritidae). Environ Entomol. 23: 827-831. [RA2006]

{Eren et al. 2004} Eren M; Uyanik F; Kucukersan S. 2004. The Influence of Dietary Boron Supplementation on Egg Quality and Serum Calcium, Inorganic Phosphorus, Magnesium Levels and Alkaline Phosphatase Activity in Laying Hens. Research in Veterinary Science. 76(3): 203-210. [ECOTOX - 166581]

{Esim et al. 2013} Esim N; Tiryaki D; Karadagoglu O; Atici O. 2013. Toxic Effects of Boron on Growth and Antioxidant System Parameters of Maize (*Zea mays* L.) Roots. Toxicology and Industrial Health. 29(9):800-5. [Set01]

{European Commission 2008} European Commission. 2008. Assessment of the Risk to Consumers from Borates and the Impact of Potential Restrictions on their Marketing and Use. Report prepared by DG Enterprise and Industry for the European Commission. Report dated November 2008. Available at: http://ec.europa.eu/enterprise/sectors/chemicals/files/docs_studies/final_report_borates_en.pdf. [Set00]

{European Commission 2009a} European Commission. 2009a. Boric acid, Product-type 8 (Wood preservative), Directive 98/8/EC concerning the placing of biocidal products on the market. CA-Feb09-Doc.3.9a. Report dated Feb. 20, 2009. Available at: https://circabc.europa.eu/sd/a/16d3573d-8626-4352-926c-8f0c9b5fd209/Draft%20assessment%20report%20Boric%20acid.pdf. [Set00]

{European Commission 2009b} European Commission. 2009b. Disodium octaborate tetrahydrate Product-type 8 (Wood preservative). Assessment Report. Directive 98/8/EC concerning the placing biocidal products on the market. Report dated Feb. 20, 2009. Available at: https://circabc.europa.eu/sd/a/6ba0bde3-b159-48f5-9c8a-931d31cc69e1/Draft%20assessment%20report%20DOT.pdf. [Set00]

{Fail et al. 1998} Fail PA; Chapin RE; Price CJ; Heindel JJ. 1998. General, reproductive, developmental, and endocrine toxicity of boronated compounds. Reproductive Toxicology. 12(1): 1-18. [RA2006]

{FDA 2013} FDA (U.S. Food and Drug Administration). 2013. Guidance for Industry: A Food Labeling Guide (14. Appendix F: Calculate the Percent Daily Value for the Appropriate Nutrients). Available at: http://www.fda.gov/Food/GuidanceRegulation/GuidanceDocumentsRegulatoryInformation/LabelingNutrition/ucm064928.htm. [Set02]

{Ferreira et al. 2013} Ferreira RA; Silva Zacarin EC; Malaspina O; Bueno OC; Tomotake ME; Pereira AM. 2013. Cellular Responses in the Malpighian Tubules of *Scaptotrigona postica* (Latreille, 1807) Exposed to Low Doses of Fipronil and Boric Acid. Micron (Oxford, England). 46:57-65. [Set01]

{Findlay 1953} Findlay W. 1953. The toxicity of borax to wood-rotting fungi. Timber Technology and Machine Woodworking 611(2168):275-276. MRID 00159240. As summarized in SERA 2006a. [RA2006]

{Findlay 1960} Findlay W. 1960. Boron compounds for the preservation of timber against fungi and insects. Pest Technology March:124-127. MRID 40196514. As summarized in SERA 2006a. [RA2006]

{Fink et al. 1982a} Fink R; Beavers J; Joiner G; et al. 1982a. Final Report: Acute Oral LD50--Bobwhite Quail: 20 Mule Team Borax, Granular: Project No. 135-106. (Unpublished study received Apr 30, 1982 under 1624-94; prepared by Wildlife International Ltd., submitted by United States Borax & Chemical Corp., Los Angeles, CA; CDL:247369-A). MRID 00090308. As summarized in SERA 2006a. [RA2006]

{Fink et al. 1982b} Fink R; Beavers J; Joiner G; et al. 1982b. Final Report: Eight-day Dietary LC50--Mallard Duck: Polybor: Project No. 135- 104. (Unpublished study received Apr 30, 1982 under 1624-2; prepared by Wildlife International Ltd., submitted by United States Borax & Chemical Corp., Los Angeles, CA; CDL:247364-C). MRID 00100635. As summarized in SERA 2006a. [RA2006]

{Fink et al. 1982c} Fink R; Beavers J; Joiner G; et al. 1982c. Final Report: Eight-day Dietary LC50--Bobwhite Quail: Polybor: Project No. 135-103. (Unpublished study received Apr 30, 1982 under 1624-2; prepared by Wildlife International Ltd., submitted by United States Borax & Chemical Corp., Los Angeles, CA; CDL: 247364-D). MRID 00100636. As summarized in SERA 2006a. [RA2006]

{Fink et al. 1982d} Fink R; Beavers J; Joiner G; et al. 1982d. Final Report: Acute Oral LD50--Bobwhite Quail: Polybor: Project No. 135-105. (Unpublished study received Apr 30, 1982 under 1624-2; prepared by Wildlife International Ltd., submitted by United States Borax & Chemical Corp., Los Angeles, CA; CDL:247364-B). MRID 00100637. As summarized in SERA 2006a. [RA2006]

{Fitzpatrick and Reid 2009} Fitzpatrick KL; Reid RJ. 2009. The Involvement of Aquaglyceroporins in Transport of Boron in Barley Roots. Plant, Cell and Environment. 32(10):1357-65. [Set01]

{Fort et al. 1998} Fort DJ; Propst TL; Stover EL; Strong PL; Murray FJ. 1998. Adverse Reproductive and Developmental Effects in Xenopus from Insufficient Boron. Biological Trace Element Research. 66(1-3): 237-259. [ECOTOX - 166577]

{Fort et al. 2001} Fort DJ; Stover EL; Bantle JA; Dumont JN; Finch RA. 2001. Evaluation of a Reproductive Toxicity Assay Using *Xenopus laevis*: Boric Acid, Cadmium and Ethylene Glycol Monomethyl Ether. Journal of Applied Toxicology. 21:41-52 [ECOTOX - 66626]

{Fort et al. 2002} Fort DJ; McLaughlin DW; Rogers RL; Buzzard BO. 2002. Effect of Endocrine Disrupting Chemicals on Germinal Vesicle Breakdown in Xenopus *In Vitro*. Drug and Chemical Toxicology. 25(3): 293-308. [ECOTOX - 105901]

{Frank and Stuanes 2003} Frank J; Stuanes AO. 2003. Short-term effects of liming and vitality fertilization on forest soil and nutrient leaching in a Scots Pine ecosystem in Norway. For Ecol Manage. 176: 371-386. [RA2006]

{Frick 1985} Frick H. 1985. Boron Tolerance and Accumulation in the Duckweed, *Lemna minor*. Journal of Plant Nutrition. 8(12): 1123-1129. [ECOTOX - 5947]

{Furuta et al. 2007} Furuta T; Iwata N; Kikuchi K. 2007. Effects of Fish Size and Water Temperature on the Acute Toxicity of Boron to Japanese Flounder *Paralichthys olivaceus* and Red Sea Bream *Pagrus major* . Fisheries Science.73(2): 356-363. [ECOTOX - 166696]

{Garabrant et al. 1985} Garabrant DH; Bernstein L; Peters JM; Smith TJ; Wright WE. 1985. Respiratory effects of borax dust. British Journal of Industrial Medicine. 42(12): 831-837. [RA2006]

{Garcia and Morrell 2010} Garcia CM and J.J. Morrell. 2010. Efficacy and Economic Benefits of Prophylactic Treatments of Newly Felled Bamboo. Journal of Economic Entomology. 103(1): 101-107. [ECOTOX - 120915]

{Geeraerts and Belpaire 2010} Geeraerts C1; Belpaire C. 2010. The effects of contaminants in European eel: a review. Ecotoxicology. 19(2):239-66. [Set01]

{Gersich 1984} Gersich FM. 1984. Evaluation of a static renewal chronic toxicity test method for *D. magna* using boric acid. Environmental Toxicology and Chemistry 3:1, 89-94. [RA2006]

{Gestring and Soltanpour 1987} Gestring WD; Soltanpour PN. 1987. Comparison of soil tests for assessing boron toxicity to alfalfa. SOIL SCI SOC AM J; 51 (5). 1987. 1214-1219. [RA2006]

{Geyikoglu and Turkez 2008} Geyikoglu F; Turkez H. 2008. Boron Compounds Reduce Vanadium Tetraoxide Genotoxicity in Human Lymphocytes. Environmental Toxicology and Pharmacology. 26(3):342-7. [Set01]

{Goodell and Pendlebury 1991} Goodell B; Pendlebury AJ. 1991. Preservative treatment and field test monitoring of spruce pole stock: pressure and diffusible chemical treatments. For Prod J. 41: 39-44. [RA2006]

{Gordon et al. 1973} Gordon AS; Prichard JS; Freedman MH. 1973. Seizure disorders and anemia associated with chronic borax intoxication. Can. Med. Assoc. J.; VOL 108 ISS Mar 17 1973, P719-721, 724, (REF 6). [RA2006]

{Grace and Abdallay 1990} Grace JK; Abdallay A. 1990. Termiticidal activity of boron dusts (Isoptera, rhinotermitidae). J Appl Entomol. 109(3): 283-288. [RA2006]

{Grace and Yamamoto 1994} Grace JK; Yamamoto RT. 1994. Simulation of remedial borate treatments intended to reduce attack on douglas-fir lumber by the formosan subterranean termite (Isoptera: rhinotermitidae). Journal of Economic Entomology. 87(6): 1547-1554. [RA2006]

{Graham 1970} Graham DA. 1970. Evaluation of borax for prevention of Annosus root rot in California. Disease Report 3, File 5230, USDA/Forest Service Report dated October 1970.. [RA2006]

{Graham 1971} Graham DA. 1971. Evaluation of borax for prevention of Annosus root rot in California. Plant Disease Reporter. 55(6):490-494. [RA2006]

{Grizzard and Matthews 1942} Grizzard AL; Matthews EM. 1942. The effect of boron on seed production of alfalfa. Am Soc Agron. 34: 365-368. [RA2006]

{Gu et al. 2006} Gu D; He J; Duan X; et al. 2006. Body Weight and Mortality Among Men and Women in China. JAMA. 295(7); 776-783. [Std]

{Guhl 1992} Guhl W. 1992. Okologische Aspekte von Bor. SOFW-Journal, 118 (18/92), 1159-1168. As cited in ECETOC Working Group 1997. [RA2006]

{Hall et al. 2014} Hall S; Lockwood R; Harrass MC. 2014. Application of a Unique Test Design to Determine the Chronic Toxicity of Boron to the Aquatic Worm *Lumbriculus variegatus* and Fatmucket Mussel *Lampsilis siliquoidea*. Archives of Environmental Contamination and Toxicology. 66(1):58-68. [Set01/ECOTOX 166414]

{Hamilton 1995} Hamilton SJ. 1995. Hazard Assessments of Inorganics to Three Endangered Fish in the Green River, Utah. Ecotoxicology and Environmental Safety. 30:134-142. [RA2006]

{Hamilton and Buhl 1990} Hamilton SJ; Buhl KJ. 1990. Acute Toxicity of Boron, Molybdenum, and Selenium to Fry of Chinook Salmon and Coho Salmon. Arch. Environ. Contam. Toxicol. 19:366-373. [RA2006]

{Hamilton and Wolf 2007} Hamilton RA; Wolf BC. 2007. Accidental Boric Acid Poisoning Following the Ingestion of Household Pesticide. Journal of Forensic Science. 52(3):706-8. [Set01]

{Handler 1978} Handler R. 1978. Monograph on Borax, Boric Acid, and Borates. Washington, D.C.: Food and Drug Administration. Prepared by Informatics for FDA, Bureau of Foods. (FDA report no. FDA/BF- 79/6; PB287761). MRID 42931800. As summarized in SERA 2006a. [RA2006]

{Hanstveit et al. 2001} Hanstveit AO; de Vette HQ; van Asten JG. 2001. A study or the adsorption/desorption of Boric Acid to two sediment types, TNO Unpublished report to Borax Europe. IMW-99-9047-03. Unpublished study as summarized in HERA (2005). [Sec]

{Harrouk et al. 2005} Harrouk WA; Wheeler KE; Kimmel GL; Hogan KA; Kimmel CA. 2005. Effects of Hyperthermia and Boric Acid on Skeletal Development in Rat Embryos. Birth Defects Research. Part B, Developmental and Reproductive Toxicology. 74(3):268-76. [Set01]

{Heederik et al. 1994} Heederik D; De Cock J; Endlich E. 1994. Dust exposure indices and lung function changes in longshoremen and dock workers. American Journal of Industrial Medicine. 26(4): 497-509. [RA2006]

{Heindel et al. 1994} Jeindel JJ; Price CJ; Schwetz BA. 1994. The developmental toxicity of boric acid in mice, rats, and rabbits. Environmental Health Perspectives. 102(Suppl 7): 107–112. [Set00]

{Henderson and Eckhert 2006} Henderson KA; Eckhert C. 2006. Boric Acid Induces EF Stress in Du-145 and LNCAP Prostate Cancer Cell Lines. Toxicological Sciences 2006 Mar;90(1-S):289 [Set01]

{Henderson et al. 2009} Henderson K; Stella SL; Kobylewski S; Eckhert CD. 2009. Receptor Activated $Ca(2^{+})$ Release Is Inhibited by Boric Acid in Prostate Cancer Cells. PloS one. 4(6):e6009. [Set01]

{Henderson et al. 2015} Henderson KA; Kobylewski SE; Yamada KE; Eckhert CD. 2015. Boric Acid Induces Cytoplasmic Stress Granule Formation, eIF2α Phosphorylation, and Atf4 in Prostate Du-145 Cells. Biometals. 28(1):133-41. [Set01]

{HERA 2005} HERA (Human and Environmental Risk Assessment). 2005. Substance: Boric Acid (CAS No 10043-35-3), Edition 1.0. Human and Environmental Risk Assessment on ingredients of Household Cleaning Products. Available at: http://www.heraproject.com/Index.cfm. [Set00]

{Hickey 1989} Hickey CW. 1989. Sensitivity of Four New Zealand Cladoceran Species and *Daphnia magna* to Aquatic Toxicants. New Zealand Journal of Marine and Freshwater Research. 23(1): 131-137. [ECOTOX - 8764]

{Hillis et al. 2011} Hillis DG; Fletcher J; Solomon KR; Sibley PK. 2011. Effects of Ten Antibiotics on Seed Germination and Root Elongation in Three Plant Species. Archives of Environmental Contamination and Toxicology. 60(2): 220-232. [ECOTOX - 161023]

{Hodges 1970} Hodges CS. 1970. Evaluation of stump treatment chemicals for control of Fomes annosus. In: Proceedings of the 3rd International Conference on Fomes annosus. (IUFRO). Pages 43-53. [RA2006]

{Hoffman et al. 1990} Hoffman DJ; Camardese MB; Lecaptain LJ; Pendleton GW. 1990. Effects of Boron on Growth and Physiology in Mallard Ducklings. Environmental Toxicology and Chemistry. 9: 335-346. [RA2006]

{Hogsette and Koehler 1992} Hogsette JA; Koehler PG. 1992. Comparative toxicity of aqueous solutions of boric acid and Polybor 3 to house flies (Diptera: Muscidae). J Econ Entomol. 85: 1209-1212. [RA2006]

{Hovatter and Ross 1995} Hovatter PS; Ross RH. 1995. A comparative analysis of the toxicity of boron compounds to freshwater and saltwater species. [RA2006]

{HSDB 2014} HSDB (Hazardous Substances Database). Borax. Available at: http://toxnet.nlm.nih.gov/cgi-bin/sis/search/a?dbs+hsdb:@term+@DOCNO+328. Last Revision Date: 20140904. [Set00]

{Hu et al. 1992} Hu X; Wegman DH; Eisen EA; Woskie SR; Smith RG. 1992. Dose related acute irritant symptom responses to occupational exposure to sodium borate dusts. British Journal of Industrial Medicine, Vol. 49, No. 10, pages 706-713, 11 references, 1992. [RA2006]

{Hubbard 1998} Hubbard SA. 1998. Comparative toxicology of borates. Biol Trace Elem Res 1998 Winter. 66(1-3): 343-57. [RA2006]

{Hubbard and Sullivan 1995} Hubbard SA; Sullivan FM. 1995. Toxicological effects of inorganic boron compounds in animals: a review of the literature. Journal of Trace Elements in Experimental Medicine 1995;8(2):133. [RA2006]

{Hubbard and Sullivan 1996} Hubbard SA; Sullivan FM. 1996. Toxicological effects of inorganic boron compounds in animals: a review of the literature. Journal of Trace Elements in Experimental Medicine. 9(4): 165-173. [RA2006]

{Humphrey and Dykes 2008} Humphrey JAC; Dykes ES. 2008. Thermal energy conduction in a honey bee comb due to cell-heating bees. J Theoretical Biology. 250 (1): 194-208. [Std]

{Hunt 1994} Hunt CD. The biochemical effects of physiologic amounts of dietary boron in animal nutrition models. Environmental Health Perspectives. 102(Suppl 7):35-43. [Set03]

{Hunt 1996} Hunt CD. 1996. Biochemical effects of physiological amounts of dietary boron. Journal of Trace Elements in Experimental Medicine. 9:185–213. [Set03]

{Hunt 1998} Hunt CD. 1998. Regulation of enzymatic activity: One possible role of dietary boron in higher animals and humans. Biological Trace Element Research. 66:205–225. (As summarized in Institute of Medicine 2001) [Set02]

{Hunt et al. 1991} Hunt CD; Shuler TR; Mullen LM. 1991. Concentration of Boron and Other Elements in Human Foods and Personal-care Products. Journal of the American Dietetic Association. 91:558-568. [Set02]

{Hyrsl et al. 2007} Hyrsl P; Buyukguzel E; Buyukguze K. 2007. The Effects of Boric Acid-Induced Oxidative Stress on Antioxidant Enzymes and Survivorship in *Galleria mellonella*. Archives of Insect Biochemistry and Physiology. 66(1):23-31. [Set01]

{ICRP (International Commission on Radiologic 1975} ICRP (International Commission on Radiologic Protection). 1975. Report of the Task Group on Reference Man. Recommendations of the International Commission on Radiological Protection (ICRP) Publ. No. 23. Pergamon Press, New York, NY. [Std]

{Imbus et al. 1963} Imbus JR; Cholak J; Miller LJ; Sterling T. 1963. Boron, cadmium, chromium, and nickel in blood and urine. A survey of American working men. Archives of Environmental Health. 6: 286-295. [Set05]

{Ince et al. 2010} Ince S; Kucukkurt I; Cigerci IH; Fatih Fidan A; Eryavuz A. 2010. The Effects of Dietary Boric Acid and Borax Supplementation on Lipid Peroxidation, Antioxidant Activity, and DNA Damage in Rats. Journal of Trace Elements in Medicine and Biology. 24(3):161-4. [Set01]

{Ince et al. 2011} Ince S; Turkmen R; Yavuz H. 2011. The Effect of Boric Acid on Acethylcholine, Bethanechol and Potasssium-Evoked Responses on Ileum of Rat. Autonomic and Autacoid Pharmacology. 31(3-4):50-6. [Set01]

{Ince et al. 2012} Ince S; Keles H; Erdogan M; Hazman O; Kucukkurt I. 2012. Protective Effect of Boric Acid Against Carbon Tetrachloride-Induced Hepatotoxicity in Mice. Drug and Chemical Toxicology. 35(3):285-92. [Set01]

{Institute of Medicine 1997} Institute of Medicine. 1997. Dietary Reference Intakes for Calcium, Phosphorus, Magnesium, Vitamin D, and Fluoride. Standing Committee on the Scientific Evaluation of Dietary Reference Intakes; Food and Nutrition Board; Institute of Medicine, National Academy of Sciences. ISBN 0-309-06350-7. 449 pp. Available at: http://www.nap.edu/catalog/5776/dietary-reference-intakes-for-calcium-phosphorus-magnesium-vitamin-d-and-fluoride. [Set00]

{Institute of Medicine 2001} Institute of Medicine. 2001. Dietary Reference Intakes for Vitamin A, Vitamin K, Arsenic, Boron, Chromium, Copper, Iodine, Iron, Manganese, Molybdenum, Nickel, Silicon, Vanadium, and Zinc. Report of the Panel on Micronutrients, Subcommittees on Upper Reference Levels of Nutrients and of Interpretation and Uses of Dietary Reference Intakes, and the Standing Committee on the Scientific Evaluation of Dietary Reference Intakes, Food and Nutrition Board, Institute of Medicine. Available at: http://www.nap.edu/catalog/10026/dietary-reference-intakes-for-vitamin-a-vitamin-k-arsenic-boron-chromium-copper-iodine-iron-manganese-molybdenum-nickel-silicon-vanadium-and-zinc. [Set02]

{IPCS/WHO 1998} IPCS/WHO (International Program on Chemical Safety/World Health Organization). 1998. Environmental Health Criteria 204: Boron. United Nations Environment Programme, the International Labour Organisation, and the World Health Organization. Available at: http://apps.who.int/iris/bitstream/10665/42046/1/9241572043_eng.pdf. [Set00]

{Jamjod and Rerkasem 1999} Jamjod S; Rerkasem B. 1999. Genotypic variation in response of barley to boron deficiency. Plant Soil. 215: 65-72. [RA2006]

{Jansen et al. 1984a} Jansen JA: Andersen J; Schou JS. 1984a. Boric acid single dose pharmacokinetics after intravenous administration to man. Archives of Toxicology. 55(1): 64-67. [Set05]

{Jansen et al. 1984b} Jansen JA: Andersen J; Schou JS. 1984b. Gastro-intestinal absorption and *in vitro* release of boric acid from water-emulsifying ointments. Food and Chemical Toxicology. 22(1): 49-53. [Set05]

{Jirakova et al. 2015} Jirakova A; Rajsk L; Rob F; Gregorova J; Hercogova J. 2015. Dermatitis Toxica Faciei After Boric Acid. Dermatology and Therapy. 28(1):52-5. [Set01]

{Kabu and Akosman 2013} Kabu M; Akosman MS. 2013. Biological Effects of Boron. Reviews of Environmental Contamination and Toxicology of Boron. 225: 57-75. [Set00]

{Karsky 1999} Karsky R . 1999. Dry Borax Applicator: Operator's Manual. 9934 2812. Missoula, MT: U.S. Department of Agriculture, Forest Service, Missoula Technology and Development Center. Available at: http://www.fs.fed.us/t-d/php/library_card.php?p_num=9934%202812. [Set00]

{Karsky et al. 1998} Karsky R; Cram M; Thistle HW. 1998. New methods of application of borax to tree stumps for control of *Heterobasidion annosum*. USDA/Forest Service T&D Publicaiton 9834 2834. Available at: http://www.fs.fed.us/t-d/pubs/htmlpubs/htm98342834/paper.htm. [Set00]

{Kato et al. 2009} Kato Y; Miwa K; Takano J; Wada M; Fujiwara T. 2009. Highly Boron Deficiency-Tolerant Plants Generated by Enhanced Expression of NIP5;1, a Boric Acid Channel. The Plant Cell Physiol. 50(1):58-66. [Set01]

{Katsoyannos et al. 1999} Katsoyannos BI; Heath RR; Papadopoulos NT; Epsky ND; Hendrichs J. 1999. Field evaluation of Mediterranean fruit fly (Diptera: tephritidae) female selective attractants for use in monitoring programs. J Econ Entomol. 92: 583-589. [RA2006]

{Khangarot and Das } Khangarot BS; Das S. 2009. Acute Toxicity of Metals and Reference Toxicants to a Freshwater Ostracod, *Cypris subglobosa* Sowerby, 1840 and Correlation to EC_{50} Values of Other Test Models. Journal of Hazardous Materials. 172(2/3): 641-649. [ECOTOX - 151495]

{Kirkland 1992} Kirkland R. 1992. Efficacy of Disodium Octaborate Tetrahydrate in the Control of Flea Larvae: Lab Project Number: 134-92. Unpublished study prepared by Bio Research. 11 p. MRID 42745200. [RA2006]

{Kissel 2010} Kissel JC. 2010. The mismeasure of dermal absorption. Journal of Exposure Science and Environmental Epidemiology. 21: 302–309. [Std]

{Klasing and Pilch 1988} Klasing SA; Pilch SM. 1988. Agricultural drainage water contamination in the San Joaquin Valley: A public health perspective for selenium, boron, and molybdenum. San Joaquin Valley Drainage Program, 2800 Cottage Way, Sacramento, CA. As cited in ECETOC Working Group 1997. [RA2006]

{Kliejunas 1989} Kliejunas JT. 1989. Borax stump treatment for control of annosus root disease in the Eastside pinte type forests of Northeastern California. Presented at Sumposium on Research and Management of Annosus Root Disease in Western North America. April 18-21, 1989 at Monterey, CA. USDA Forest Service Gen. Tech. Rep. PSW-116: 159-166. Available at: http://www.fs.fed.us/psw/publications/documents/psw_gtr116/psw_gtr116_07_kliejunas.pdf. [RA2006]

{Klotz et al. 2000} Klotz JH; Greenberg L; Amrhein C; Rust MK. 2000. Toxicity and repellency of borate-sucrose water baits to argentine ants (Hymenoptera: Formicidae). J Econ Entomol 2000 Aug;93(4):1256-8. [RA2006 ECOTOX]

{Kluge 1990} Kluge R. 1990. Symptom-related toxic threshold in plants for the evaluation of excess boron in crops. Agribiol Red 43(3):234-243. As cited in SERA 2006a from ECETOC 1997. [RA2006]

{Knisel and Davis 2000} Knisel WG; Davis FM. 2000. GLEAMS (Groundwater Loading Effects of Agricultural Management Systems), Version 3.0, User Manual. U.S. Department of Agriculture, Agricultural Research Service, Southeast Watershed Research Laboratory, Tifton, GA. Pub. No.: SEWRL-WGK/FMD-050199. Report Dated May 1, 1999 and revised August 15, 2000. 194pp.[Std]

{Koenigs 1971} Koenigs JWJr. 1971. Borax: its toxicity to Fomes annosus in wood and its diffusion, persistence and concentration in treated stumps of southern pines. Phytopathology; 61(2): 269-74 1971; (REF:12). [RA2006]

{Koh 1995} Koh D. 1995. An outbreak of occupational dermatosis in an electronics store. Contact Dermatitis, Vol. 32, No. 6, pages 327-330, 4 references, 1995. [RA2006]

{Kopf and Wilk 1995} Kopf W; Wilk A. 1995. Investigation on aquatic toxicity against plant organisms. Unpublished results from the BayLFw – Institut fur Wasserforschung, Kaulbachstr. 37, D-80539, Munich, Germany. As cited in ECETOC Working Group 1997. [RA2006]

{Korkmaz et al. 2007} Korkmaz M; Uzgoren S; Bakırdere S; Aydin F; Ataman OY. 2007. Effects of dietary boron on cervical cytopathology and on micronucleus frequency in exfoliated buccal cells. Environmental Toxicology. 22:17–25. [Set05]

{Kreij and Basar 1997} Kreij C; Basar H. 1997. Leaf tip yellowing in eggplant is caused by boron deficiency. J Plant Nutr. 20: 47-53. [RA2006]

{Krieger et al. 1996} Krieger RI; Dinoff TM; Peterson J. 1996. Human Disodium Octaborate Tetrahydrate DOT Exposure Following Carpet Treatment Not Associated with Significant Dermal Absorption. Journal of Exposure Analysis and Enviornmental Epidemiology. 6(3): 279-288. [Set01]

{Krise et al. 1995} Krise WF; Hendrix MA; Bonney WA; Baker-Gordon SE. 1995. Evaluation of sperm-activating solutions in Atlantic salmon Salmo salar fertilization tests. J World Aquac Soc. 26: 384-389. [RA2006]

{Ku and Chapin 1994} Ku WW; Chapin RE. 1994. Mechanism of the Testicular Toxicity of Boric Acid in Rats, *In Vivo* and *In Vitro* Studies. Environmental Health Perspectives. 102 (Suppl. 7):99-105. [Set02]

{Ku et al. 1991} Ku WW; Chapin RE; Moseman RF; Brink RE; Pierce KD; Adams KY. 1991. Tissue disposition of boron in male Fischer rats. Toxicology and Applied Pharmacology. 111:145–151. [Set05]

{Kucukkurt et al. 2015} Kucukkurt I; Akbel E; Karabag F; Ince S. 2015. The Effects of Dietary Boron Compounds in Supplemented Diet on Hormonal Activity and Some Biochemical Parameters in Rats. Toxicology and Industrial Health. 31(3):255-60. [Set01]

{Kudo et al. 2000} Kudo S; Tanase H; Yamasaki M; et al. 2000. Collaborative Work to Evaluate Toxicity on Male Reproductive Organs by Repeated Dose Studies in Rats 23). A Comparative 2- and 4-Week Repeated Oral Dose Testicular Toxicity Study of Boric Acid in Rats. Journal Of Toxicological Sciences. 25:223-232. [ECOTOX - 105982]

{Kukulinski 1988} Kukulinski M. 1988. Timbor Rods: Eye Irritation, Primary Skin Irritation, Acute Oral Toxicity, Acute Dermal Toxicity, Sensitization: Laboratory Project ID TM 87-549. Unpublished study prepared by Tox Monitor Laboratories, Inc. 25 p. MRID 40534003. As summarized in SERA 2006a. [RA2006]

{Laks et al. 1993} Laks PE; Park CG; Richter DL. 1993. Anti-sapstain efficacy of borates against Aureobasidium pullulans. For Prod J. 43: 33-34. [RA2006]

{LaLievre 1998, MRID 40594602, as cited in S} LaLievre 1998, MRID 40594602, as cited in U.S. EPA 1993b. [RA2006]

{Landauer 1953} Landauer W. 1953. Complex formation and chemical specificity of boric acid in production of chick embryo malformations. Proc Soc Exp Biol Med. 82:633-636. [RA2006]

{Landolph 1985} Landolph JR. 1985. Cytotoxicity and negligible genotoxicity of borax and borax ores to cultured mammalian cells. American Journal of Industrial Medicine. 7(1): 31-43. [RA2006]

{Laposata and Dunson 1998} Laposata MM; Dunson WA. 1998. Effects of Boron and Nitrate on Hatching Success of Amphibian Eggs. Arch Environ Contam Toxicol 35: 615-619. [RA2006]

{Lee et al. 1978} Lee IP; Sherins RJ; Dixon RL. 1978. Evidence for induction of germinal aplasia in male rats by environmental exposure to boron. Toxicology and Applied Pharmacology. 45 (2): 577-590. [RA2006]

{Lehtijarvi et al. 2011} Lehtijarvi A; Dogmus-Lehtijarvii HT; Aday AG; Oskay F. 2011. The Efficacy of Selected Biological and Chemical Control Agents Against *Heterobasidion abietinum* on *Abies cilicica*. Forest Pathology. 41(6): 470-476. [ECOTOX - 166419]

{Lewis and Valentine 1981} Lewis MA and Valentine LC. 1981. Acute and Chronic Toxicities of Boric Acid to Daphnia magna Straus. Bull. Environ. Contam. Toxicol. 27:309-315. [RA2006]

{Li et al. 2008} Li E; Xiong Z; Chen L; Zeng C; Li K. 2008. Acute Toxicity of Boron to Juvenile White Shrimp, *Litopenaeus vannamei*, at Two Salinities. Aquaculture. 278(1-4): 175-178. [ECOTOX - 111738]

{Linden et al. 1986} Linden CH; Hall AH; Kulig KW; et al. 1986. Acute ingestions of boric acid. Clin Toxicol 24:269-279. [RA2006]

{Linden et al. 1986} Linden CH; Hall AH; Kulig KW; et al. 1986. Acute ingestions of boric acid. Clinical Toxicology. 24:269-279. [RA2006]

{Linder et al. 1990} Linder RE; Strader LF; Rehnberg GL. 1990. Effect of Acute Exposure to Boric Acid on the Male Reproductive System of the Rat. Journal of Toxicology and Environmental Health. 31:133-146. [ECOTOX - 105864]

{Litovitz et al. 1988} Litovitz TL; Klein-Schwartz W; Oderda GM; Schmitz BF. 1988. Clinical manifestation of toxicity in a series of 784 boric acid ingestions. Am J Emerg Med, 6: 209-213. Cited in WHO 1998. [RA2006]

{Litovitz et al. 1988} Litovitz TL; Klein-Schwartz W; Oderda GM; Schmitz BF. 1988. Clinical manifestation of toxicity in a series of 784 boric acid ingestions. Am J Emerg Med, 6: 209-213. [Set05]

{Lloyd 1998} Lloyd J. 1998. Borates and their biological applications. The International Research Group on Wood Preservation. Report No. IRG/WP 98-30178. Copy courtesy of Jeff Lloyd, Nisus Corporation. [Nisus]

{Lloyd 2012} Lloyd J. 2012. Control of Heterobasidion using Borate Stump Treatment. PowerPoint presentation courtesy of Jeff Lloyd, Nisus Corporation. [Nisus]

{Lloyd and Pratt 1997} Lloyd JD; Pratt JE. 1997. The Use of Disodium Octaborate Tetrahydrate to Control Conifer Butt Rot Caused by *Heterobasidion annosum*. in International Conference on Wood Protection with Diffusible Preservatives and Pesticides; pp. 135-139. Copy courtesy of Jeff Lloyd. [Nisus]

{Locksley and Farr 1955} Locksley JB; Farr LE. 1955. The tolerance of large doses of sodium borate intravenously by patients receiving neutron capture therapy. Journal of Pharmacology and Experimental Theraputics. 114(4):484-489. [Set05]

{Loewengart 2001} Loewengart G. 2001. Toxicity of boron to rainbow trout: a weight-of-the-evidence assessment. Environ Toxicol Chem. 20(4):796-803. [RA2006]

{Lung and Clancy 2009} Lung D; Clancy C. 2009. "Boiled Lobster" Rash of Acute Boric Acid Toxicity. Clinical Toxicology (Philadelphia, Pa.). 47(5):432. [Set01]

{Mahabir et al. 2008} Mahabir S; Spitza M; Barrera S; Dong Y; Eastham C; Forman M. 2008. Dietary boron and hormone replacement therapy as risk factors for lung cancer in women. American Journal of Epidemiology. 167:1070–1080. [Set02]

{Maier and Knight 1991} Maier KJ; Knight AW. 1991. The toxicity of waterborne boron to D. magna and C. decorus and the effect of water hardness and sulfate on boron toxicity. Arch Environ Contam Toxicol 20:282-287. [RA2006]

{Malouf 1987} Malouf G. 1987. Wood Penetration Studies Using Aqueous TIM-BOR: Lab. Proj. ID 1598. Unpublished study prepared by US Borax Research Corp. 7 p. MRID 40196521. As summarized in SERA 2006a. [RA2006]

{Mascari and Foil 2010} Mascari TM; Foil LD. 2010. Laboratory Evaluation of Insecticide-Treated Sugar Baits for Control of Phlebotomine Sand Flies (Diptera: Psychodidae). Journal of the American Mosquito Control Association. 26(4):398-402. [Set01]

{Mathieson et al. 2012} Mathieson M; Toft R; Lester PJ. 2012. Influence of Toxic Bait Type and Starvation on Worker and Queen Mortality in Laboratory Colonies of Argentine Ant (Hymenoptera: Formicidae). Journal of Economic Entomology. 105(4):1139-44. [Set01]

{Maudlin and Kard 1996} Maudlin JK; Kard BM. 1996. Disodium Octaborate Tetrahydrate Treatments to Slash Pine for Protection against Formosan Subterranean Termite and Eastern Subterranean Termite (Isoptera: Rhinotermitidae). Journal of Economic Entomology. 89 (3): 682-688. [Set01]

{Mauldin and Beal 19??} Mauldin J; Beal R. 19??. Feeding and Survival of Subterranean Termites on Southern Pine Pressure-treated with a Borate. Unpublished study prepared by USDA Forest Service. 18 p. MRID 40196501. As summarized in SERA 2006a. [RA2006]

{Meacham and Hunt 1998} Meacham SL; Hunt CD. 1998. Dietary Boron Intakes of Selected Populations in the United States. Biological Trace Element Research. 66: 65-76.

{Meacham et al. 2010} Meacham S; Karakas S; Wallace A; Altun F. 2010. Boron in Human Health: Evidence for Dietary Recommendations and Public Policies. The Open Mineral Processing Journal. 3:36-83. [Set00]

{Miwa and Fujiwara 2010} Miwa K; Fujiwara T. 2010. Boron Transport in Plants: Co-Ordinated Regulation of Transporters. Ann Bot. 105(7):1103-8. [Set01]

{Miwa et al. 2007} Miwa K; Takano J; Omori H; Seki M; Shinozaki K; Fujiwara T. 2007. Plants Tolerant of High Boron Levels. Science. 318(5855):1417. [Set01]

{Mondy and Munshi 1993} Mondy NI; Munshi CB. 1993. Effect of boron on enzymatic discoloration and pH and ascorbic acid contents of potatoes. J Agric Food Chem. 41: 554-556. [RA2006]

{Moore 1997} Moore JA. 1997. An assessment of boric acid and borax using the IEHR evaluative process for assessing human developmental and reproductive toxicity of agents. Reproductive Toxicology. 11(1): 123-160. [RA2006]

{Moseman 1994} Moseman RF. 1994. Chemical disposition of boron in animals and humans. Environmental Health Perspectives. 102(Suppl 7): 113–117. [Set02]

{Mullens and Rodriguez 1992} Mullens BA; Rodriguez JL. 1992. Effects of Disodium Octaborate Tetrahydrate on Survival, Behavior, and Egg Viability of Adult Muscoid Flies (Diptera: Muscidae). Journal of Economic Entomology. 85 (1): 137-143. [Set01]

{Murray 1995} Murray FJ. 1995. A human health risk assessment of boron (Boric acid and borax) in drinking water. Regul Toxicol Pharmacol. 22: 221-230. [RA2006]

{Murray 1998} Murray FJ. 1998. A comparative review of the pharmacokinetics of boric acid in rodents and humans. Biological Trace Element Research. 66(1):331–341. [Set05]

{Muzny et al. 2012} Muzny C; Barnes A; Mena L. 2012. Symptomatic Trichomonas vaginalis Infection in the Setting of Severe Nitroimidazole : Successful Treatment with Boric Acid. Sex Health. 9(4):389-91. [Set01]

{Naderi and Palmer 2006} Naderi AS; Palmer BF. 2006. Successful Treatment of a Rare Case of Boric Acid Overdose with Hemodialysis. American Journal of Kidney Diseases. 48(6):e95-7. [Set01]

{Nagai et al. 2010} Nagai N; Murao T; Okamoto N; Ito Y. 2010. Comparison of Corneal Wound Healing Rates After Instillation of Commercially Available Latanoprost and Travoprost in Rat Debrided Corneal Epithelium. Journal of Oleo Science. 59(3):135-41. [Set01]

{Naranjo et al. 2013} Naranjo DP; Qualls WA; M ller GC; Samson Xue RD. 2013. Evaluation of Boric Acid Sugar Baits against *Aedes albopictus* (Diptera: Culicidae) in Tropical Environments. Parasitology Research. 112(4):1583-7. [Set01]

{National Boron Research Institute 2016} National Boron Research Institute. 2016. Boron Reserves. Available at: http://www.boren.gov.tr/en/boron/reserves. [Set00]

{Neary et al. 1975} Neary DG; Schneider G; White DP. 1975. Boron toxicity in red pine following municipal waste water irrigation. Soil Sci Soc Am Proc. 39(5): 981-982. [RA2006]

{Nicolotti and Gonthier 2005} Nicolotti G; Gonthier P. 2005. Stump Treatment against Heterobasidion with Phlebiopsis gigantea and Some Chemicals in Picea abies Stands in the Western Alps. Forest Pathology. 35(5): 365-374. [ECOTOX - 105866]

{Nielsen 1994} Nielsen FH. 1994. Biochemical and physiologic consequences of boron deprivation in humans. Environmental Health Perspectives. 102(Suppl 7): 59–63. [Set02]

{Nielsen 1997} Nielsen FH. 1997. Boron. Chapter 15 in: O'Dell BL; Sunde RA. Editors. 1997. Handbook of Nutritionally Essential Mineral Elements. CRC Press. pp. 453-484. [Set02]

{Nisus 2005} Nisus (Nisus Corporation). 2005. NiBor Borate Insecticide and Fungicide. Product Label approved by EPA on 7/13/2005. Available at: http://www3.epa.gov/pesticides/chem_search/ppls/064405-00008-20050713.pdf. [Set00]

{Nisus 2009} Nisus (Nisus Corporation). 2009. DOT Cellu-Treat® Wood Preservative. Material Safety Data Sheet. Issued 8/2001, Updated 1/2009. Available at: http://www.fs.usda.gov/Internet/FSE_DOCUMENTS/stelprdb5329557.pdf. [Set00]

{Nisus 2010} Nisus (Nisus Corporation). 2010. Cellu-Treat® DOT Wood Preservative. Product Label dated 2010. Available at: http://www.fs.usda.gov/Internet/FSE_DOCUMENTS/stelprdb5329557.pdf. [Set00]

{Nisus 2015} Nisus (Nisus Corporation). 2015. General Use Label, Nibor® Borate Insecticide and Fungicide. Product Label dated 9/24/2015. 64405-8 12-8-14 SAL + 3-9-2015 NOTIF. Available at: http://www3.epa.gov/pesticides/chem_search/ppls. [Set00]

{Nobel 1981} Nobel W. 1981. Effect of boron pollution of submerged softwater-macrophytes. Angew Bot. 55(5-6): 501-514. As cited in WHO 1998. [RA2006]

{Noirot 1992} Noirot M. 1992. Final Report on the TIM-BOR Experimental Use Permit Study. Unpublished study prepared by U S. Borax Research Corp. 130 p. MRID 42381800. As summarized in SERA 2006a. [RA2006]

{Nolte et al. 1995} Nolte T; Harleman JH; Jahn W. 1995. Histopathology of chemically induced testicular atrophy in rats. Experimental and Toxicologic Pathology. 47 (4): 267-286. [RA2006]

{Nondillo et al. 2014} Nondillo A; Chaves CC; Fialho FB; Bueno OC; Botton M. 2014. Evaluation of Insecticides for the Control of *Linepithema* (Hymenoptera: Formicidae). Journal of Economic Entomology. 107(1):215-22. [Set01]

{NPCI 2013} NPCI (National Pesticide Information Center). 2013. Boric Acid General Fact Sheet. Available at: http://npic.orst.edu/factsheets/boricgen.html. [Set00]

{NPTN 2001} NPTN (National Pesticide Telecommunications Network). 2001. Boric Acid (Technical Fact Sheet). Available at: https://www.livingwithbugs.com/PDFiles/Boric_Acid_Factsheet.pdf. [Set00]

{NRC (National Research 1983} NRC (National Research Council). 1983. Risk assessment in the Federal government: managing the process. Washington, DC: National Academy Press; 176 p. + app. [RA2006]

{Nusus 2015} Nisus (Nisus Corporation). 2010. General Use Label. Nibor® Borate Insecticide and Fungicide (previously approved Tim-Bor Professional, Nibor-D, Nibor D, Cellutreat, Cellu-Treat). Marked Label dated 9/24/2015. Available at: http://www3.epa.gov/pesticides/chem_search/ppls/064405-00008-20150924.pdf. [Set00]

{O'Dell and Sunde 1997} O'Dell BL; Sunde RA. 1997. Handbook of Nutritionally Essential Mineral Elements. CRC Press. Available at: https://books.google.com/books?hl=en&lr=&id=8ldsXzd9QQAC&oi=fnd&pg=PR3&dq=Handbook+of+Nutritionally+Essential+Mineral+Elements&ots=lvKP2yO3Am&sig=pBjM7iJRw-0kkm-7TWQFnDdIgRY#v=onepage&q=Handbook%20of%20Nutritionally%20Essential%20Mineral%20Elements&f=false. [Set02]

{Ogleby 1988} Ogleby J. 1988. Timbor Rods: Analysis and Certification of Product Ingredients. Unpublished study prepared by Laporte Industries, Ltd. 25 p. MRID 40534001. As summarized in SERA 2006a. [RA2006]

{Ohlendorf et al. 1986} Ohlendorf HM; Hoffmann DJ; Saiki MK; Aldrich TW. 1986. Embryonic mortality and abnormalities of aquatic birds: apparent impacts of selenium from irrigation drainwater. Sci. Total Environ. 52:49-63. As cited in ECETOC Working Group 1997. [RA2006]

{Olgun et al. 2012} Olgun O; Yazgan O; Cufadar Y. 2012. Effects of Boron and Copper Dietary Supplementation in Laying Hens on Egg Shell Quality, Plasma and Tibia Mineral Concentrations and Bone Biomechanical Properties. Revue de Médecine Vétérinaire. (Toulouse). 163:335-342 [ECOTOX - 169959]

{Otten et al. 1957} Otten R; Dawson J; Schreiber M. 1957. The effects of several herbicides on nitrification in soil. Pages 120-127, In Proc. Northeastern Weed Control Conf., 11th Annual Meeting: Vol. 11. S.l.: s.n. (Also In unpublished submission received Mar 18, 1976 under 464-402; submitted by Dow Chemical U.S.A., Midland, MI; CDL:095212-W). MRID 00107904. As summarized in SERA 2006a. [RA2006]

{Owojori et al. 2011} Owojori OJ; Healey J; Princz J; Siciliano SD. 2011. Can Avoidance Behavior of the Mite Oppia nitens Be Used as a Rapid Toxicity Test for Soils Contaminated with Metals Or Organic Chemicals? Environmental Toxicology and Chemistry. 30(11):2594-601. [Set01]

{Owojori et al. 2014} Owojori OJ; Waszak K; Roembke J. 2014. Avoidance and Reproduction Tests with the Predatory Mite *Hypoaspis aculeifer*: Effects of Different Chemical Substances. Environmental Toxicology and Chemistry. 33(1):230-7. [Set01]

{Ozturkcan et al. 2009} Ozturkcan S; Dundar R; Katilmis H; Liknur AE; Aktaq S; Haciomeroglu S. 2009. The Ototoxic Effect of Boric Acid Solutions Applied Into the Middle Ear of Guinea Pigs. European Archives of Oto-Rhino-Laryngology. 266(5):663-7. [Set01]

{Padilla et al. 2012} Padilla S; Corum D; Padnos B; et al. 2012. Zebrafish Developmental Screening of the ToxCast Phase I Chemical Library. Reproductive Toxicology. 33(2): 174-187. [ECOTOX - 161191]

{Pahl et al. 2005} Pahl MV; Culver BD; Vaziri ND. 2005. Boron and the Kidney. Journal of Renal Nutrition. 15(4):362-70. [Set01]

{Pandey and Gupta 2013} Pandey N; Gupta B. 2013. The Impact of Foliar Boron Sprays on Reproductive Biology and Seed Quality of Black Gram. Journal of Trace Elements in Medicine and Biology. 27(1):58-64. [Set01]

{Park et al. 2004} Park M. et al. 2004. NaBC1 is a ubiquitous electrogenic Na+-coupled borate transporter essential for cellular boron homeostasis and cell growth and proliferation. Molecular Cell. 16, 331–341. [Set02]

{Park et al. 2005} Park M; Li Q; Scheynikov N; Muallem S; Zeng W. 2005. Borate Transport and Cell Growth and Proliferation: Not Only in Plants. Cell Cycle. 4(1): 24-26. [Set02]

{Parker et al. 1999} Parker BJ; Veness RG; Evans CS. 1999. A biochemical mechanism whereby paecilomyces variotii Can overcome the toxicity of the wood protectant, borate. Enzyme and Microbial Technology. 24(7): 402-406. [RA2006]

{Pauli et al. 2000} Pauli BD; Perrault JA; Money SL. 2000. RATL: A Database of Reptile and Amphibian Toxicology Literature. National Wildlife Research Centre 2000, Canadian Wildlife Service, Environmental Conservation Branch, Technical Report Series Number 357. Available at: http://dsp-psd.communication.gc.ca/Collection/CW69-5-357E.pdf. [Std]

{Paulson 1988a} Paulson J. 1988a. Timbor Rods: Product Chemistry. Unpublished study. 13 p. MRID 40534000. As summarized in SERA 2006a. [RA2006]

{Paulson 1988b} Paulson J. 1988b. Timbor Rods: Product Chemistry. Unpublished study. 4 p. MRID 40534002. As summarized in SERA 2006a. [RA2006]

{Pawa and Ali 2006} Pawa S; Ali S. 2006. Boron Ameliorates Fulminant Hepatic Failure by Counteracting the Changes Associated with the Oxidative Stress. Chemico-Biological Interactions. 160(2):89-98. [Set01]

{Paynter 1963} Paynter OE. 1963. 90-Day Dietary Feeding - Dogs with 20 MULE TEAM® Borax (Sodium tetraborate decahydrate). MRID 406923-07. As summarized in SERA 2006a. [RA2006]

{Pazirandeh et al. 2009} Pazirandeh A; Jameie B; Zargar M. 2009. Determination of Boron Distribution in Rat's Brain, Kidney and Liver. Applied Radiation and Isotopes. 67(7-8 Suppl):S369-73. [Set01]

{Peters et al. 2008} Peters AK; Steemans M; Hansen E; Mesens N; Verheyen GR; Vanparys P. 2008. Evaluation of the Embryotoxic Potency of Compounds in a Newly Revised High Throughput Embryonic Stem Cell Test. Toxicological Sciences. 105(2):342-50. [Set01]

{Peters et al. 2008a} Peters AK; Wouwer GV; Weyn B; Verheyen GR; Vanparys P; Gompel JV. 2008a. Automated Analysis of Contractility in the Embryonic Stem Cell Test, a Novel Approach to Assess Embryotoxicity. Toxicology *In Vitro*. 22(8):1948-56. [Set01]

{Peyton and Green 1941} Peyton HA; Green 0. 1941. Boric acid poisoning: Case report. Southern Medical Journal. 34: 1286-1287. [Set05]

{Polanco et al. 2008b} Polanco MC; Zwiazek JJ; Jones MD; MacKinnon MD. 2008b. Responses of Mycorrhizal Jack Pine (*Pinus banksiana*) Seedlings to NaCl and Boron. Trees. 22(6): 825-834. [ECOTOX - 166679]

{Pongsavee 2009a} Pongsavee M. 2009a. Effect of Borax on Immune Cell Proliferation and Sister Chromatid Exchange in Human Chromosomes. Journal of Occupational Medicine and Toxicology. 4:27. [Set01]

{Pongsavee 2009b} Pongsavee M. 2009b. Genotoxic Effects of Borax on Cultured Lymphocytes. Southeast Asian Journal of Tropical Medicine and Public Health. 40(2):411-8. [Set01]

{Pratt and Quill 1996} Pratt JE; Quill K. 1996. A Trial of Disodium Octaborate Tetrahydrate for the Control of *Heterobasidion annosum*. European Journal of Forest Pathology. 26 (6): 297-305. [Set01]

{Pratt et al. 1996} Pratt JE; Nisbet TR; Tracy DR; Davidson J. 1996. Boron Content in Surface Water Run-Off from a Clear-Felled Conifer Crop in West Scotland Following Stump Treatment with Disodium Octaborate Tetrahydrate. Scandinavian Journal of Forest Research. 11 (4): 370-374. [Set01]

{Presnell and Nicholas 1990} Presnell TL; Nicholas DD. 1990. Evaluation of combinations of low hazard biocides in controlling mold and stain fungi on southern pine. For Prod J. 40: 57-61. [RA2006]

{Price et al. 1991} Price CJ; Marr MC; Myers CB; Heindel JJ; Schwetz BA. 1991. Final report on the developmental toxicity of boric acid (CAS No. 10043-35-3) in New Zealand white rabbits. NIEHS/NTP Order No. B92-129550. As cited in Hubbard 1998. [RA2006]

{Price et al. 1996a} Price CJ; Strong PL; Marr CB; Myers CB; Murray FJ. 1996a. Developmental toxicity NOAEL and postnatal recovery in rats fed boric acid during gestation. Fundam. Appl. Toxicol. 32:179-193. [RA2006]

{Price et al. 1996b} Price CJ; Marr CB; Myers CB; Seely JC; Heindel JJ; Schwetz BA. 1996b. The Developmental Toxicity of Boric Acid in Rabbits. Fundam. Appl. Toxicol. 34:176-178. [RA2006]

{Price et al. 1996b} Price CJ; Marr CB; Myers CB; Seely JC; Heindel JJ; Schwetz BA. 1996b. The Developmental Toxicity of Boric Acid in Rabbits. Fundamental and Applied Toxicology. 34:176-178. [RA2006]

{Princz et al 2010} Princz JI; Behan-Pelletier VM; Scroggins RP; Siciliano SD. 2010. Oribatid Mites in Soil Toxicity Testing - The Use of *Oppia nitens* (C.L. Koch) as a New Test Species. Environmental Toxicology and Chemistry. 29(4): 971-979. [ECOTOX - 166372]

{Quaranta et al. 2009} Quaranta A; Bellantuono V; Cassano G: Lippe C. 2009. Why Amphibians Are More Sensitive than Mammals to Xenobiotics. PLoS ONE. 4: (11): 1-4. [Std]

{Rainey et al. 1999} Rainey CJ; Nyquist LA; Christensen RE; et al. 1999. Daily boron intake from the American diet. Journal of the American Dietetic Association. 99:335-340. [Set02]

{Rainey et al. 2002} Rainey CJ; Nyquist LA; Christensen RE; et al. 1999. Daily boron intake from the United States. J Food Comp Anal. 15:237-250. [Set02]

{Rani and Meena 2013} Rani M; Meena MC. 2013. Multiple Organ Damage Due to Boric Acid Toxicity. Asia Pacific Journal of Medical Toxicology. http://apjmt.mums.ac.ir December 2013. [Set00]

{Rawlins 2016} Rawlins S. 2016. Email dated September 28, 2016 from Scott Rawlins (Director, Regulatory and Governmental Affairs, Wilbur-Ellis Company) to Patrick Durkin (SERA Inc.). [Set05]

{Ray et al. 2007} Ray D; Goswami R; Banerjee U; Dadhwal V; Goswami D; Mandal P; Sreenivas V; Kochupillai N. 2007. Prevalence of *Candida glabrata* and its Response to Boric Acid Vaginal Suppositories in Comparison with Oral Fluconazole in Patients with Diabetes and Vulvovaginal candidiasis. Diabetes Care. 30(2):312-7. [Set01]

{Reagan 1985a} Reagan E. 1985a. Acute Dermal Toxicity Study of 20 Mule Team Sodium Tetraborate Decahydrate in New Zealand White Rabbits: Lab Project Number: 8403A. Unpublished study prepared by Food & Drug Research Labs, Inc. 9 p. MRID 43553200. As summarized in SERA 2006a. [RA2006]

{Reagan 1985b} Reagan E. 1985b. Primary Dermal Irritation Study of 20 Mule Team Sodium Tetraborate Decahydrate in New Zealand White Rabbits: Lab Project Number: 8403B. Unpublished study prepared by Food & Drug Research Labs, Inc. 8 p. MRID 43553201. As summarized in SERA 2006a. [RA2006]

{Reagan 1985c} Reagan E. 1985c. Primary Eye Irritation Study of 20 Mule Team Sodium Tetraborate Decahydrate in New Zealand White Rabbits: Lab Project Number: 8403B. Unpublished study prepared by Food & Drug Research Labs, Inc. 21 p. MRID 43553202. As summarized in SERA 2006a. [RA2006]

{Reichle et al. 1973} Reichle DE, Goldstein RA; Van Hook RI; Dodson DJ. 1973. Analysis of Insect Consumption in a Forest Canopy. Ecology. 54: 1076-1084. [Std]

{Reid 2006} Reid FA. 2006. A Field Guide to Mammals of North America North of Mexico. Fourth Edition. The Peterson Field Guide Series. Houghton Mifflin Company, Boston MA. 570 pp. [Std]

{Reinart and Fletcher 1977} Reinart D; Fletcher D. 1977. 8-Day Dietary LC_{50} Study with Borax in Bobwhite Quail: IBT No. 8580-10597. Unpublished study prepared by Industrial Bio-Test Laboratories, Inc. 14 p. MRID 00142633. As summarized in SERA 2006a. [RA2006]

{Robbins et al. 2010} Robbins WA; Xun L; Jia J; Kennedy N; Elashoff DA; Ping L. 2010. Chronic Boron Exposure and Human Semen Parameters. Reproductive Toxicology. 29(2):184-90. [Set01]

{Roessner et al. 2006} Roessner U; Patterson JH; Forbes MG; et al. 2006. An Investigation of Boron Toxicity in Barley Using Metabolomics. Plant Physiology. 142(3): 1087-1101 [ECOTOX - 166716]

{Rogers 1947} Rogers HT. 1947. Boron response and tolerance of several legumes to borax. J Am Soc Agron. 39: 897-913. [RA2006]

{Rogers et al. 2005} Rogers JM; Lau C; Andrews JE; Chernoff N; Thibodeaux JR; Barbee BD; Grey BE. 2005. Effect of Varying Maternal Folate Status and Dietary Folate Intake on Response to Diverse Developmental Toxicants in the Rat. Birth Defects Research Part A: Clinical and Molecular Teratology. 73(5):314 [Set01]

{Roldan-Pallares et al. 2005} Roldan-Pallares M; Avila MI; Refojo MF. 2005. The Use of Boric Acid Solution to Help in the Removal of Biodegraded Miragel Episcleral Buckles. Retina. 25(1):90-3. [Set01]

{Rossi et al. 1993} Rossi AF; Miles RD; Bootwalla SM; Wilson HR; Eldred AR. 1993. The effect of feeding two sources of boron on broiler breeder performance. Poultry Sci. 72: 1931-1934. [RA2006]

{Roudabush et al. 1965} Roudabush R; Terhaar C; Fassett D; et al. 1965. Comparative acute effects of some chemical on the skin of rabbits and guinea pigs. Toxicology and Applied Pharmacology. 7(4): 559-565. MRID 00150903. [RA2006]

{Roudabush et al. 1965} Roudabush R; Terhaar C; Fassett D; et al. 1965. Comparative acute effects of some chemical on the skin of rabbits and guinea pigs. Toxicology and Applied Pharmacology. 7(4): 559-565. [RA2006]

{Rowe et al. 1998} Rowe RI; Bouzan C; Nabili S; Eckhert CD. 1998. The Response of Trout and Zebrafish Embryos to Low and High Boron Concentrations is U-Shaped. Biological Trace Element Research. 66(1-3): 261-270. [ECOTOX - 105984]

{Rozelle and Ableson 1988} Rozelle D; Ableson A. 1988. Manufacturing Procedures--Production of TIM-BOR: Lab Project Number: WE-8801. Unpublished study prepared by United States Borax & Chemical Corp. 52 p. MRID 43297900. As summarized in SERA 2006a. [RA2006]

{Rust et al. 2004} Rust MK; Reierson DA; Klotz JH. 2004. Delayed Toxicity as a Critical Factor in the Efficacy of Aqueous Baits for Controlling Argentine Ants (Hymenoptera: Formicidae). Journal of Economic Entomology. 97(3):1017-24. [Set01]

{Sabuncuoglu et al. 2006} Sabuncuoglu BT; Kocaturk PA; Yaman O; Kavas GO; Tekelioglu M. 2006. Effects of Subacute Boric Acid Administration on Rat Kidney Tissue. Clinical Toxicology (Philadelphia, Pa.). 44(3):249-53. [Set01]

{Sample and Arenal 1999} Sample BE; Arenal CA. 1999. Allometric models for interspecies extrapolation of wildlife toxicity data. Bulletin of Environmental Contamination and Toxicology. 62(6): 653-663. [RA2006]

{Savini et al. 2009} Savini V; Catavitello C; Bianco A; Balbinot A; D'antonio F; D'antonio D. 2009. Azole Resistant *Candida glabrata* Vulvovaginitis Treated with Boric Acid. European Journal of Obstetrics and Gynecology and Reproductive Biology. 147(1):112. [Set01]

{Scheffrahn et al. 1997} Scheffrahn RH; Su N-Y; Busey P. 1997. Laboratory and Field Evaluations of Selected Chemical Treatments for Control of Drywood Termites (Isoptera: Kalotermitidae). Journal of Economic Entomology. 90 (2): 492-502. [Set01]

{Schmitt et al. 2000} Schmitt CL; Parmeter JR; Kliejunas JT. 2000. Annosus Root Disease of Western Conifers. USDA/Forest Service, Forest Insect and Disease Leaflet 172. Available at: http://www.fs.usda.gov/Internet/FSE_DOCUMENTS/fsbdev2_043457.pdf. [FS]

{Schoberl and Huber 1988} Schoberl P; Huber L. 1988. Ecologically relevant data of non-tenside compounds in detergents and cleaners. Tenside Deterg, 25:99-107 (in German). As cited in WHO 1998. [RA2006]

{Schroeder and Mitechener 1975} Schroeder HA; Mitechener M. 1975. Life-term effects of mercury, methyl mercury, and nine other trace metals on mice. J Nutr. 105(4): 452-458. [RA2006]

{Seaby and Schaible 2000} Seaby DA; Schaible RC. 2000. Preventing heterobasidion annosum from colonizing chemically thinned Sitka Spruce stems. Forestry. 73: 351-359. [RA2006]

{Seal and Weeth 1980} Seal BS; Weeth HJ. 1980. Effect of boron in drinking water on the male laboratory rat. Bull Environ Contam Toxicol. 25:782-789. [RA2006]

{Selderslaghs et al. 2012} Selderslaghs IWT; Blust R; Witters HE. 2012. Feasibility Study of the Zebrafish Assay as an Alternative Method to Screen for Developmental Toxicity and Embryotoxicity Using a Training Set of 27 Compounds. Reproductive Toxicology. 33(2): 142-154. [ECOTOX - 158995]

{SERA 2006a} SERA (Syracuse Environmental Research Associates, Inc.). 2006a. Human Health and Ecological Risk Assessment for Borax (Sporax®) – FINAL REPORT. SERA TR 04-43-21 06-30-02b. Report dated February 24, 2006. Available at: http://www.fs.fed.us/foresthealth/pesticide/risk.shtml. [Std]

{SERA 2007a} SERA (Syracuse Environmental Research Associates, Inc.). 2007a. Gleams-Driver User Guide (Version 1.8). SERA TR 07-52-05-08a. Report dated December 31, 2007. Available at: www.sera-inc.com. [Std]

{SERA 2007b} SERA (Syracuse Environmental Research Associates, Inc.). 2007b. Aminopyralid Human Health and Ecological Risk Assessment – FINAL REPORT. SERA TR-052-04-04a. Report dated June 28, 2007. Available at: http://www.fs.fed.us/foresthealth/pesticide/risk.shtml. [Std]

{SERA 2009} SERA (Syracuse Environmental Research Associates, Inc.). 2009. Technical Comparison of EPA, BLM and Forest Service Pesticide Risk Assessments, Final Report. SERA TR-052-19-02. Report dated July 29, 2009. Available at: http://www.fs.fed.us/foresthealth/pesticide/pdfs/SERA_TR-052-19-02_Risk_Comparison.pdf. [Std]

{SERA 2011a} SERA (Syracuse Environmental Research Associates, Inc.). 2011a. WorksheetMaker Version 6.00, User Guide. SERA TR-052-20-01b. Document dated December 21, 2011. Syracuse Environmental Research Associates, Inc., Fayetteville, NY. Available at www.sera-inc.com. [Std]

{SERA 2011b} SERA (Syracuse Environmental Research Associates, Inc.). 2011b. Memorandum on Release of Gleams-Driver 1.9.3. Memo dated November 6, 2011. Available at: www.sera-inc.com. [Std]

{SERA 2013a} SERA (Syracuse Environmental Research Associates, Inc.). 2013a. Reassessment of Worker Exposure Rates – Corrected and Revised Final Report. SERA TR-052-30-03a. Document dated October 13, 2013. Syracuse Environmental Research Associates, Inc., Fayetteville, NY. Available at: http://www.fs.fed.us/foresthealth/pesticide/risk.shtml. [Std]

{SERA 2014a} SERA (Syracuse Environmental Research Associates, Inc.). 2014a. Preparation of Environmental Documentation and Risk Assessments, SERA MD-2014-02b. Document dated November 17, 2014. Syracuse Environmental Research Associates, Inc., Manlius, NY. Available at www.sera-inc.com. [Std]

{SERA 2014b} SERA (Syracuse Environmental Research Associates, Inc.). 2014b. Reassessment of Worker Exposure Rates – FINAL REPORT. SERA TR-056-06-02b. Document dated November 17, 2014. Syracuse Environmental Research Associates, Inc., Manlius, NY. Available at: http://www.fs.fed.us/foresthealth/pesticide/risk.shtml. [Std]

{Shaipanich et al. 1978} Shaipanich C; Anukrahanon T; Mekanonchai R; Tiptabiankarn L. 1978. Toxicity of alcohol-borax in the rat. Mahidol Univ. J. Pharm. Sci. (Varasarn Paesachasarthara). 5: 35-40. [RA2006]

{Sharma et al. 1978} Sharma MP; Mathur RS; Mehta K. 1978. Effect of borax on testis of indian desert gerbil meriones-hurriane. Experientia (Basel). 34(10): 1374-137. [RA2006]

{Sims and Appel 2012} Sims SR; Appel AG. 2012. Efficacy of Commercial Baits and New Active Ingredients against Firebrats and Silverfish (Zygentoma: Lepismatidae). Journal of Economic Entomology. 105(4):1385-91. [Set01]

{Smit et al. 2012} Smit CE; Moser T; R"mbke J. 2012. A New OECD Test Guideline for the Predatory Soil Mite Hypoaspis Aculeifer: Results of An International Ring Test. Ecotoxicology and Environmental Safety. 82:56-62. [Set01]

{Smith 1970} Smith RSJr. 1970. Borax to control *Fomes annosus* infection of white fir stumps. Plant Disease Reporter. 54(10): 872-875. [RA2006]

{Smith and Anders 1989} Smith GJ; Anders VP. 1989. Toxic effects of boron on mallard reproduction. Environmental Toxicology and Chemistry. 8:943-950. [RA2006]

{Smith et al. 1946} Smith NR; Dawson VT; Wenzel ME. 1946. The effect of certain herbicides on soil microorganisms. Pages 197-201,In Proceedings of the Soil Science Society of America. Vol. 10. Madison, Wis.: Soil Science Society of America. MRID 05001564. As summarized in SERA 2006a. [RA2006]

{Sola et al. 2013} Sola F; Falibene A; Josens R. 2013. Asymmetrical Behavioral Response towards Two Boron Toxicants Depends on the Ant Species (Hymenoptera: Formicidae). Journal of Economic Entomology. 106(2):929-38. [Set01]

{Sopova et al. 1981} Sopova M; Petrovska D; Musalevski A; Najcevska C; Sekovski Z. 1981. Cytogenetical and morphological effect of general toxicity caused with different concentrations of boron. Mutat Res. 85: 229. [RA2006]

{Soriano-Ursua et al. 2014} Soriano-Ursua MA; Farfan-Garcia ED; L¢pez-Cabrera Y; Querejeta E; Trujillo-Ferrara JG. 2014. Boron-Containing Acids: Preliminary Evaluation of Acute Toxicity and Access to the Brain Determined by Raman Scattering Spectroscopy. NeuroToxicology. 40:8-15. [Set01]

{Spears 1999} Spears JW. 1999. Reevaluation of the metabolic essentiality of the minerals. Asian Australasian Journal of Animal Sciences. 12(6):1002-1008. [Set02]

{Sprando et al. 2009} Sprando RL; Olejnik N; Cinar HN; Ferguson M. 2009. A Method to Rank Order Water Soluble Compounds According to Their Toxicity Using *Caenorhabditis elegans*, a Complex Object Parametric Analyzer and Sorter, and Axenic Liquid Media. Food and Chemical Toxicology. 47(4):722-8. [Set01]

{Stangoulis and Reid 2002} Stangoulis JCF; Reid RJ. 2002. Boron Toxicity in Plants and Animals. In: Boron in Plant and Animal Nutrition. Editors: Goldbach, H., Rerkasem, B., Wimmer, M.A., Brown, P.H., Thellier, M., Bell, R.W. (Eds.). pp. 227-239. Available at: http://link.springer.com/chapter/10.1007%2F978-1-4615-0607-2_21. [Set02]

{Stanley and Robinson 2007} Stanley MC; Robinson WA. 2007. Relative Attractiveness of Baits to *Paratrechina longicornis* (Hymenoptera: Formicidae). Journal of Economic Entomology. 100(2):509-16. [Set01]

{Stanley and Tapp 1982} Stanley RD; Tapp JF. 1982. An assessment of Ecotoxicological Test Methods, Part VIII. ICI Brixham Laboratory Report BL/A/2164. Brixham, Devon, UK. As cited in Windeatt et al. 1991. [RA2006]

{Stegger et al. 2011} Stegger P; Ebke KP; Rombke J. 2011. Boric Acid as Alternative Reference Substance for Earthworm Field Tests. Journal of Soils and Sediments. 11:330-335. [ECOTOX - 166375]

{Stewart et al. 2013} Stewart ZP; Oxborough RM; Tungu PK; Kirby MJ; Rowland MW; Irish SR. 2013. Indoor Application of Attractive Toxic Sugar Bait (ATSB) in Combination with Mosquito Nets for Control of Pyrethroid-Resistant Mosquitoes. PloS one. 8(12):e84168. [Set01]

{Stokinger 1981} Stokinger HE. 1981. The halogens and nonmetals boron and silicon. In: Clayton GD, Clayton FE, eds. Patty's Industrial Hygiene and Toxicology, Vol. 2B. New York: John Wiley and Sons. pp. 2978–3005. [Set05]

{Strong et al. 1993} Strong CA; Koehler PG; Patterson RS. 1993. Oral Toxicity and Repellency of Borates to German Cockroaches (Dictyoptera: Blattellidae). Journal of Economic Entomology. 86 (5): 1458-1463. [Set01]

{Sumida et al. 2010} Sumida S; Silva-Zacarin EC; Decio P; Malaspina O; Bueno FC; Bueno OC. 2010. Toxicological and Histopathological Effects of Boric Acid on *Atta sexdens* Rubropilosa (Hymenoptera: Formicidae) Workers. Journal of Economic Entomology. 103(3):676-90. [Set01]

{Suomi and Akre 1992} Suomi DA; Akre RD. 1992. Control of the Structure-Infesting Beetle (Hemicoelus Gibbicollis) (Coleoptera: Anobiidae) with Borates. Journal of Economic Entomology. 85 (4): 1188-1193. [Set01]

{Sylvain et al. 1998} Sylvain IC; Berry JP; Galle P. 1998. Ultrastructural apoptotic lesions induced in rat thymocytes after borax ingestion. Anticancer Research. 18(4A):2455-2461. As summarized in HSDB 2014. [Set05]

{Tagawa et al. 2000} Tagawa T; Kono K; Dote T; Usuda K; Nishiura H; Koizumi C; Saito M; Nakaya H; Nagaie H. 2000. Pharmacokinetics and effects after intravenous administration of high-dose boron to rat. Int Arch Occup Environ Health. 73(Suppl): S98-100. [RA2006]

{Tagawa et al. 2000} Tagawa T; Kono K; Dote T; Usuda K; Nishiura H; Koizumi C; Saito M; Nakaya H; Nagaie H. 2000. Pharmacokinetics and effects after intravenous administration of high-dose boron to rat. International Archives of Occupational and Environmental Health. 73(Suppl): S98-100. [RA2006]

{Takano et al. 2006} Takano J; Wada M; Ludewig U; Schaaf G; Von Wiren N; Fujiwara T. 2006. The *Arabidopsis* Major Intrinsic Protein Nip5;1 Is Essential for Efficient Boron Uptake and Plant Development Under Boron Limitation. The Plant Cell. 18(6):1498-509. [Set01]

{Takano et al. 2008} Takano J; Miwa K; Fujiwara T. 2008. Boron Transport Mechanisms: Collaboration of Channels and Transporters. Trends in Plant Science. 13(8):451-7. [Set01]

{Takano et al. 2010} Takano J; Tanaka M; Toyoda A; Miwa K; Kasai K; Fuji K; Onouchi H; Naito S; Fujiwara T. 2010. Polar Localization and Degradation of *Arabidopsis* Boron Transporters through Distinct Trafficking Pathways. Proceedings of the National Academy of Sciences of the United States of America. 107(11):5220-5. [Set01]

{Tan 1970} Tan TG. 1970. Occupational toxic alopecia due to borax. Acta Dermatovener (Stockholm). 50: 55-58. [RA2006]

{Tanaka et al. 2008} Tanaka M; Wallace IS; Takano J; Roberts DM; Fujiwara T. 2008. Nip6;1 Is a Boric Acid Channel for Preferential Transport of Boron to Growing Shoot Tissues in Arabidopsis. The Plant Cell. 20(10):2860-75. [Set01]

{Tanaka et al. 2011} Tanaka M; Takano J; Chiba Y; Lombardo F; Ogasawara Y; Onouchi H; Naito S; Fujiwara T. 2011. Boron-Dependent Degradation of Nip5;1 mRNA for Acclimation to Excess Boron Conditions in Arabidopsis. The Plant Cell. 23(9):3547-59. [Set01]

{Tanji 1990} Tanji KK. 1990. Agricultural Salinity Assessment and Management. American Society of Civil Engineers, New York, New York. [RA2006]

{Taylor 1967} Taylor JM. 1967. Toxicity of boron compounds to the common furniture and house longhorn beetles. International Pest Control. January/February 1967:14-17. [RA2006]

{Teixido et al. 1999} Teixido N; Usall J; Magan N; Vinas I. 1999. Microbial population dynamics on golden delicious apples from bud to harvest and effect of fungicide applications. Annals of Applied Biology. 134(1): 109-116. [RA2006]

{Teixido et al. 2013} Teixido E; Piqu, E; G¢mez-Catal n J; Llobet JM. 2013. Assessment of Developmental Delay in the Zebrafish Embryo Teratogenicity Assay. Toxicology *In Vitro*. 27(1):469-78. [Set01/ECOTOX 166376]

{Thompson 2015} Thompson J. 2015. Extrapolation of Acute Toxicity Across Bee Species. Integrated Environmental Assessment and Management. doi: 10.1002/ieam.1737. [Std]

{Tomlin 2004} Tomlin C. 2004. The e-Pesticide Manual, Thirteenth Edition, Crop Protection Publications; British Crop Protection Council. Entry for borax. Available at: http://www.bcpcbookshop.co.uk.[Std]

{Tomlinson and Faithfull 1979} Tomlinson JA; Faithfull EM. 1979. Effects of fungicides and surfactants on the zoospores of Oipidium brassicae. Ann Appl Biol. 93: 13-19. [RA2006]

{Toyoshima et al. 1997} Toyoshima I; Yoshimura T; Tsunoda K; Takahashi M. 1997. Comparative toxicity, residual nature and effect on respiration of boron compounds in a lower termite, Coptotermes formosanus Shiraki (Isoptera: rhinotermitidae). Material Und Organismen (Berlin). 31(3): 217-226. [RA2006]

{Treinen and Chapin 1991} Treinen KA; Chapin RE. 1991. Development of testicular lesions in F344 rats after treatment with boric acid. Toxicology and Applied Pharmacology 107:325-335. [Set02]

{Tunnicliffe and Rosenheim 1901} Tunnicliffe FW; Rosenheim O. 1901. On the Influence of Boric Acid and Borax upon the General Metabolism of Children. Journal of Hygiene (London). 1(2): 168–201. [Set00]

{Turkez 2008} Turkez H. 2008. Effects of Boric Acid and Borax on Titanium Dioxide Genotoxicity. Journal of Applied Toxicology. 28(5):658-64. [Set01]

{Turkez and Geyikoglu 2010} Turkez H; Geyikoglu F. 2010. Boric Acid: A Potential Chemoprotective Agent Against Aflatoxin b_1 Toxicity in Human Blood. Cytotechnology. 62(2):157-65. [Set01]

{Turkez et al. 2007} Turkez H; Geyikoqlu F; Tatar A; Keles S; Ozkan A. 2007. Effects of Some Boron Compounds on Peripheral Human Blood. Zeitschrift für Naturforschung C. 62(11-12):889-96. [Set01]

{Turkez et al. 2010} Turkez H; Tatar A; Hacimuftuoglu A; Ozdemir E. 2010. Boric Acid as a Protector Against Paclitaxel Genotoxicity. Acta Biochim Pol. 57(1):95-7. [Set01]

{Turkez et al. 2012a} Turkez H; Geyikoqlu F; Dirican E; Tatar A. 2012a. *In vitro* Studies on Chemoprotective Effect of Borax Against Aflatoxin B1-Induced Genetic Damage in Human Lymphocytes. Cytotechnology. 64(6):607-12. [Set01]

{Turkez et al. 2012b} Turkez H; Geyikoglu F; Tatar A; Keles MS; Kaplan I. 2012b. The Effects of Some Boron Compounds Against Heavy Metal Toxicity in Human Blood. Experimental and Toxicologic Pathology. 64(1-2):93-101. [Set01]

{Turkez et al. 2013} Turkez H; Geyikoqlu F; Tatar A. 2013. Borax Counteracts Genotoxicity of Aluminum in Rat Liver. Toxicology and Industrial Health. 29(9):775-9. [Set01]

{Turkoqlu 2007} Turkoqlu S. 2007. Genotoxicity of Five Food Preservatives Tested on Root Tips of *Allium cepa* L. Mutation Research. 626(1-2):4-14. [Set01]

{Tyl et al. 2007} Tyl RW; Chernoff N; Rogers JM. 2007. Altered Axial Skeletal Development. Birth defects research. Part B, Developmental and reproductive Toxicology. 80(6):451-72. [Set01]

{U.S. Borax Corporation 1981a } U.S. Borax Corporation. 1981a. Toxicology 20 Mule Team Boric Acid. Vol. I. (Compilation: unpublished study received March 5, 1981 under 1623-117; CDL:244539). As summarized in SERA 2006a. [RA2006]

{U.S. Borax Corporation 1981b} U.S. Borax Corporation. 1981b. Toxicology 20 Mule Team Boric Acid. Vol. II. (Compilation: unpublished study received March 5, 1981 under 1624-117; CDL:244540). As summarized in SERA 2006a. [RA2006]

{U.S. Borax Corporation 1981c} U.S. Borax Corporation. 1981c. Toxicology 20 Mule Team Boric Acid. Vol. III. (Compilation: unpublished study received March 5, 1981 under 1624-117; CDL:244541). As summarized in SERA 2006a. [RA2006]

{U.S. Borax Corporation 1981d}{U S} U.S. Borax Corporation. 1981d. Toxicology 20 Mule Team Boric Acid. Vol. IV. (Compilation: unpublished study received March 5, 1981 under 1624-117; CDL:244542). As summarized in SERA 2006a. [RA2006]

{U.S. Borax Inc. 1994} U.S. Borax Inc. 1994. Submittal of Product Chemistry and Toxicity Data in Support of Reregistration Eligibility Document for Disodium Octaborate Tetrahydrate Containing Product TIM-BOR. Transmittal of 5 Studies. MRID 43493901. As summarized in SERA 2006a. [RA2006]

{U.S. EPA 2014} U.S. EPA (U.S. Environmental Protection Agency). 2014. U.S. Environmental Protection Agency Endocrine Disruptor Screening Program, Comprehensive Management Plan. Jointly developed by the Office of Chemical Safety and Pollution Prevention and the Office of Water. Report dated Feb. 14, 2015. Available at: https://www.epa.gov/sites/production/files/2015-08/documents/edsp_comprehesive_management_plan_021414_f.pdf. [Std]

{U.S. EPA/NCEA 2004} U.S. EPA/NCEA (U.S. Environmental Protection Agency/National Center for Environmental Assessment). Integrated Risk Information System (IRIS). Boron and Compounds; CASRN 7440-42-8. Available at: https://cfpub.epa.gov/ncea/iris. Last Updated 8/5/2004 [Set00]

{U.S. EPA/NCEA 2011} U.S. EPA (U.S. Environmental Protection Agency/National Center for Environmental Assessment). 2011. Exposure Factors Handbook (Final Report). National Center for Environmental Assessment, U.S. EPA, Washington, DC. EPA/600/R-090/052F, September 2011. Available at: https://cfpub.epa.gov/ncea/risk/recordisplay.cfm?deid=236252. [Std]

{U.S. EPA/OCSPP 2015} U.S. EPA/OCSPP (U.S. Environmental Protection Agency/ Office of Chemical Safety and Pollution Prevention). 2015. OCSPP Harmonized Test Guidelines. OPPTS Harmonized Test Guidelines - Master List. Last Updated November 2015. Available at: https://www.epa.gov/sites/production/files/2015-11/documents/ocspp-testguidelines_masterlist-2015-11-19.pdf. [Std]

{U.S. EPA/OPP 1993a} U.S. EPA/OPP (U.S. Environmental Protection Agency/Office of Pesticide Programs). 1993a. RED on Boric Acid and Sodium Salts. [RA2006]

{U.S. EPA/OPP 1993b} U.S. EPA/OPP (U.S. Environmental Protection Agency/Office of Pesticide Programs). 1993b. RED FACTS, Boric Acid. [RA2006]

{U.S. EPA/OPP 2006a} U.S. EPA/OPP (U.S. Environmental Protection Agency/Office of Pesticide Programs). 2006a. Report of the Food Quality Protection Act (FQPA) Tolerance Reassessment Eligibility Decision (TRED) for Boric Acid/Sodium Borate Salts. Notice of availability dated August 2, 2006 in Fed. Reg. 71(148): 43744-43745. EPA-HQ-OPP-2005-0062-0024. [Docket02]

{U.S. EPA/OPP 2009a} U.S. EPA/OPP (U.S. Environmental Protection Agency/Office of Pesticide Programs). 2009a. Boric Acid and Sodium Borate Salts, Final Work Plan, Registration Review, October 2009, Case # 0024. EPA-HQ-OPP-2009-0306-0012. [Docket01]

{U.S. EPA/OPP 2009b} U.S. EPA/OPP (U.S. Environmental Protection Agency/Office of Pesticide Programs). 2009b. Boric Acid and Sodium Borate Salts, Summary Document, Registration Review: Initial Docket, June 2009. EPA-HQ-OPP-2009-0306-0003. [Docket01]

{U.S. EPA/OPP 2013a} U.S. EPA/OPP (U.S. Environmental Protection Agency/Office of Pesticide Programs). 2013a. Part 158 Toxicology Data Requirements: Guidance for Neurotoxicity Battery, Subchronic Inhalation, Subchronic Dermal and Immunotoxicity Studies. Available at: https://www.epa.gov/sites/production/files/2014-02/documents/part158-tox-data-requirement.pdf. [Std]

{U.S. EPA/OPP 2013b} U.S. EPA (U.S. Environmental Protection Agency/Office of Pesticide Programs). 2013b. Occupational Pesticide Handler Unit Exposure Surrogate Reference Table. Report dated March, 2013. Available at: http://www.epa.gov/pesticides/science/handler-exposure-table.pdf. [Std]

{U.S. EPA/OPP 2014a} U.S. EPA/OPP (U.S. Environmental Protection Agency/Office of Pesticide Programs). 2014b. Overview of Registration Review Program. Last updated April 17, 2014. Available at: http://www.epa.gov/oppsrrd1/registration_review/highlights.htm#nn. [Std]

{U.S. EPA/OPP 2014b} U.S. EPA/OPP (U.S. Environmental Protection Agency/Office of Pesticide Programs). 2014c. InertFinder. Last updated August 6, 2014. Available at: http://iaspub.epa.gov/apex/pesticides/f?p=101:1:. [Std]

{U.S. EPA/OPP/EFED 1993} U.S. EPA/OPP/EFED (U.S. Environmental Protection Agency/Office of Programs/Environmental Fate and Effects Division). 1993. Science Chapter for Boric Acid/Sodium Metaborate RED (Chemicals #011001, 011103; Case #0034). June 1, 1993. [RA2006]

{U.S. EPA/OPP/EFED 2009a} U.S. EPA/OPP/EFED (U.S. Environmental Protection Agency/Office of Programs/Environmental Fate and Effects Division). 2009a. Registration Review - Final Problem Formulation for the Ecological Risk Assessment of Boric acid. May 4, 2009. EPA-HQ-OPP-2009-0306-0004. [Docket01]

{U.S. EPA/OPP/EFED 2015a} U.S. EPA/OPP/EFED (U.S. Environmental Protection Agency/Office of Programs/Environmental Fate and Effects Division). 2015a. Preliminary Environmental Fate and Ecological Risk Assessment for the Registration Review of Boric Acid and Sodium Borate Salts. Document dated November 25, 2015. EPA-HQ-OPP-2009-0306-0021. [Docket01]

{U.S. EPA/OPP/EFED 2015b} U.S. EPA/OPP/EFED (U.S. Environmental Protection Agency/Office of Programs/Environmental Fate and Effects Division). 2015b. ATTACHMENT 2: Boric Acid and Sodium Borate Salts Case—ECOTOX Studies Summary Tables. Document dated July, 2014. EPA-HQ-OPP-2009-0306-0022. [Docket01]

{U.S. EPA/OPP/EFED 2015c} U.S. EPA/OPP/EFED (U.S. Environmental Protection Agency/Office of Programs/Environmental Fate and Effects Division). 2015c. ATTACHMENT 1: Boric Acid and Sodium Borate Salts Case—ECOTOX Bibliographies. Document dated June 15, 2015. EPA-HQ-OPP-2009-0306-0023. [Docket01]

{U.S. EPA/OPP/HED 1993} U.S. EPA/OPP/HED. (U.S. Environmental Protection Agency/Office of Programs/Health Effects Division). 1993. Science Chapter for the Reregistration Eligibility Document (RED) for Boric Acid, Case #0024. April 2, 1993. [RA2006]

{U.S. EPA/OPP/HED 2005a} U.S. EPA/OPP/HED. (U.S. Environmental Protection Agency/Office of Programs/Health Effects Division). 2005a. Boric Acid/Sodium Borate Salts: Supplement to HED Chapter of the Tolerance Reassessment Eligibility Decision Document (TRED). EPA-HQ-OPP-2005-0062-0005. [Docket02]

{U.S. EPA/OPP/HED 2005b} U.S. EPA/OPP/HED. (U.S. Environmental Protection Agency/Office of Programs/Health Effects Division). 2005b. Boric Acid: Residential Exposure Assessment for the Tolerance Reregistration Eligibility Decision Document. EPA-HQ-OPP-2005-0062-0006. [Docket02]

{U.S. EPA/OPP/HED 2005c} U.S. EPA/OPP/HED. (U.S. Environmental Protection Agency/Office of Programs/Health Effects Division). 2005c. Review of Boric Acid Incident Reports. EPA-HQ-OPP-2005-0062-0007. [Docket02]

{U.S. EPA/OPP/HED 2006a} U.S. EPA/OPP/HED. (U.S. Environmental Protection Agency/Office of Programs/Health Effects Division). 2006a. Boric Acid/Sodium Borate Salts: HED Chapter of the Tolerance Reassessment Eligibility Decision Document (TRED). EPA-HQ-OPP-2005-0062-0026. [Docket02]

{U.S. EPA/OPP/HED 2009a} U.S. EPA/OPP/HED. (U.S. Environmental Protection Agency/Office of Programs/Health Effects Division). 2009a. Boric Acid/Sodium Salts of Boric Acid. Human Health Assessment Scoping Document in Support of Registration Review. EPA-HQ-OPP-2009-0306-0005. [Docket01]

{U.S. EPA/OPP/HED 2009b} U.S. EPA/OPP/HED. (U.S. Environmental Protection Agency/Office of Programs/Health Effects Division). 2009b. Updated Review of Boric Acid Incident Reports. EPA-HQ-OPP-2009-0306-0006. [Docket01]

{U.S. EPA/OPP/HED 2015a} U.S. EPA/OPP/HED. (U.S. Environmental Protection Agency/Office of Programs/Health Effects Division). 2015a. Boric Acid/Sodium Salts of Boric Acid. Occupational and Residential Exposure and Risk Assessment for Registration Review. EPA-HQ-OPP-2009-0306-0025. [Docket01]

{U.S. EPA/OPPTS 1998a} U.S. EPA/OPPT (U.S. Environmental Protection Agency/Office of Pollution Prevention and Toxic Substances). 1998. Health Effects Test Guidelines, OPPTS 870.1200, Acute Dermal Toxicity. EPA 712–C–98–192. Document dated August 1998a. Available at: https://www.regulations.gov/#!documentDetail;D=EPA-HQ-OPPT-2009-0156-0004 . [Std]

{U.S. EPA/OPPTS 1998b} U.S. EPA/OPPT (U.S. Environmental Protection Agency/Office of Pollution Prevention and Toxic Substances). 1998b. Health Effects Test Guidelines, OPPTS 870.1300, Acute Inhalation Toxicity. EPA 712–C–98–193. Document dated August 1998. Available at: https://www.regulations.gov/#!documentDetail;D=EPA-HQ-OPPT-2009-0156-0005. [Std]

{U.S. EPA/OPPTS 2000} U.S. EPA/OPPTS (U.S. Environmental Protection Agency/Office of Prevention, Pesticides, and Toxic Substances). 2000. Health Effects Test Guidelines, OPPTS 870.3550, Reproduction/Developmental Toxicity Screening Test. EPA712–C–00–367. July 2000. [Std]

{U.S. EPA/OPPTS 2003} U.S. EPA/OPPTS (U.S. Environmental Protection Agency/Office of Prevention, Pesticides, and Toxic Substances). 2003a. Health Effects Test Guidelines, OPPTS 870.2600, Skin Sensitization. EPA 712–C–03–197, Report dated March 2003. Available at: https://www.regulations.gov/#!documentDetail;D=EPA-HQ-OPPT-2009-0156-0008. [Std]

{U.S. EPA/OPPTS 2004} U.S. EPA/OPPTS (U.S. Environmental Protection Agency/Office of Prevention, Pesticides, and Toxic Substances). 2004. Overview of the Ecological Risk Assessment Process in the Office of Pesticide Programs, Endangered and Threatened Species Effects Determinations. Available at https://www.epa.gov/sites/production/files/2014-11/documents/ecorisk-overview.pdf.[Std]

{U.S. EPA/ORD 1992} U.S. EPA/ORD (U.S. Environmental Protection Agency/Office of Research and Development). 1992. Dermal Exposure Assessment: Principles and Applications. EPA/600/8-91/011B. Interim Report. Exposure Assessment Group, Office of Health and Environmental Assessment, Washington, DC. Available at: http://cfpub.epa.gov/ncea/cfm/recordisplay.cfm?deid=12188. [Std]

{U.S. EPA/ORD 1993} U.S. EPA/ORD (U.S. Environmental Protection Agency/Office of Research and Development). 1993. Wildlife Exposure Factors Handbook. Volumes 1 and 2. EPA/600/R-93/187a,b. Pagination not continuous. NTIS PB94-174778 and PB94-174779. Available at: http://rais.ornl.gov/homepage. [Std]

{U.S. EPA/ORD 2004} U.S. EPA (U.S. Environmental Protection Agency/Office of Research and Development). 2004. United State Environmental Protection Agency Integrated Risk Information System. Boron (Boron and Borates only) (CASRN 7440-42-8). Last updated 8/5/2004. Available at http://www.epa.gov.iris.subst.0410.htm [RA2006]

{U.S. EPA/ORD 2007} U.S. EPA/ORD (U.S. Environmental Protection Agency/Office of Research and Development). 2007. Dermal Exposure Assessment: A Summary of EPA Approaches. EPA/600/R-07/040F. Report dated September 2007. Available at http://www.epa.gov/ncea. [Std]

{U.S. EPA/OSWER 1998} U.S. EPA/ORD (U.S. Environmental Protection Agency/Solid Waste and Emergency Response). 1998. Soil Screening Guidance: Technical Background Document. Second Edition. EPA/540/R95/128. Report dated May 1996. Available at http://www2.epa.gov/superfund/soil-screening-guidance-technical-background-document. [Std]

{U.S. EPA/OW 2008} U.S. EPA/OW (U.S. Environmental Protection Agency/Office of Water). 2008. Drinking Water Health Advisory for Boron. Health and Ecological Criteria Division, Office of Science and Technology. Report dated May 2008. Available at: http://www2.epa.gov/sites/production/files/2014-09/documents/drinking_water_health_advisory_for_boron.pdf.

{USDA/FS 1991). USDA/FS (USDA/Forest Service). 1991. Evaluation of the use of TIM-BOR for the control of annosum root disease. FPM Report No. N91-12. Prepared by G. DeNitto, Forest Pathologist, USDA Forest Service Pest Management. Redding, CA. [RA2006]

{USDA/FS 1993} USDA/FS (USDA/Forest Service). 1993. Biological evaluation of the efficacy of TIM-BOR for the control of annosus root disease. Memorandum to J Borrecco from GA DeNitto, dated Feb 08, '93. USDA Forest Service, Shasta-Trinity National Forest. Not paginated. [RA2006]

{USDA/FS 1994} USDA/FS (USDA/Forest Service). 1994. Borax background document. Internal memorandum from MM Ollieu to Forest Supervisor, NF, dated May 5, 1994. USDA Forest Service. Not paginated. [RA2006]

{USDA/FS 2011) USDA/FS (USDA/Forest Service). 2011. Annosus Root disease Infects fresh stumps and spreads root-to-root. Prepared by Forest Health Protection, Rocky Mountain Region. Available at: http://www.fs.usda.gov/Internet/FSE_DOCUMENTS/stelprdb5299327.pdf. [Set00]

{USDA/NSERL 2005} USDA/NSERL (United States Department of Agriculture/National Soil Erosion Research Laboratory). 2004. Cligen Weather Generator, expanded and improved by USDA Agricultural Research Service and U. S. Forest Service. Available at: http://horizon.nserl.purdue.edu/Cligen/. [Std]

{USGS 2014} USGS (U.S. Geological Survey). 2007. An Overview Comparing Results from Two Decades of Monitoring for Pesticides in the Nation's Streams and Rivers, 1992–2001 and 2002–2011. Scientific Investigations Report 2014–5154. Available at: http://pubs.usgs.gov/sir/2014/5154/pdf/sir2014-5154.pdf. [Std]

{USGS 2014} USGS (U.S. Geological Survey). 2014. Preliminary Pesticide Use Maps for 2011. Available at: http://water.usgs.gov/nawqa/pnsp/usage/maps/compound_listing.php. Accessed on August 17, 2014. [Std]

{Usta et al. 2009} Usta M; Ustaomer D; Kartal SN; Ondaral S. 2009. Termite Resistance of MDF Panels Treated with Various Boron Compounds. International Journal of Molecular Sciences. 10(6):2789-97. [Set01]

{Ustundaq et al. 2014} Ustundaq A; Behm C; Follmann W; Duydu Y; Degen GH. 2014. Protective Effect of Boric Acid on Lead- and Cadmium-Induced Genotoxicity in V79 Cells. Archives of Toxicology. 88(6):1281-9. [Set01]

{van Hemmen 1992} van Hemmen JJ. 1992. Agricultural pesticide exposure data bases for risk assessment. Rev. Environ. Contam. Toxicol. 126: 1-85. [Std]

{VanderZaag et al. 2010} VanderZaag AC; Campbell KJ; Jamieson RC; et al. 2010. Survival of Escherichia coli in agricultural soil and presence in tile drainage and shallow groundwater. Canadian Journal of Soil Science, 2010, 90(3): 495-505.

{Venditti et al. 2013} Venditti T; Cubaiu L; Ladu G; D'hallewin G. 2013. Effect of Different GRAS Compounds in the Control of Apples Blue Mould. Communications in Agricultural and Applied Biological Sciences. 78(3):599-604. [Set01]

{Verce et al. 2012} Verce MF; Stiles AR; Chong KC; Terry N. 2012. Isolation of An Extremely Boron-Tolerant Strain of *Bacillus firmus*. Canadian Journal of Microbiology. 58(6):811-4. [Set01]

{Waldbauer 1968} Waldbauer GP. 1968. The consumption and utilization of food by insects. Advan Insect Physiol. 5: 229-288. [Std]

{Wallen et al. 1957} Wallen IE; Greer WC; Weston RF. 1957. Toxicity to Gambusia affinis of certain pure chemicals in turbid waters. Sewage Industrial Wastes. 29(6): 695-711. As cited in Hovatter and Ross 1995. [RA2006]

{Wang et al. 2008} Wang Y; Zhao Y; Chen X. 2008. Experimental Study on the Estrogen-Like Effect of Boric Acid. Biological Trace Element Research. 121(2):160-70. [Set01]

{Warne et al. 1990} Warne MS; Connell DW; Hawker DW; Schueuermann G. 1990. Prediction of aqueous solubility and the octanol-water partition coefficient for lipophilic organic compounds using molecular descriptors and physiochemical properties. Chemosphere. 21(7): 877-888. [RA2006]

{Webb et al. 2013} Webb DV; Stowman AM; Patterson JW. 2013. Boric Acid Ingestion Clinically Mimicking Toxic Epidermal Necrolysis. Journal of Cutaneous Pathology. 40(11):962-5. [Set01]

{Wegman et al. 1994} Wegman DH; Eisen EA; Hu X; Woskie SR; Smith RG; Garabrant DH. 1994. Acute and chronic respiratory effects of sodium borate particulate exposures. Environmental Health Perspectives, Vol. 102, Supplement 7, pages 119-128, 29 references, 1994. [RA2006]

{Weir 1966} Weir RJ. 1966. Final Report: Three-Generation Reproduction Study--Rats: Project No. 182-105. (Unpublished study received Jan 17, 1969 under 9F0783; prepared by Hazleton Laboratories, Inc., submitted by United States Borax & Chemical Corp., Los Angeles, Calif.; CDL:091344-D). MRID 00005623. [Set No. CBI01] As summarized in SERA 2006a. [RA2006]

{Weir 1967} Weir RJ. 1967. Final Report: 38-Week Dietary Feeding--Dogs: Borax (Sodium tetraborate decahydrate). (Unpublished study received Jan 17, 1969 under 9F0783; prepared by Hazleton Labora- tories, Inc., submitted by United States Borax & Chemical Corp., Los Angeles, Calif.; CDL:091344-B). MRID 00005620. As summarized in SERA 2006a. [RA2006]

{Weir and Fisher 1972} Weir RJ; Fisher RS. 1972. Toxicologic studies on borax and boric acid. Toxicol Appl Pharmacol. 23:351-364. [RA2006]

{Weis and Weis 1991} Weis P; Weis JS. 1991. The developmental toxicity of metals and metalloids in fish. Metal Ecotoxicology: Concepts & Applications. pp. 145-69. [RA2006]

{Weiss et al. 1978} Weiss MJ; Peacher PH; Knighten JL; Affeltranger. 1978. Annosa root rot stump treatment. USDA Forest Service, Southeastern Area, State and Private Forestry. Forestry Report SA-FR 1. 21 p. [RA2006]

{Wester et al. 1998} Wester RC; Hui X; Hartway T; Maibach HI; Bell K; Schell MJ; Northington DJ; Strong P; Culver BD. 1998. *In vivo* percutaneous absorption of boric acid, borax, and disodium octaborate tetrahydrate in humans compared to in vitro absorption in human skin from infinite and finite doses. Toxicological Sciences. 45(1): 42-51. [RA2006]

{Westlund and Nohrstedt 2000}Westlund A; Nohrstedt HO. 2000. Effects of Stump-Treatment Substances for Root-Rot Control on Ground Vegetation and Soil Properties in a *Picea abies* Forest in Sweden. Scandinavian Journal of Forestry Research. 15(5): 550-560. [ECOTOX - 166641]

{WHO 1998} WHO (World Health Organization). 1998. Boron. Guidelines for drinking-water quality, 2nd ed. Addendum to Vol. 2. Health criteria and other supporting information. World Health Organization, Geneva, 1998. Available at: http://www.who.int/water_sanitation_health/dwq/boron.pdf?ua=1. [Set00]

{WHO 1999} WHO (World Health Organization). 1999. Hazard prevention and control in the work environment: Airborne dust. Chapter 1. Dust: Definitions and Concepts. Available at: http://www.who.int/occupational_health/publications/en/oehairbornedust3.pdf. [Set00]

{Whorton et al. 1994} Whorton MD; Haas JL; Trent L; Wong O. 1994. Reproductive effects of sodium borates on male employees: birth rate assessment. Occupational and Environmental Medicine. 51(11): 761-767. [RA2006]

{Wilbur-Ellis 2002} Wilbur-Ellis. 2002. MSDS for Sporax®. Prepared March 31, 1993, Last Revised Feb 5, 2002. Note: This is the most current MSDS. [RA2006]

{Wilbur-Ellis 2013} Wilbur-Ellis. 2013. Product Label for Sporax®. EPA Approval for label dated January 31, 2013. Available at: http://www3.epa.gov/pesticides/chem_search/ppls/002935-00501-20130131.pdf. [RA2006]

{Wilding et al. 1959} Wilding JL; Smith WJ; Yevich P; et al. 1959. The toxicity of boron oxide. American Industrial Hygiene Association Journal. 20:284289. [Set02]

{Wiley 1904} Wiley WW. 1904. Influence of food preservatives and artificial colors on digestion and health. I. Boric acid and borax. U.S. Department of Agriculture, Bureau of Chemistry, Bulletin No. 84, Part I, July 5, p 1-477. Available at: https://ia800309.us.archive.org/33/items/influenceoffoodp00wile/influenceoffoodp00wile.pdf [Set05]

{Williams and Amburgey 1987} Williams L; Amburgey T. 1987. Integrated protection against lyctid beetle infestations. IV. Resistance of Boron-treated wood (Virola spp.) to insect and fungal attack. Forest Products J. 37(2):10-17. MRID 40196505. As summarized in SERA 2006a. [RA2006]

{Willis and McDowell. 1987} Willis, GH; McDowell, LL. 1987. Pesticide persistence on foliage. Reviews of Environmental Contamination and Toxicology. 100: 23-73. [Std]

{Willis and Piland 1938} Willis LG; Piland JR. 1938. A response of alfalfa to borax. J Am Soc Agron. 30: 63-67. [RA2006]

{Wilson et al. 2005} Wilson JR; Mills JG; Prather ID; Dimitrijevich SD. 2005. A Toxicity Index of Skin and Wound Cleansers Used on *in vitro* Fibroblasts and Keratinocytes. Advances in Skin and Wound Care. 18(7):373-8. [Set01]

{Wimmer et al. 1993} Wimmw MJ; Smith RK; Wallinga DI; Toney SR; Faber DC; Miracle JE; Carnes JT; Rutherford AB. 1993. Persistence of Diflubenzuron on Appalachian Forest Leaves after Aerial Application of Dimilin. J Agric Food Chem. 41: 2184-2190. [Std]

{Windeatt et al. 1991} Windeatt AJ; Tapp JF; Stanley RD. 1991. The use of soil-based plant tests based on the OECD guidelines. Gorsuch, J. W., et Al. (Ed.). ASTM (American Society for Testing Materials) Special Technical Publications, 1115. Plants for Toxicity Assessment: Second Volume; Symposium, San Francisco, California, USA, April 23-24, 1990. [RA2006]

{Winegardner 1996} Winegardner DL. 1996. An Introduction to Soils for Environmental Professionals. CRC Press, Boca Raton, Florida. 270 pp.[Std]

{Winston 1987} Winston ML. 1987. The Biology of the Honey Bee. Harvard University Press, Cambridge, MA. ISBN 0-674-07409-2 280 pp. [Std]

{Wise and Winkelmann 2009} Wise LD; Winkelmann CT. 2009. Micro-Computed Tomography and Alizarin Red Evaluations of Boric Acid-Induced Fetal Skeletal Changes in Sprague-Dawley Rats. Birth defects research. Part B, Developmental and reproductive Toxicology. 86(3):214-9. [Set01]

{Wnorowski 1994a} Wnorowski G. 1994a. Sodium Tetraborate Decahydrate: Acute Inhalation Toxicity Limit Test (in Rats). Lab Project Number: 3309. Unpublished study prepared by Product Safety Labs. 24 p. MRID 43500800. As summarized in SERA 2006a. [RA2006]

{Wnorowski 1994b} Wnorowski G. 1994b. Sodium Tetraborate Decahydrate: Dermal Sensitization (in Guinea Pigs). (Buehler Method): Lab Project Number: 3308. Unpublished study prepared by Product Safety Labs. 28. MRID 43500801. As summarized in SERA 2006a. [RA2006]

{Wnorowski 1994c} Wnorowski G. 1994c. Disodium Octaborate Tetrahydrate: Acute Inhalation Toxicity Limit Test: Lab Project Number: 3313. Unpublished study prepared by Product Safety Labs. 24 p. MRID 43500103. As summarized in SERA 2006a. [RA2006]

{Wnorowski 1994d} Wnorowski G. 1994d. Disodium Octaborate Tetrahydrate: Dermal Sensitization Test--Buehler Method(in Guinea Pigs). Lab Project Number: 3312. Unpublished study prepared by Product Safety Labs. 28 p. MRID 43500104. As summarized in SERA 2006a. [RA2006]

{Wnorowski 1996a} Wnorowski G. 1996a. Acute Dermal Toxicity Limit Test (in Rats): Sodium Tetraborate Decahydrate (Borax). Lab Project Number: 4513: P322. Unpublished study prepared by Product Safety Labs. 15 p. MRID 44048600. As summarized in SERA 2006a. [RA2006]

{Wnorowski 1996b} Wnorowski G. 1996b. Acute Dermal Toxicity Limit Test (in Rats): Disodium Octaborate Tetrahydrate(Polybor). Lab Project Number: 4516: P322. Unpublished study prepared by Product Safety Labs. 15 p. MRID 44048600. As summarized in SERA 2006a. [RA2006]

{Wong et al. 1964} Wong LC; Heimbach MD; Truscott DR; et al. 1964. Boric acid poisoning: Report of 11 cases. Can Med Assoc J 90:1018-1023. Summarized in ATSDR 1992. [RA2006]

{Woods 1994} Woods WG. 1994. An introduction to boron: history, sources, uses, and chemistry. Environmental Health Perspectives. 102(7): 5-11. [RA2006]

{Woskie et al. 1993} Woskie SR; Shen P; Finkel M; Eisen EA; Smith TJ; Smith R; Wegman DH. 1993. Calibration of a continuous-reading aerosol monitor (Miniram) to measure borate dust exposures. Applied Occupational and Environmental Hygiene. 8(1): 38-45. [RA2006]

{Woskie et al. 1994} Woskie SR; Shen P; Eisen EA; Finkel MH; Smith TJ; Smith R; Wegman DH. 1994. The real-time dust exposures of sodium borate workers: examination of exposure variability. American Industrial Hygiene Association Journal, Vol. 55, No. 3, pages 207-217, 29 references, 1994. [RA2006]

{Woskie et al. 1998} Woskie SR; Eisen EE; Wegman DH; Hu X; Kriebel D. 1998. Worker sensitivity and reactivity: indicators of worker susceptibility to nasal irritation. American Journal of Industrial Medicine. 34(6): 614-622. [RA2006]

{Xing et al. 2008}Xing X; Wu G; Wei F; et al. 2008. Biomarkers of environmental and workplace boron exposure. Journal of Occupational and Environmental Hygiene. 5:141-147. [Set02]

{Xu and Peak 2007} Xu D; Peak D. 2007. Adsorption of Boric Acid on Pure and Humic Acid Coated Am-Al(oh)3: A Boron K-Edge Xanes Study. Environmental Science and Technology. 41(3):903-8. [Set01]

{Xue et al. 2008} Xue RD; Ali A; Kline DL; Barnard DR. 2008. Field Evaluation of Boric Acid- and Fipronil-Based Bait Stations Against Adult Mosquitoes. Journal of the American Mosquito Control Association. 24(3):415-8. [Set01]

{Xue et al. 2011} Xue RD; M [illegible] GC; Kline DL; Barn
of Boric Acid Sugar Baits Applied to Plants for Control of *Aedes albopictus*. Journal of the American Mosquito Control Association. 27(1):56-60. [Set01]

{Yeslibag and Eren 2008} Yeslibag D; Eren M. 2008. Effects of Dietary Boric Acid Supplementation on Performance, Eggshell Quality and Some Serum Parameters in Aged Laying Hens. Turk. J. Vet. Anim. Sci.32(2): 113-117 [ECOTOX - 111573]

{Yildiz et al. 2013} Yildiz G; Koksal BH; Sizmax O. 2013. Effects of dietary boric acid addition on growth performance, cholesterolemia, some carcass and tibia characteristics in different rearing periods in broiler chickens. Revue de Médecine Vétérinaire. 164(4): 219-224. [Set01]

{Ying et al. 2011} Ying X; Cheng S; Wang W; Lin Z; Chen Q; Zhang W; Kou D; Shen Y; Cheng X; Rompis FA; Peng L; Zhu Lu C. 2011. Effect of Boron on Osteogenic Differentiation of Human Bone Marrow Stromal Cells. Biological Trace Element Research. 144(1-3):306-15. [Set01]

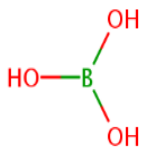
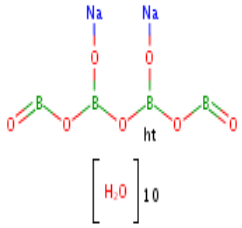
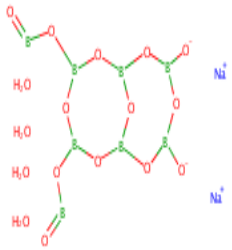
{Yoon et al. 2010} Yoon J; Miwa H; Ahmed I; Yokota A; Fujiwara T. 2010. *Rhodococcus baikonurensis* BTM4c, a Boron-Tolerant Actinobacterial Strain Isolated from Soil. Bioscience Biotechnology and Biochemistry. 74(1):178-81. [Set01]

{Yoshinari et al. 2012} Yoshinari A; Kasai K; Fujiwara T; Naito S; Takano J. 2012. Polar Localization and Endocytic Degradation of a Boron Transporter, Bor1, Is Dependent on Specific Tyrosine Residues. Plant Signaling and Behavior. 7(1):46-9. [Set01 - Toxline]

{Yu et al. 2013} Yu D; Yong D; Dong S. 2013. Toxicity Detection of Sodium Nitrite, Borax and Aluminum Potassium Sulfate Using Electrochemical Method. Journal of Environmental Sciences (China). 25(4):785-90. [Set01]

{Zhang et al. 2005} Zhang YC; Perzanowski MS; Chew GL. 2005. Sub-Lethal Exposure of Cockroaches to Boric Acid Pesticide Contributes to Increased Bla G 2 Excretion. Allergy. 60(7):965-8. [Set01]

Table 1: Overview of Sporax® and Cellu-Treat

Property	Boron	Boric Acid	Sodium Tetraborate Decahydrate [Borax]	Disodium Octaborate Tetrahydrate [DOT]
CAS No.[1]	7440-42-8	10043-35-3	1303-96-4	12280-03-4
Molecular Formula[1, 3]	B	$BH_3 0_3$	$B_4Na_2O_7$ $\cdot 10\ H_20$	$B_8Na_2O_{13}$ $\cdot 4\ H_2O$
Structure[1]	B			
Molecular Weight[1]	10.811	61.8317	381.365	412.5142
Boron Content[2]	1	0.175	0.113	0.210
Boron Content[3]		0.1748	0.1134	0.2096
K_{ow}		0.175 [4]		
Water Solubility[5]		55.6 g/L (cold) 250 g/L (boiling)	62.5 g/L at 25°C	223.65 g/L at 20°C
EPA PC Code	N/A	011001	029601 or 011102	011103
Common synonyms	N/A	N/A	Borax Sodium borate decahydrate	DOT Boron sodium oxide (many more)
Formulations/ Suppliers	N/A	N/A	Sporax®/ Wilbur-Ellis	Cellu-Treat®/Nisus
EPA Reg. No. for Formulation	N/A	N/A	2935-501	64405-8
% a.i. in formulation	N/A	N/A	100%	98%

[1] ChemIDplus 2015

[2] Molecular weight of boron in compound (i.e., #B x 10.881 g B/mole) divided by molecular weight of compound, rounded to three significant places.

[3] U.S. EPA/OPP/EFED 2015a, Table 3.1, p. 28.

[4] Barres 1967

[5] Detailed documentation of temperature dependence in Crapse and Kyser 2011. Value for boric acid at 25°C (77°F) is 54,300 mg/L (Crapse and Kyser 2011, Table 1, p. 11).

Table 2: Selected Monitoring in Different Media

Source Group	Level	Units	Source
Air			
Gar phase	0.016	ng/ m^3	ECETOC 1997, p. 39
NOS	<0.5 – 80	ng/m^3	IPCS/WHO 1998, p. 21; ATSDR 2010, p. 9
Soil			
Earth's crust	10 (5 – 100)	mg B/kg	IPCS/WHO 1998
Rocks	1.5 – 60	mg B/kg	ECETOC 1997, p. 37
Low borate soils	<10	mg B/kg	ECETOC 1997, p. 40
Average (world-wide)	10-20	mg B/kg	ECETOC 1997, p. 40
High borate soils	Up to 100	mg B/kg	ECETOC 1997, p. 40
U.S.	26 to 300[2]	mg B/kg	IPCS/WHO 1998, p. 36
Trees			
Eucalypt forests (n=2)	2.1 and 2.5	kg/ha	IPCS/WHO 1998, p. 26
Water, Surface			
USA overall	0.076 – 0.387	mg B/L	ECETOC 1997, p. 30 [1]
USA overall	0.1 (<0.01 – 1.5)	mg B/L	U.S. EPA/OPP/EFED 2015a, p. 29
USA Illinois	0.050 – 0.112	mg B/L	ECETOC 1997, p. 30 [1]
USA North Dakota	0.228 – 0.519	mg B/L	ECETOC 1997, p. 30 [1]
North America	0.1 – 0.4	mg B/L	IPCS/WHO 1998, p. 33
North America (max.)	360	mg B/L	IPCS/WHO 1998, p. 33
USA	<1 – 3	mg B/L	ATSDR 2010, p. 9
Europe	<0.01 – 7	mg B/L	IPCS/WHO 1998, p. 33
Water, Ground			
World wide	<0.3 to >100	mg B/L	IPCS/WHO 1998, p. 32
Water, Ocean			
	4.6 (0.5 to 9.6)	mg B/kg	ECETOC 1997, p. 16

Note: Monitoring data are extensive. The above is a brief summary selected from reputable reviews.

[1] Values expressed as median to 90th percentile covering monitoring from January 1984 to December 1993. The two states reflect the lowest and highest median values. Data on other state are available.

[2] Geometric mean to maximum.

See Section 2.2 for initial discussion.

Table 3: Use of Borax by the Forest Service from 2000 to 2004

Year	Region	Forest	Amount (lbs)	Acres Treated	lbs/acre
2000	5	1	15	40	0.4
2000	5	4	240	519	0.5
2000	5	5	5965	5480	1.1
2000	5	7	15	20	0.8
2000	5	11	585	2234	0.3
2000	5	12	125	460	0.3
2000	5	13	200.5	417	0.5
2000	5	13	27	58	0.5
2000	5	15	10	40	0.3
2000	5	17	8573.5	4675	1.8
2000	5	6	5125.5	4469	1.1
2000	5	9	830	2353	0.4
2000	6	14	217	1074	0.2
2001	5	1	5	10	0.5
2001	5	4	563	1870	0.3
2001	5	5	43	370	0.1
2001	5	6	2515	4472	0.6
2001	5	9	4815	4938	1.0
2001	5	11	663	2168	0.3
2001	5	12	125	380	0.3
2001	5	15	10	10	1.0
2001	5	17	3417	2185	1.6
2001	5	19	30	111	0.3
2001	6	1	80	259	0.3
2001	6	14	125	258	0.5
2002	5	1	10	20	0.5
2002	5	11	698	2333	0.3
2002	5	17	5274	2822	1.9
2002	5	19	58	210	0.3
2002	5	4	555	1700	0.3
2002	5	5	1012	2441	0.4
2002	5	6	9327.5	5837	1.6
2002	5	9	190	483	0.4
2002	6	14	145	1302	0.1
2003	5	1	10	20	0.5
2003	5	4	938	1700	0.6
2003	5	5	1490	1918	0.8
2003	5	6	4847.8	8339.6	0.6
2003	5	9	523.5	1475	0.4
2003	5	11	136	135	1.0
2003	5	17	843	1605	0.5
2003	5	19	47	170	0.3
2003	6	14	155	1058	0.1
2003	8	11	17	25	0.7
2004	5	1	150	247	0.6
2004	5	4	227	370	0.6
2004	5	5	5673	3995	1.4
2004	5	6	6181	4234.1	1.5
2004	5	9	204	488	0.4
2004	5	11	1130	1130	1.0
2004	5	13	300	1897	0.2
2004	5	17	7932	5010	1.6
2004	5	19	77	280	0.3
2004	6	14	164	340	0.5
2004	8	11	40	12	3.3
				Min:	0.1
				Max:	3.3
				Number of Applications	55

Table 4: Regional Summary of Borax Use by the Forest Service from 2000 to 2004

Use Parameter	Region 5	Region 6	Region 8	All
Number of Applications	47	6	2	55
Total Pounds	81731.3	886	57	82674.3
Total Acres	86138.7	4291	37	90466.7
Average lbs/acre	0.95	0.21	1.54	0.91
Minimum lbs/acre	0.1	0.1	0.7	0.1
Maximum lbs/acre	1.9	0.5	3.3	3.3

Table 5: Acute Toxicity Data in Humans

Subject/Population	Dose (Agent)	Effect	Reference
Volunteers, males, n=8, 22-28 years, BW≈70 kg	IV, 562-611 mg BA/day 1.4-1.53 mg B/kg bw.	No signs of toxicity.	Jansen et al. 1984a
Volunteers, males, n=6, 30-58 years, BW 67-76 kg	750 mg BA 1.7-2.08 mg B/kg bw, IV	No effect. 1-2 mg B/L blood at 25 minutes post-administration.	Jansen et al. 1984b
Patients, n=10, B^{10} therapy for glioblastoma	25 (19-46) mg B/kg bw IV	Rapid onset of nausea (2 min.). Facial flush, vomiting, incontinence.	Locksley and Farr 1955
Patient (n=1), male, accidental	Subcutaneous, 28,000 mg boric acid ≈70 mg B/kg bw,	Severe skin reaction, cough, vomiting, abdominal pain.	Peyton and Green 1941
56 year old male, suicide attempt.	Oral, no estimate of dose	Lethargy, stiffness, skin reaction, alopecia. Serum boron: 34 mg B/L	Webb et al. 2013
45 year old male	Oral, boric acid, no estimate of dose	Severe skin reaction, nausea, vomiting 130 mg borate/dL blood	Lung and Clancy 2009
26 year old woman	Oral, 21,000 mg boric acid [≈61.25 mg B/kg bw]	Survived with aggressive medical treatments	IPCS/WHO 1998 citing Teshima et al. 1992
85 year old male	Oral, 30 g boric acid [≈74.9 mg B/kg bw]	Acidosis, renal failure, shock. Survived with treatment Serum BA of 1800 mg/L [315 mg B/L]	Corradi et al. 2010
45 year old male, suicide attempt	Potential dose up to 75 g boric acid [≈187 mg B/kg bw]. Mixed exposure to cocaine.	Vomiting. Initial level of 154.44 mg/L in arterial serum. Survived.	Naderi and Palmer 2006
77 year old male	Oral, 85 mg B/kg, boric acid	Vomiting, diarrhea, erythema, cyanotic extremities, acute renal failure, cardiopulmonary and hypotension **Death** from cardiac insufficiency.	ATSDR 2010 citing Ishii et al. 1993
Not specified	640 mg/kg bw boric acid [112 mg B/kg bw]	**"Lowest" Lethal dose**	Stokinger 1981
Infants, 2, accidental	Oral 500 mg B/kg bw and 735 mg B/kg bw	**Death** Degenerative changes of liver, kidney, and brain. Aggressive medical treatment.	Wong et al. 1964
45 year old mail, suicidal	Oral, 700 mg B/kg bw	**Death**. Vomiting, diarrhea, skin reaction, renal failure.	ATSDR 2010 citing Restuccio et al. 1992
Infant, 18 months, 18 lbs.	Oral, Uncertain, orthoboric acid	**Death** 83 mg borate/L blood	Hamilton and Wold 2007
19 year old male	Oral, boric acid, no estimate of dose	**Death.** Severe damage to stomach. No assay of blood boron.	Rani and Meena 2013

See Section 3.1.4.2 for discussion.

Table 6: Summary of Repeated Dose Studies in Mammals

Species	Days	NOAEL (mg B/kg bw/day)	LOAEL (mg B/kg bw/day)	Endpoint	Reference
Rats	7	68		No overt toxicity	Ku and Chapin 1994
Rats	21		175	Decrease bw. Overt toxicity.	Dani et al. 1971
Rats, M	28		21.9	Testicular pathology	Kudo et al. 2000
Rats, M	28		61	Testicular pathology, decreased testosterone, decrease in sperm number.	Treinen and Chapin 1991
Rats	45	48	70	Renal tubule degeneration and kidney weight loss up to 30 days.	Sabuncuoglu et al. 2006
Rats, M	60	25	50	Testicular atrophy and pathology	Lee et al. 1978
Dogs, F	90	2.6	23	Decrease hematocrit	MRID 40692307
Dogs, M	90	4.1	32	Testicular atrophy and pathology	MRID 40692307
Rats	90	42	125	Testicular atrophy, decreases in body, testes, and ovarian weights	MRID 40692305
Rats, M	90	41		No effects	MRID 40692306
Dogs	266		40	Testicular atrophy, decreased bw	MRID 40692308
Dogs	266		28	Testicular atrophy and pathology	MRID 40692310
Dogs	730	**8.8**[1]		No effects.	MRID 40692310
Mice	730		48	Testicular atrophy.	Dieter et al. 1991 MRID 41863101
Rats	730	17	58	Testicular atrophy.	MRID 40692309
Rats	730	17.5	58.5	Testicular atrophy.	Weir and Fisher 1972

Includes only studies for which mg B/kg bw doses are available. Other studies discussed in text.

[1] The NOAEL of 8.8 mg B/kg bw/day is used in U.S. EPA/OPP/HED 2015a, p. 8 at the point of departure for the dose-response assessment for incidental oral and short- and intermediate-term inhalation exposures. UF of 100. This study also used by U.S. EPA/OPP/HED 1993 to derive a chronic RfD of 0.09 mg/kg bw.

See Appendix 1, Table A1-2, for details.
See Section 3.1.5 for initial discussion.

Table 7: Summary of Developmental and Reproduction Studies

Species	NOAEL (mg B/kg bw/day)	LOAEL (mg B/kg bw/day)	Effect(s)	Reference
			Developmental	
Mice	27	111	Fetal: Decreases in pup weight and survival.	MRID 41589101
	27	111	Parental: Decrease in fertility.	
Mice	43.3	79	Fetal: Decreased body weight.	Heindel et al. 1992, 1994,
	79	175	Fetal: Skeletal malformations.	
	N.D.	43.3	Maternal: renal tubular dilatation.	MRID 41725402
Rabbits	21.8	43.7	Fetal: Decreased survival, cardiovascular malformations.	Price et al. 1996b MRID 42164202
	21.8	43.7	Maternal: Intrauterine bleeding.	
Rats [1, 2]	9.6	13.7	Fetal: Fetal mortality, skeletal malformations and reduced fetal weight.	Price et al. 1996a MRID 43340101
	25	N.D.	Parental: No effects.	
Rats [1]	13.6	28.8	Fetal: Skeletal anomalies.	Heindel et al. 1992, 1994
	28.8	57.7	Maternal: Decrease in uterine weights.	MRID 41725401
	57.7	94.3	Fetal: Fetal mortality and soft tissue anomalies.	
Rats	N.D.	43.75	Fetal: Skeletal anomalies.	Harrouk et al. 2005
	87.5	N.D.	Maternal: No effects	
Rats	N.S	40	Fetal: Skeletal anomalies.	Wise and Winkelmann 2009
	87.5	N.D.	Maternal: No effects	
Rats	N.S	21.9	Paternal: Decreased testosterone	El-Dakdoky and Abd El-Wahab 2013
	21.9	43.75	Paternal: Decreased testes weight.	
	21.9	43.75	Fetal: Decreased fetal viability.	
			Reproductive	
Rats	45	150	Paternal: Testicular atrophy, pathology and abnormal sperm. Reversible sterility.	Dixon et al. 1979
	150	450	Paternal: Irreversible sterility.	
Rats	25	82	Paternal: Testicular atrophy, pathology and abnormal sperm.	MRID 40692311
	25	82	Reproduction: Decreased fertility.	
	25	82	Offspring: Decreased pup survival	
	27	92	Maternal: Decreased ovulation. No offspring when mated with control males.	

N.D.: Not determined.

[1] Used by Allen et al. 1996 in benchmark dose analysis to derive the IRIS chronic RfD of 0.2 mg/kg bw/day using an uncertainty factor of 100 (U.S. EPA/OPP/NCEA 2004).

[2] The NOAEL of 9.6 mg B/kg bw used by Institute of Medicine (2001) to derive acceptable dose of 0.3 mg B/kg bw/day using an uncertainty factor of 30.

See Appendix 1, Table A1-3, for details.
See Section 3.1.9 for discussion.

Table 8: Levels of Human Exposure to Boron

Source Group	Exposure Mean (95% CI) or Range [Low – High] mg B/day[1]	Source
Dietary		
United States	1.28 [M] 1.0 [F]	ATSDR 2010, p. 9
United States	1 – 3	Meacham et al. 2010
United States, 1989-91[4]	1.17 (0.43-2.42), High=9.64 [M] 0.96 (0.33-1.94), High=8.50 [F]	Rainey et al. 1996
United States, 1994-96[4]	1.28 (0.53-2.40), 99th %=3.18 [M] 1.00 (0.41-1.87), 99th %=2.47 [M]	Rainey et al. 2002
United States	1.21 to 1.52 (averages)	IPCS/WHO 1998, p. 49
United States, children (4-18 years)	0.80±0.040 to 1.02±0.04	ATSDR 2010, Table 6-4, p. 152 [2]
United States, adults (>19 years)	1.28±0.04 [M] 1.00±0.01 [F]	ATSDR 2010, Table 6-4, p. 152 [2]
United States, toddlers	0.548	Meacham and Hunt 1998
United States, adults	0.89 [M], 0.69 [F]	Meacham and Hunt 1998
China	2.3 (0.4-12.7)	Xing et al. 2008, Table III
Egypt	1.31 (0.63-2.15) [M] 1.24 (0.71-1.90) [F]	Pahl et al. 2005, Table 1
Great Britain	1.3 (0.56-2.49) [M] 1.12 (0.44-2.25) [F]	Pahl et al. 2005, Table 1
Germany	1.72 (0.72-3.45) [M] 1.62 (0.67-3.02) [F]	Pahl et al. 2005, Table 1
Kenya	1.95 (1.09-2.82) [M] 1.80 (1.16-2.62) [F]	Pahl et al. 2005, Table 1
Korea	0.93	Meacham et al. 2010
Mexico	2.12 (1.02-3.29) [M] 1.75 (1.05-2.61) [F]	Pahl et al. 2005, Table 1
Turkey	6.8 (1.8 – 23)	Bolt et al. 2012, Table 1
Turkey	6 – 8 (common)	Meachem et al. 2010, p. 38
Turkey	29 (upper bound)	Meachem et al. 2010, p. 38
Water		
United States[3]	0.2 – 0.6	Meacham et al. 2010, p. 37
Air		
Background	0.00044	IPCS/WHO 1998, p. 45
Occupational (NOS)		
U.S. workers, borax packaging and shipping	4.0 ±1.69 [Low] 16.18 ± 11.64 [Medium] 24.77 ± 15.35 [High]	Culver et al. 1994
NOS	3.5 - 46.5	Pahl et al. 2005, Table 1
NOS	28.4	IPCS/WHO 1998, p. 52
China	41.2 [11.6-111.4]	Xing et al. 2008
China	37 (2.3-470)	Bolt et al. 2012, Table 1
Turkey	14.5 (3.3 – 36)	Bolt et al. 2012, Table 1

[1] Sex of groups specified in [] when available: [M]=Males; [F]=Females.

[2] More detailed breakdowns by age and sex based on data from Rainey et al. (1999; 2002). Adult data for 1994-1996. Consumption of wine can increase intake by 3-4 mg/day.

[3] Estimate consistent with IPCS-WHO (1998, p. 46) estimates of 0.1 to 0.3 mg B/L in ground water and the consumption of 2 liters/day. Anderson et al. (1994. p. 77) estimates that drinking water will typically account for only 1% to 2% of boron intakes or 2% to 4% of boron intake if drinking water is used to reconstitute beverages or fruit juices.

[4] More detailed data are given in papers for different age groups. See Table 1 in Rainey et al. (1996) and Rainey et al. (2002).

Table 9: Backpack Foliar - Derivation of Worker Exposure Rates

Item	Value	Reference/Note
Reference Chemical	Glyphosate	Section 3.2.2.1.3.
First-order dermal absorption rate coefficient for reference chemical (hour^{-1}) [ka_{Ref}]	0.00041	SERA 2014b, Table 14
Occupational Exposure Rates for Reference Chemical		
Central Estimate	0.0003	SERA 2014b, Table 14
Lower 95% Prediction Bound	0.00006	SERA 2014b, Table 14
Upper 95% Prediction Bound	0.002	SERA 2014b, Table 14
Subject Chemical	Borates (Boric acid)	
First-order dermal absorption rate coefficient for subject chemical (hour^{-1}) [ka_P]	0.0000876	Section 3.1.3.2.2
$ka_P \div ka_{Ref}$	0.213658536585	
Occupational Exposure Rates for Subject Chemical (borates)		
Central Estimate	0.000064097561	SERA 2014b, Eq. 22
Lower 95% Prediction Bound	0.000012819512	SERA 2014b, Eq. 22
Upper 95% Prediction Bound	0.000427317073	SERA 2014b, Eq. 22

See Section 3.2.1 for discussion.

Documentation for Table: The above table implements the adjustment of worker exposure rates based dermal absorption rates. The table uses MS Word "fields" rather than macros.

- Determine the first-order dermal absorption rate coefficient for the chemical under review. See SERA 2014a, Section 3.1.3.2.2.
- Select the reference chemical. See SERA 2014b, Section 4.1.6.1.
- Fill in the information on the reference chemical in the upper section of the above table.
- Fill in the first-order dermal absorption rate coefficient for the chemical under review in the Value column of Row 9 in the above table.

Update the estimated values for ratio of the k_a values and the occupational exposure rates for the chemical under review – i.e., the green shaded cells in the above table. The simplest way to update these fields is to select each of the 4 green shaded cells (one at a time and in order), press the right mouse button, and select 'Update field'.

See Section 3.2.2.1.1.1 for discussion.

Table 10: Precipitation, Temperature and Classifications for Standard Sites

Location	Precipitation	Temperature	Average Annual Rainfall (inches)	Average Annual Temperature (◦F)
HI, Hilo	Wet	Warm	126.06	73.68
WA, Quillayute [1]	Wet	Temperate	95.01	49.14
NH, Mt. Washington	Wet	Cool	98.49	27.12
FL, Key West	Average	Warm	37.68	77.81
IL, Springfield	Average	Temperate	34.09	52.79
MI, Sault Ste. Marie	Average	Cool	32.94	40.07
AR, Yuma Test Station	Dry	Warm	3.83	73.58
CA, Bishop	Dry	Temperate	5.34	56.02
AK, Barrow	Dry	Cool	4.49	11.81

[1] Based on composite estimation in WEPP using a latitude of 47.94 N and a longitude of -124.54 W.

Table 11: Input Parameters for Fields and Waterbodies Used in Gleams-Driver Modeling

Field Characteristics	Description	Pond Characteristics	Description
Type of site and surface (FOREST)	Field (0)	Surface area	1 acre
Treated and total field areas	10 acres	Drainage area:	10 acres
Field width	660 feet	Initial Depth	2 meters
Slope	0.1 (loam and clay) 0.05 (sand)	Minimum Depth	1 meter
Depth of root zone	36 inches	Maximum Depth	3 meters
Cover factor	0.15	Relative Sediment Depth	0.02
Type of clay	Mixed		
Surface cover	No surface depressions		

Stream Characteristics	Value
Width	2 meters
Flow Velocity	6900 meters/day
Initial Flow Rate	710,000 liters/day

GLEAMS Crop Cover Parameters[3]	Description	Value
ICROP	Weeds	78
CRPHTX	Maximum height in feet.	3
BEGGRO	Julian day for starting growth	32
ENDGRO	Julian day for ending growth	334

Application, Field, and Soil Specific Factors [1]	Code[3]	Clay	Loam	Sand
Percent clay (w/w/):	CLAY	50%	20%	5%
Percent silt (w/w/):	SILT	30%	35%	5%
Percent sand (w/w/):	N/A	20%	45%	90%
Percent Organic Matter:	OM	3.7%	2.9%	1.2%
Bulk density of soil (g/cc):	BD	1.4	1.6	1.6
Soil porosity (cc/cc):	POR	0.47	0.4	0.4
Soil erodibility factor (tons/acre):	KSOIL	0.24	0.3	0.02
SCS Runoff Curve Number [2]:	CN2	83	70	59
Evaporation constant (mm/d):	CONA	3.5	4.5	3.3
Saturated conductivity below root zone (in/hr):	RC	0.087	0.212	0.387
Saturated conductivity in root zone (in/hr)	SATK	0.087	0.212	0.387
Wilting point (cm/cm):	BR15	0.28	0.11	0.03
Field capacity (cm/cm):	FC	0.39	0.26	0.16

[1] The qualitative descriptors are those used in the QuickRun window of Gleams-Driver. Detailed input values for the soil types are given in the sub-table below which is adapted from SERA (2007b, Tables 2 and 3). All fields are run for about 6 months before the pesticide is applied in early summer.

[2] From Knisel and Davis (Table H-4), *Clay*: Group D, Dirt, upper bound; *Loam*: Group C, woods, fair condition, central estimate; *Sand*: Group A, meadow, good condition, central estimate.

[3]Codes used in documentation for GLEAMS (Knisel and Davis 2000) and Gleams-Driver (SERA 2007a)

Table 12: Chemical parameters used in Gleams-Driver modeling

Parameter	Values	Note/Reference
Halftimes (days)		
Aquatic Sediment	9,999	Note 1
Foliar	9,999	Note 1
Soil	9,999	Note 1
Water	9,999	Note 1
Soil $K_{o/c}$, mL/g	62 - 438	Note 2
Sediment K_d, mL/g	68-120	Note 3
Water Solubility, mg/L	54,300	Note 4
Foliar wash-off fraction	1	Note 5
Fraction applied to foliage	0	Note 5
Depth of Soil Incorporation	1 cm	Note 6
Irrigation after application	none	
Initial Application Date	June 15	Default

Notes

Number	Text
1	Borates are modeled using chemical and physical properties of boric acid. The results of the modeling are given as boron equivalents. The assumption is made that no degradation occurs in terms of boron. GLEAMS, however, requires a finite halftime for vegetation and soil. A value of 9,999 days (about 27 year) is used to set the degradation rate to a negligible value.
2	HERA 2005 citing unpublished TNO study by de Vette et al. 2000.
3	HERA 2005 citing unpublished TNO study by Hanstveit et al. 2001.
4	Water solubility for boric acid at 77°F from Crapse and Kyser (2011, Table 1, p. 11). U.S. EPA/OPP/EFED (2015a, Appendix F, p. 79) appears to have used a water solubility of 9,300 mg/L. The source of this value is unclear. This difference is inconsequential. Water solubility is not a sensitive parameter in GLEAMS for water solubilities of >10 mg/L. (Knisel and Davis 2000, p. 105).
5	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.
6	This is the incorporation depth used by GLEAMS for surface applications (Knisel and Davis, 2000, p. 102).

Table 13: Monitored and Modeled Concentrations in Surface Water

Scenario/Source	Peak Concentrations (ppb or µg B/L per lb/acre)		Long-Term Average Concentrations (ppb or µg B/L per lb/acre)	
Accidental Spill	635 (318-1,270		N/A	
GLEAMS-Driver Simulations (Appendix 8)				
Pond, Section 3.2.3.4.4, Appendix 8, Tables 7 and 8	**Soil**	**Conc.**	**Soil**	**Conc.**
	Clay	55.2 (14.5 - 228)	Clay	27.4 (7.3 - 150)
	Loam	15.7 (1.48 - 211)	Loam	7.56 (0.5 - 80)
	Sand	52.4 (0.0000012 - 430)	Sand	18.8 (0.0000006 - 229)
	Comp.[1]	41.1 (0.0000012 - 430)	Comp.[1]	17.9 (0.0000006 - 229)
Stream, Section 3.2.3.4.4, Appendix 9, Tables 5 and 6	**Soil**	**Conc.**	**Soil**	**Conc.**
	Clay	50.4 (22.4 - 285)	Clay	0.91 (0.26 - 5.2)
	Loam	17.4 (4 - 128)	Loam	0.304 (0.029 - 8)
	Sand	22.6 (0.0000029 - 169)	Sand	2.02 (0.000000024 - 12.6)
	Comp.[1]	30.1 (0.0000029 – 285	Comp.[1]	1.1 (0.000000024 - 12.6)
EPA Tier 1 Models (see Section 3.2.3.4.4)				
GENEEC, U.S. EPA/OPP/EFED 2015a [2]	58.6		58.4 (90-day)	
Monitoring (see Section 3.2.3.4.5)				
Pratt et al. 1996 [3], stream, peat soil	69			
Ambient Concentrations (See Table 2 for details)				
U.S. (ECETOC 1997, p. 30)	76 – 387		µg B/L	
U.S. (U.S. EPA/OPP/EFED 2015a, p. 29)	100 (<10 to 1,500)		µg B/L	

[1] The average composite values across soil types are calculated as the arithmetic average of the average for each soil type. The lower bound is taken as the lowest value of the lower bounds across soil types. The upper bound is taken as the highest value of the upper bound across soil types.

[2] U.S. EPA/OPP/EFED 2015a, Appendix F, p. 77. Application rate of 0.07 lb/acre with Peak of 4.10 µg/L and longer-term (90 day) average of 4.09 µg/L. Peak WCR: 4.10 µg/L ÷ 0.07 lb /acre ≈ 58.57 µg/L per lb/acre. Longer-term WCR: 4.09 µg/L ÷ 0.07 lb /acre ≈ 58.42 µg/L per lb/acre.

[3] Maximum concentration in steam of 140 µg/L after application of 2 kg B/ha (as DOT) or ≈ 1.784 lb B/acre. Background concentration: 17 µg/L. WCR: (140 µg/L - 17 µg/L) / 1.784 lb B/acre ≈ 68.946 µg B/L per lb B/acre. 200-220 cm (78.7 to 86.6 inches)/year. Near Glasgow Scotland with an average temperature of about 10°C or 50°F (https://www.yr.no/place/United_Kingdom/Scotland/Glasgow/statistics.html). Peat soil (most similar to clay SERA 2007a, Table 2, p. 78). Site is closest to Wet/Temperate for GLEAMS-Driver sites. See Section 3.2.3.4.5 for a more detailed discussion.

See Section 3.2.3.4 for discussion.

Table 14: WCRs in surface water used in this risk assessment

	Peak WCR[1]	Longer-term WCR[1]
Central	0.041	0.018
Lower	0.0000000012	0.0000000006
Upper	0.43	0.23

[1] WCR (Water contamination rates) – concentrations in units of mg a.i./L expected at an application rate of 1 lb a.i./acre for a small pond. Units of mg a.i./L are used in the EXCEL workbook that accompanies this risk assessment. Note that the central estimate is taken as the arithmetic average of the average for each soil type. The lower bound is taken as the lowest value of the lower bounds across soil types. The upper bound is taken as the highest value of the upper bound across soil types. See Table 13 for a summary of the values. See Appendix 9 for details by sites and soil types – i.e., Table A9-7 for peak values and Table A9-10 for longer-term averages.

See Section 3.2.3.4.6 for discussion

Table 15: Summary of toxicity values used in human health risk assessment

Acute – single exposure

Element	Derivation of RfD
EPA Document	U.S. EPA/OPP/HED 2015a, p. 11
Study	MRID 40692303
NOAEL Dose	350 mg B/kg bw
LOAEL Dose	≥350 mg B/kg bw
LOAEL Endpoint(s)	Clinical signs of toxicity and mortality
Species, sex	Rats, M/F
Uncertainty Factor/MOE	100
Equivalent RfD	3.5 mg/kg bw

Chronic exposures

Element	Derivation of RfD
EPA Document	U.S. EPA/OPP/HED 2015a, p. 11
Study	Weir and Fisher 1972, MRID 40692310
NOAEL Dose	8.8 mg B/kg bw/day
LOAEL Dose	32 mg B/kg bw/day
LOAEL Endpoint(s)	Testicular atrophy. Reproductive effects.
Species, sex	Dogs
Uncertainty Factor/MOE	100
Equivalent RfD	0.088 mg/kg bw/day

See Section 3.3 for discussion

Table 16: Summary of human health toxicity values

Type of Value	Equivalent RfD (mg B/kg bw)	Species, Uncertainty Factor NOAEL LOAEL	Study	Derived by
Short-term Oral				
Minimal Risk Level (1-14 days)	0.2	Rats, UF: 100 NOAEL: 22 mg B/kg bw LOAEL: 44 mg B/kg bw	Price et al. 1996b	ATSDR 2010, p. 17
10-Day Health Advisory[1]	0.25	Rats, UF: 100 NOAEL: 25 mg B/kg bw LOAEL: 50 mg B/kg bw	Lee et al. 1978	U.S. EPA/OW 2008, p. 28
Acute Incidental	3.5	Rats, UF: 100 NOAEL: 350 mg B/kg bw LOAELs: ≥439 mg B/kg bw	MRID 40692303	U.S. EPA/OPP/HED 2015a, p. 11
Longer-term Oral				
Incidental Intermediate oral (1-6 months)	0.088	Dog, UF: 100 NOAEL: 8.8 mg B/kg bw/d LOAEL: 32 mg B/kg bw/d	Weir and Fisher 1972, MRID 40692310	U.S. EPA/OPP/HED 2015a, p. 11 [3]
Chronic Health Advisory for Adults[1]	0.156	Rats, UF: 66 BMD: 10.3 mg B/kg bw/d	Allen et al. 1996 [2]	U.S. EPA/OW 2008, p. 30
Chronic Health Advisory for Children[1]	0.175	Rats, UF: 100 NOAEL: 17.5 mg B/kg bw/d LOAEL: 58.5 mg B/kg bw/d	Weir and Fisher 1972	U.S. EPA/OW 2008, p. 30
Tolerable Daily Intake	0.16	Rats, UF: 60 NOAEL: 9.6 mg/kg bw LOAEL: 13.7 mg/kg bw	Price et al. 1996a	WHO 1998 (Drinking Water)
Chronic RfD	0.2	Rats, UF: 66 BMD: 10.3 mg B/kg bw/d	Allen et al. 1996 [2]	U.S. EPA/NCEA 2004
Tolerable Upper Intake Level	0.3	Rats, UF: 30 NOAEL: 9.6 mg/kg bw LOAEL: 13.7 mg/kg bw	Price et al. 1996a	Institute of Medicine 2001, p.519
Tolerable Daily Intake	0.4	Rats, UF: ≈25 [$10^{(0.5+0.9)}$] NOAEL: 9.6 mg/kg bw LOAEL: 13.7 mg/kg bw	Price et al. 1996a	IPCS/WHO 1998 (Health Criteria)
Inhalation				
Minimal Risk Level [4]	0.1	Humans, UF: 3 NOAEL: 0.8 mg B/m^3 LOAEL: 1.5 mg B/m^3	Cain et al. 2004, 2008	ATSDR 2010

[1] The Health Advisory is given as a concentration in water for a 10 kg child. The values in this table simply reflect the NOAEL and the uncertainty factor rounded to 3 significant digits.

[2] Benchmark dose analysis by Allen et al. 1996 using data from Heindel et al. (1992) and Price et al. (1996a). See text for discussion.

[3] As summarized in U.S. EPA/NCEA (2004), this had been the early (1989) chronic RfD entered into IRIS.

[4] The MRL is given as 0.3 mg B/m^3. Under the assumption that an 80 kg male breathes 22.8 m^3/day (U.S. EPA/NCEA 2011, p. 6-64) and 100% absorption (U.S. EPA/OPP/HED 2015a, p. 9), the MRL corresponds to a dose of about 0.1 mg B/kg bw [0.3 mg B/m^3 x 22.8 m^3/day ÷ 80 kg ≈ 0.097714 mg B/kg bw].

Note: Typical background human exposure is about 0.01 to 0.03 mg/kg bw/day. See Section 3.2 for discussion.

See Section 3.3 for discussion.

Table 17: Terrestrial Nontarget Animals Used in Ecological Risk Assessment

MAMMALS [1]

Animal	Representative Species	W[4]	Food Consumption[5]	Water Consumption
Small mammal	Mice	20	$2.514\ W^{0.507}$ [Eq 3-48]	$0.099\ W^{0.9}$ [Eq 3-17]
Larger mammal	Squirrels	400	$2.514\ W^{0.507}$ [Eq 3-48]	$0.099\ W^{0.9}$ [Eq 3-17]
Canid	Fox	5,000	$0.6167\ W^{0.862}$ [Eq 3-47]	$0.099\ W^{0.9}$ [Eq 3-17]
Large Herbivorous Mammal	Deer	70,000	$1.518\ W^{0.73}$ [Eq 3-46]	$0.099\ W^{0.9}$ [Eq 3-17]
Large Carnivorous Mammal	Bear	70,000	$0.6167\ W^{0.862}$ [Eq 3-47]	$0.099\ W^{0.9}$ [Eq 3-17]

BIRDS [2]

Animal	Representative Species	W[4]	Food Consumption[5]	Water Consumption
Small bird	Passerines	10	$2.123\ W^{0.749}$ [Eq 3-36]	$0.059\ W^{0.67}$ [Eq 3-15]
Predatory bird	Owls	640	$1.146\ W^{0.749}$ [Eq 3-37]	$0.059\ W^{0.67}$ [Eq 3-15]
Piscivorous bird	Herons	2,400	$1.916\ W^{0.704}$ [Eq 3-38]	$0.059\ W^{0.67}$ [Eq 3-15]
Large herbivorous bird	Geese	4,000	$1.146\ W^{0.749}$ [Eq 3-37]	$0.059\ W^{0.67}$ [Eq 3-15]

INVERTEBRATES [3]

Animal	Representative Species	W[4]	Food Consumption[5]
Honey bee [7]	*Apis mellifera*	0.000116	≈2 (1.2 to 4)[6]
Herbivorous Insects	Various	Not used	1.3 (0.6 to 2.2)

[1] Sources: Reid 2006; U.S. EPA/ORD 1993.
[2] Sources: Sibley 2000; Dunning 1993; U.S. EPA/ORD 1993.
[3] Sources: Humphrey and Dykes 2008; Reichle et al. 1973; Winston 1987
[4] Body weight in grams.
[5] For vertebrates, based on allometric relationships estimating field metabolic rates in kcal/day for rodents (omnivores), herbivores, and non-herbivores. For mammals and birds, the estimates are based on Nagy (1987) as adapted by U.S. EPA/ORD (1993). The equation numbers refer to U.S. EPA/ORD (1993). See the following table for estimates of caloric content of food items. For herbivorous insects, consumption estimates are based on fractions of body weight (g food consumed/g bw) from the references in Note 3.
[6] For honeybees, food consumption based on activity and caloric requirements. Used only when estimates of concentrations in nectar and/or pollen can be made, which is not the case in the current risk assessment.
[7] A surface area of 1.42 cm2 is used for the direct spray scenario of the honey bee. This value is based on the algorithms suggested by Humphrey and Dykes (2008) for a bee with a body length of 1.44 cm.

See data on food commodities in following table.
See Sections 4.2.2 and 4.2.3.2 for discussion.

Table 18: Summary of toxicity values used in ecological risk assessment

Group/Duration	Organism	Endpoint	Toxicity Value (all in units of boron)	Reference
Terrestrial Animals				
Acute				
Mammals (including canids)		Rat NOAEL	350 mg B/kg bw	Section 4.3.2.1.
Birds		Quail NOAEL (gavage)	113 mg B/kg bw	Section 4.3.2.2
Honey Bee (contact)		NOAEL (mortality)	540 mg B/kg bw	Section 4.3.2.4.2
Longer-term				
Mammals		NOAEL (dogs)	8.8 mg B/kg bw	Section 4.3.2.1
Bird		NOAEL (mallards)	3.7 mg B/kg bw	Section 4.3.2.2.
Terrestrial Plants				
Soil	Sensitive	Monocots	0.11 lb B/acre	Section 4.3.2.5
	Tolerant	Dicots	>0.87 lb B/acre	Section 4.3.2.5
Foliar	Sensitive	Note determined		Section 4.3.2.5
	Tolerant	NOAEL, monocots and dicots	≥0.03 lb B/acre	Section 4.3.2.5
Aquatic Animals				
Acute				
Amphibians	Sensitive	African clawed frog (Fort et al. 1998)	5.0 mg B/L	Section 4.3.3.2
	Tolerant	Use chronic value	25 mg B/L	
Fish	Sensitive	Fathead, LC_{50} ÷ 20	3.53 mg B/L	Section 4.3.3.1
	Tolerant	Trout, NOAEC (mortality)	192 mg B/L	
Invertebrates	Sensitive	Shrimp LC_{50} ÷ 20	0.7 mg B/L	Section 4.3.3.3
	Tolerant	Chironomus sp., NOAEC	10 mg B/L	
Longer-term				
Amphibians	Sensitive	African clawed frog (Fort et al. 2001)	1.75 mg B/L	Section 4.3.3.2
	Tolerant	LC_1 (Fowler's Toad)	25 mg B/L	
Fish	Sensitive	Catfish, LC_{50} ÷ 20	1.1 mg B/L	Section 4.3.3.1
	Tolerant	Fathead minnow, NOAEC	7.4 mg B/L	
Invertebrates	Sensitive	Use acute value	0.7 mg B/L	Section 4.3.3.3
	Tolerant	Use acute value	10 mg B/L	
Aquatic Plants				
Algae	Sensitive	*Anabaena flosaquae*, NOAEC	1.6 mg B/L	Section 4.3.3.4
	Tolerant	*Skeletonema costatum*, NOAEC	47.1 mg B/L	Section 4.3.3.4
Macrophytes	Sensitive	*Phragmites australis*, NOAEC	4 mg B/L	Section 4.3.3.4
	Tolerant	*Lemna gibba*, NOAEC	11 mg B/L	Section 4.3.3.4

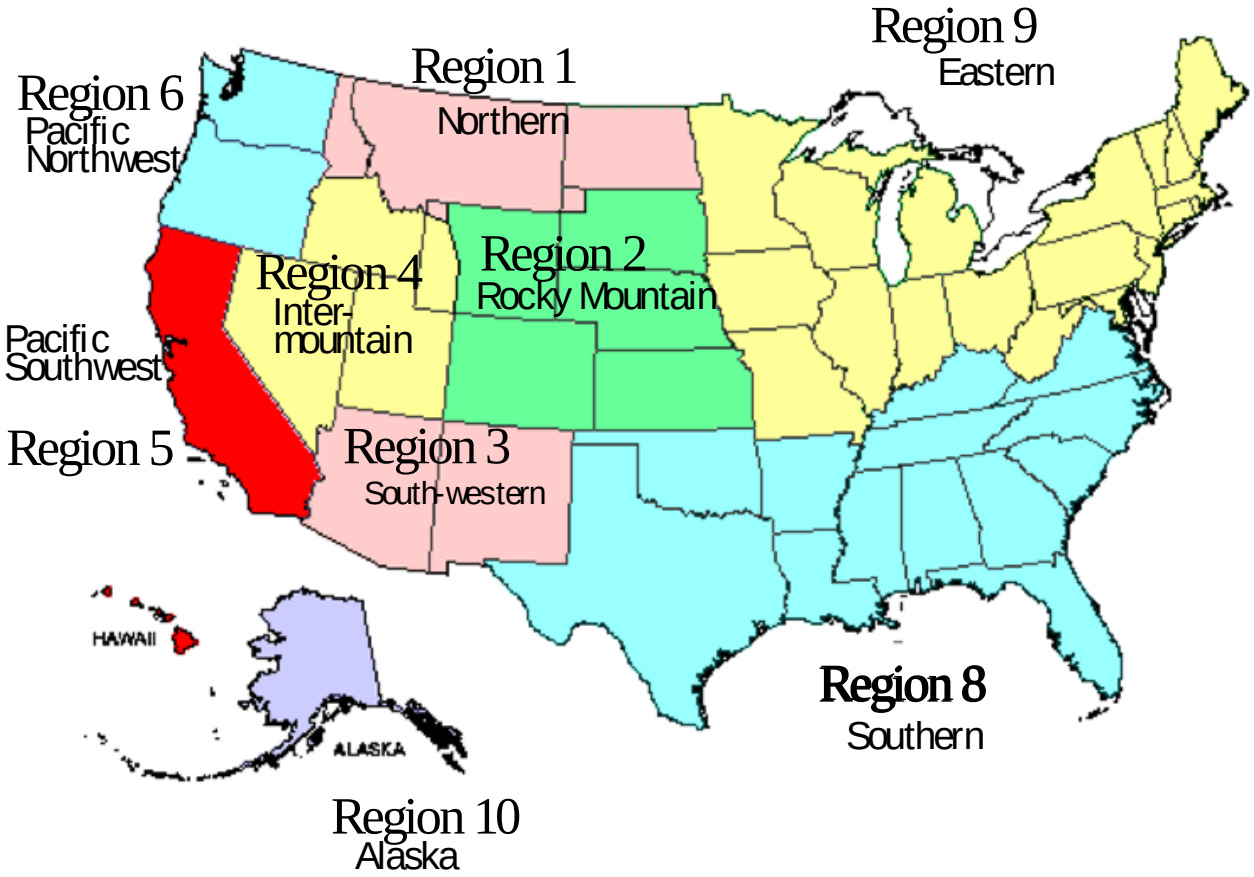


Figure 1: Forest Service Regions

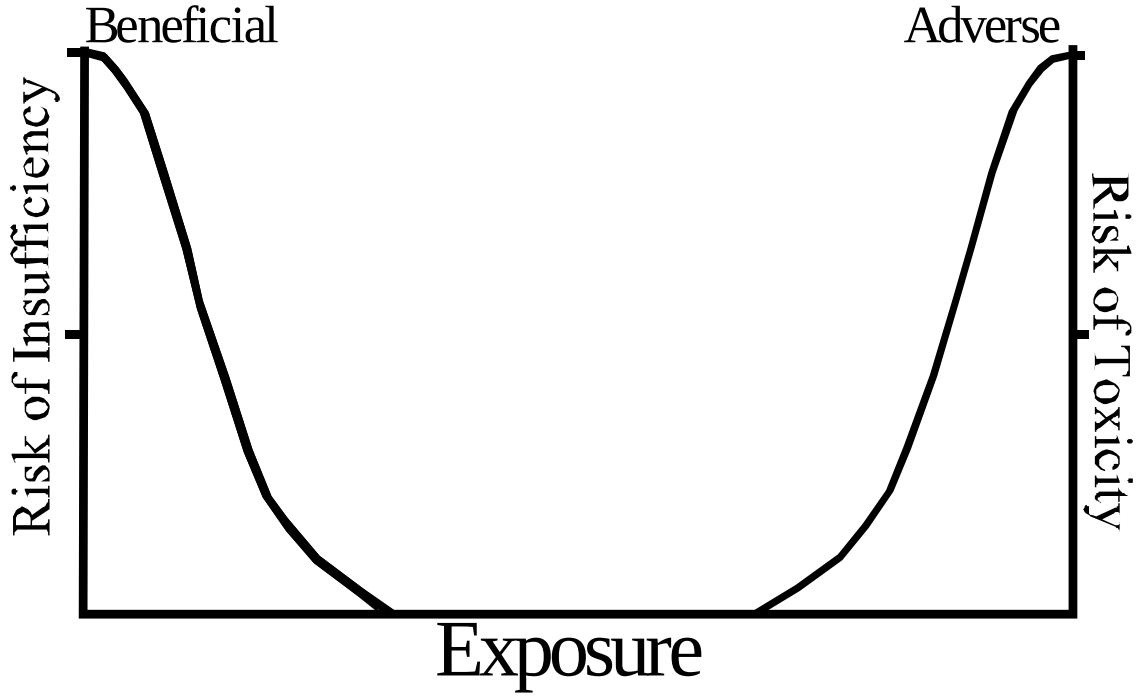


Figure 2: Range of Deficiency, Optimal, and Toxic Doses

Modified from Institute of Medicine, 2001, Figure 1-1

Appendix 1: Toxicity to mammals.

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Table A1-1: Acute Oral Toxicity

Species	Compound	Response	Reference
Gavage			
Dogs	Boric acid	LD_{50} >631 mg/kg bw [≈>110 mg B/kg bw] Category III	U.S. EPA/ OPP/HED 2006a citing Keller, 1962 MRID 00064208
Dogs	Borax acid	LD_{50} >974 mg/kg bw [≈>166 mg B/kg bw] Category III	U.S. EPA/ OPP/HED 2006a citing Keller, 1962 MRID 40692304
Dogs	Borax (1.54-6.51 g borax/kg bw or 0.174-0.736 g B/kg) Boric acid (1.0-3.98 g boric acid/kg or 0.175-0.697 g B/kg) Capsule administration 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 vomiting within 1 hour of dosing.	Weir and Fisher 1972 This study appears to identical to MRIDs 00064208 and 40692304 as summarized by U.S. EPA/ OPP/HED 2006. See previous entries.
Rats	Boric Acid	LD_{50} values Males = 3450 mg/kg (2950-4040 mg/kg) ≈604 (516-707) mg B/kg bw Females = 4080 mg/kg (3640-4560 mg/kg) ≈714 (637-798) mg B/kg bw Category III	U.S. EPA/ OPP/HED 2006a, 2015a MRID 00006719

Species	Compound	Response	Reference
Rats	Borax	LD_{50} values Males = 4550 mg/kg (4140-5010 mg/kg) ≈514 (468-566) mg B/kg bw Females = 4980 mg/kg (4310-5760 mg/kg) ≈563 (487-650) mg B/kg bw Category III Clinical Signs: depression, labored/rapid breathing, diarrhea, red crusts on eye at doses ≥439 mg B/kg (HED 2015a, p. 9). NOAEL: 350 mg B/kg bw	U.S. EPA/ OPP/HED 2006a, 2015a MRID 40692303 **Working Note: NOAEL of 350 mg B/kg bw with UF of 100 used by HED 2015a, p. 11 for functional acute RfD.**
Rats	DOT	LD_{50}: 2,550 mg/kg bw ≈535.5 mg B/kg bw	European Commission 2009b; Nisus 2009 MSDS for Cellu-Treat
Rats, Sprague-Dawley (SD) and Long-Evans (LE)	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 This study appears to identical to MRIDs 00006719 and 4069230 as summarized by U.S. EPA/ OPP/HED 2006. See previous entries.
I.P.			
Mice, CD-1 male, 20-25 g, 3 per group	Boric Acid Intraperitoneal Doses: 0, 10, 100, 1000 mg/kg bw. B equivalent doses: 0, 1.75, 17.5, 175 mg/kg bw. Observations at 24 hours.	24-hour LD_{50}: 2150 mg/kg bw (376 mg B/kg bw) No tissue pathology.	Soriano-Ursua et al. 2014
Testes			
Rats, males, Sprague-Dawley	Borax Gavage oral dose: 45, 150, 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 1976

Species	Compound	Response	Reference
Rats, Sprague-Dawley, male, 6 rats per group	Boric acid Gavage Doses: 0 or 2000 mg/kg bw B Equiv: 0, 350 mg B/kg bw Sacrificed on 2, 14, 28, and 57 DAT	No overt signs of toxicity. Transient weight loss (Days 2-14). Slight but significant decrease in absolute testes weights on Day 2 and Day 14. Marginal but significant decrease in absolute epididymis weight on Day 14. Significant increase in prostate on Days 28 and 57 (Table 1 of paper). Transient changes in sperm morphology on Days 2, 14, and 28 (Tables 2 and 3).	Linder 1990
Rats, Sprague-Dawley, male, 8 per dose	Boric acid Gavage Doses: 0, 250, 500, 1000, or 2000 mg BA/kg. B equivalent doses: 0, 43.75, 87.5, 175, and 350 mg B/kg bw. Sacrificed on 14 DAT	No overt signs of toxicity. No changes in organ weights (Table 1 of study). At 1000 and 2000 mg BA/kg bw, Decreased sperm counts (Table 2) and abnormal sperm morphology (Table 3). No significant changes in luteinizing hormone (LH), follicle stimulating hormone (FSH), thyroid-stimulating hormone (TSH), and prolactin (Prl) on Day 14.	Linder 1990

See Section 3.1.4 for general discussion.

Table A1-2: Subchronic and Chronic Toxicity Studies

Note: Table organized by duration (subchronic/chronic), species, and then citation.

Organism	Agent/Exposure	Response	Reference
Subchronic			
Dogs	Dietary concentrations of borax (sodium tetraborate decahydrate): 0, 0.0154%, 0.154%, and 1.54% B. 90-days According to U.S. EPA/OPP/HED 2006a: Equivalent Doses: 0, 0.34/0.25, 4.1/2.6 or 32/23 [M/F] mg/kg/day boron	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. EPA/OPP/HED 2006a NOAEL = 4.1mg B/kg/day M/2.6 mg/kg/day F LOAEL = 32 mg B/kg/day M/23 mg/kg/day F, based on decreases in HCT/hemoglobin, testicular atrophy, decreases testes weight and increased hemosiderin pigment in spleen, liver, kidneys.	U.S. EPA/OPP/ HED 2006a Paynter 1963 MRID 40692307
Dogs (5M/5F)	Borax and Boric Acid Dietary concentrations in food of 17.5, 175 and 1750 ppm boron equivalents 90 days	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
Rats	Borax or Boric Acid: 1 g/kg borax and boric acid B Equiv.: 175 mg B/kg bw Duration: 1-3 weeks Route: 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. Working Note: Consistent to general data on inhibition of proliferation.	Dani et al. 1971

Organism	Agent/Exposure	Response	Reference
Rats, males, Sprague-Dawley	Borax Drinking Water: 0, 0.3, 1 and 6 mg B/L. Duration: 90 days with additional observations at 30 and 60 days. Working Note: 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). Authors state that treatment with borax had no effect on body weight, or weight of testis, prostate or seminal vesicles. Plasma levels of FSH and LH unaffected by treatment No effect in fertility at any dose level	Dixon 1976
Rats, Wistar	Borax Dietary: 2000 ppm borax, 350 ppm B Duration: 16 days Observations from 2 to 28 days	Nuclear and cytoplasmic lesions of the thymus apparent by electron microscopy. Many macrophages containing dead cells were present in the thymus.	HSDB 2014 citing Sylvain et al. 1998
Rats, Sprague Dawley male (200–350g)	Boric acid Dietary Concentration: 6.4 mg/kg diet (normal chow) or 100 mg B/kg diet (boron supplemented) Duration: 4 weeks	Decreased in DNA damage and associated measures of lipid peroxidation. Enhancement of antioxidant defense mechanisms. Consistent with large body of literature on protective effects of boron. See Sections 3.1.2 and 3.1.16 of main body of the current risk assessment.	Ince et al. 2010 Turkey
Rats	Boric acid Dietary Concentration: 9000 ppm B Equivalent: ≈68 mg B/kg bw/day Duration: 7 days	No concentration in testes, brain, or hypothalamic region (Figure 1).	Ku and Chapin 1994
Rats, Sprague Dawley male (200–350g)	Boric acid and Borax Dietary Concentration: 6.4 mg/kg diet (normal chow) or 100 mg B/kg diet (boron supplemented) Duration: 4 weeks	Decreased leptin, insulin, and glucose levels, whereas increased T_3 and carnitine levels in plasma. Borax had a greater effect on hormonal status than boric acid.	Kucukkurt et al. 2015 Turkey Same group as Ince et al. 2010

Organism	Agent/Exposure	Response	Reference
Rats, Wistar, male, 6-8 weeks old, 190.3 to 226 g.	Boric acid Gavage Doses: 125, 250, and 500 mg/kg bw. B Equivalents: 0, 21.9, 43.75, 87.5 mg B/kg bw/day Durations: 2 weeks and 4 weeks.	No overt signs of toxicity. Focus on testicular pathology and sperm. High Dose: Testes pathology (degeneration and necrotic germ cells). Decreased spermatogonia and stage VII spermatids. Mid Dose: Mild pathology (exfoliated germ cells/debris) in a few rats. Low Dose: Mild pathology of testes (exfoliated germ cells). More severe pathology at 4 weeks relative to 2 weeks. At 2 weeks, no effects on sperm motility. At 4 week, decreases in sperm motility at mid and high dose (Table 2).	Kudo et al. 2000 Japan
Rats, male	Borax Dietary Concentrations: 0, 500, 1000, and 2000 ppm boron. Duration: 60 days with additional observations at 30 days. U.S. EPA/OW 2008 gives estimated doses of 0, 25, 50, and 100 mg B/kg/day based on an assumed food factor of 0.05 kg food/kg bw.	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.	Lee et al. 1978 **Working Note: Used by U.S. EPA/OW (2008, p.30)as basis for 10-health advisory.**

Organism	Agent/Exposure	Response	Reference
Rats, Sprague-Dawley, 230-340 g,	Boric Acid Doses: 0, 100, 275, and 400 mg BA/kg bw/day B Equivalents: 17.5, 48, and 70 mg b/kg bw. Duration: 45 days. Sacrifices at 10, 30, and 45 DAT, Standard Diet: <20 ppm B Working Note: Route appears to have been gavage but not explicitly stated in paper.	Dose-related increases of boron level in the kidneys (Table 2) 70 mg/kg: Slight but significant decrease in kidney weights on Days 10 and 30 but not on Day 45 (Table 1). Proximal renal tubule pathology (degeneration).	Sabuncuoglu et al. 2006
Rats	Borax Drinking water: 0, 150 and 300 mg B/L 70 days	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 bw/day)	Seal and Weeth 1980
Rats, Fischer-344, 120 days old.	Boric Acid Dietary Concentration: 0, 9000 ppm BA Doses: 348.3 mg BA/kg bw/day. B Equivalent Dose: 60.9525 mg B/kg bw/day. Duration: 28 days Observations: 4. 7, 10, 14, 2 I. and 28 days.	Decreased testosterone (60-78%) relative to controls (Figure 8A of paper). No significant difference in testosterone from controls following challenge with human chorionic gonadotropin hormone (Figure 8B of paper) or luteinizing hormone–releasing hormone (Figure 9 of paper). Testicular pathology (epithelial disorganization) and decreased in sperm number. No boron concentration in testicular tissue.	Treinen and Chapin 1991
Rats	Borax Dietary Conc.: 0, 0.0463, 0.154, 0.463, 1.54 or 4.63%. Equivalent Doses: 0, 4.0, 14, 42, 125 or 455 mg B/kg bw/day Duration: 90 days	NOAEL = 42 mg B/kg/day LOAEL = 125 mg B/kg/day based on decreased weight gain and food consumption, decreased testes and ovarian weights, testicular atrophy.	U.S. EPA/OPP HED 2006a MRID 40692305 with 40692306.
Rats, males	Borax Dietary Conc.: 0, 0.015, 0.0463, 0.154 or 0.463%. Equivalent Doses: 0, 1.3, 4.3, 13.1 or 41 mg B/kg bw/day Duration: 90 days	NOAEL: 41mg/kg/day (males only tested) LOAEL: Not determined.	U.S. EPA/OPP HED 2006a MRID 40692306

Organism	Agent/Exposure	Response	Reference
Rats, Sprague-Dawley	Borax Dietary concentrations: 52.5, 175, 525, 1750, and 5250 ppm boron equivalents. Estimated of daily doses in units of mg B/kg bw/day not available.	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 weight 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 weights 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).	Weir and Fisher 1972
Rats, Sprague-Dawley	Boric Acid Dietary concentrations: 52.5, 175, 525, 1750, and 5250 ppm boron equivalents.	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 weight decreased for males and females at 1750 and 5250 ppm.	Weir and Fisher 1972

Organism	Agent/Exposure	Response	Reference
Chronic			
Dogs, beagles (8M/8F); 8 dogs (4M/4F) in each treatment group	Borax (sodium tetraborate decahydrate), 100% Duration: 38 weeks, 25-day recovery period following 38-week treatment period. Average daily dose of test material was approximately 378 mg borax/kg/day (43 mg B /kg bw/day). Averages calculated from weekly compound consumption and boron equivalents consumption for each dog (displayed in Table 1 of fiche from SERA 2006 risk assessment).	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 which progressed 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.	Weir 1967 MRID 00005620 Appears to be same results as reported in Weir and Fisher 1972 Not covered in U.S. EPA/ OPP/HED 2006a
Dogs	Borax Dietary Concentrations: 0 or 1.03% Equivalent Doses: 0, 40/46 [M/F] mg B/kg/day Duration: 38 weeks (266 days)	NOAEL not established (<40/46 mg/kg/day) LOAEL = 40 mg/kg/day based on decreased body weight gain, testicular atrophy.	U.S. EPA/ OPP/HED 2006a MRID 40692308 Acceptable/non-guideline when considered together with MRIDs 40692307 and 40692309.

Organism	Agent/Exposure	Response	Reference
Dogs (4M and 4 F per dose group)	Borax and Boric Acid Dietary concentrations: 58, 117 and 350 ppm boron equivalents for 2 years (≈730 days). An additional group received 38-week exposure to 1170 ppm (boron equivalents) borax or boric acid.	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 Cited in U.S. EPA/ OPP/HED 2015a as MRID 40692310 **Working Note: The NOAEL of 8.8 mg B/kg bw/day is used in U.S. EPA/OPP/HED 2015a, p. 8 at the point of departure for the dose-response assessment for incidental oral and short- and intermediate-term inhalation exposures. UF of 100. This study had been used by U.S. EPA/OPP/HED 1993 to derive an RfD of 0.09 mg/kg bw.**
Mouse	Boric acid Dietary Concentrations: 0, 2500 or 5000 ppm BA Equivalent doses: 0, 48 or 96 mg B/kg bw/day. Duration: 2 years.	NOAEL = not established <48 mg/kg/day LOAEL = 48 mg B/kg/day based on splenic lymphoid depletion in males and pulmonary hemorrhage. Decreased body weights in males and females; testicular atrophy, interstitial cell atrophy at 5000 ppm (96 mg/kg/day). No evidence of carcinogenicity	Dieter et al. 1991 U.S. EPA/ OPP/HED 2006a MRID 41863101 Acceptable/Non-guideline
Rats	Borax Dietary Concentrations: 0, 0.130, 0.308, 1.030%. Equivalent doses: 0, 7.3, 17 or 58 mg B/kg/day. Duration: 2 years.	NOAEL = 17 mg/kg/day LOAEL = 58 mg/kg/day based on decreased body weight (observed by 3-4 weeks), slight anemia, testicular atrophy. No evidence of carcinogenicity. Working Note: This could be identical to Weir and Fisher 1972 summarized below. Slight changes in dose calculations are not uncommon in EPA reevaluations.	U.S. EPA/ OPP/HED 2006a MRID 40692309 citing Weir and Crews 1967 Acceptable/Non-guideline

Organism	Agent/Exposure	Response	Reference
Rats (Sprague-Dawley)	Borax and Boric Acid Dietary concentrations: 117, 350 and 1170 ppm boron equivalents 2 years 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. (17.5 mg B/kg bw) 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 (58.5 mg B/kg/day). No evidence of carcinogenesis in any treatment group.	Weir and Fisher 1972 Working Note: See notes on MRID 40692309 below.

See Section 3.1.5 for discussion.

Table A1-3: Reproductive and Developmental Studies

Species	Exposure	Response	Reference
Standard Developmental			
Mice	Boric Acid 0, 1000, 4500 or 9000 ppm boric acid in diet (for P1 mating only 0 and 1000 ppm groups). Equivalent to 0, 27, 111 or 221 mg B/kg/day.	Parental/Systemic NOAEL = 27 mg/kg/day LOAEL = 111 mg/kg/day based on decreased testicular weight, atrophy and degeneration of seminiferous tubules. Reproductive NOAEL = 27 mg/kg/day LOAEL = 111 mg/kg/day based on decreased fertility. Offspring NOAEL = 27 mg/kg/day LOAEL = 111 mg/kg/day based on decreased pup weight, decreased survival	U.S. EPA/OPP/ HED 2006a MRID 41589101 Acceptable/ Non-guideline
Mice	Boric Acid (BA) Dietary Concentrations: 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).	Maternal toxicity Mild renal lesions, increased kidney weight, decreased weight gain for all boron treatment groups. U.S. EPA/OPP/ HED 2006a reevaluation Maternal NOAEL not established <43 mg/kg/day LOAEL = 43 mg/kg/day based on renal tubular dilatation/regeneration. 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 79 mg 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 Also as summarized in U.S. EPA/OPP/ HED 2006a, p. 17 MRID 41725402 Acceptable/ Non-guideline

Species	Exposure	Response	Reference
Rabbits	Boric Acid: Gavage Doses: 0, 62.5, 125, or 250 mg BA/kg/day Equivalent B doses: 0, 10.9, 21.8, or 43.7 mg B/kg/ day) on gestational days 6-19. Working Note: The equivalent doses given by ATSDR (2010, p. 18) are: 0, 11, 22, and 44 mg B/kg bw.	Maternal toxicity At highest exposure level only, decreased food consumption and vaginal bleeding associated with pregnancy loss. U.S. EPA/OPP/HED 2006a reassessment. Maternal NOAEL = 22 mg/kg/day LOAEL = 44 mg/kg/day based on incr. intrauterine bleeding, decreased unadjusted weight gain during treatment (due to decreased gravid uterine weight). 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) U.S. EPA/OPP/HED 2006a reassessment. Developmental NOAEL = 22 mg/kg/day LOAEL = 44 mg/kg/day based on incr. mortality (resorptions, post-implantation loss), decreased fetal weight, intraventricular septal defect, enlarged aorta.	Price et al. 1996b [Open literature and EPA submission] U.S. EPA/OPP/ HED 2006a MRID 42164202 **Working Note: The NOAEL of 22 mg B/kg is used by ATSDR (2010, p. 18) in deriving the acute MRL.**
Rats, Wister (170-190 g)	Boric Acid Gavage: 0, 125, 250 or 500 mg BA/kg bw/day Equivalent B doses: 0, 21.9, 43.75, 87.5 mg B/kg bw/day Duration: 60 days	Increases in pre-implantation loss with a resulting decrease in the number of live fetuses/litter. 500 mg/kg bw/day: None of the male rats, treated could impregnate untreated females. Almost no viable sperm (Table 2 of paper) Testes weights significantly decreased at two highest doses (Table 1 of paper). Significant decrease in viable fetuses at 250 mg BA/kg bw/day group (Table 3). Significant decreases in Testosterone (ng/mL) at doses of 21.9, 43.75, 87.5 mg B/kg bw/day (Table 5 of paper)	El-Dakdoky and Abd El-Wahab 2013 Egypt

Species	Exposure	Response	Reference
Rats, Sprague-Dawley, Body weights: males 200–225 g, females 175–200 g.	Boric Acid Single Dose to females on GD 10: 0, 250 and 500 mg BA/kg Equivalent Dose: 0, 43.75, and 87.5 mg B/kg bw	No mortality or signs of toxicity in dams. Increased incidence of axial skeletal defects including a decrease in the total number of ribs and vertebra (Table 1 of study). Effects appear to be statistically significant at lowest dose (Table 3 of study). Maternal: NOAEL: 87.5 mg B/kg bw/day LOAEL: N.D. Fetal: NOAEL: N.D. LOAEL: 43.75 mg B/kg bw/day Additive effect with hyperthermia.	Harrouk et al. 2005 FDA/EPA joint effort
Rats	Boric acid Dietary Concentrations: 0, 0.1, 0.2, or 0.4% on Days 0-20. 0.8% on Days 6-15. Doses: 0, 78, 163, 330, and 539 mg BA/kg/day Equivalent doses: 0, 13.6, 28.5, 57.7, and 94.3 mg B/kg bw/day. U.S. EPA/OPP/HED 2006a gives equivalent doses as: 0, 14, 29 or 58, and 94 mg B/kg bw/day	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. U.S. EPA/OPP/HED 2006a: Maternal NOAEL = 29 mg/kg/day LOAEL = 58 mg/kg/day based on decrease in uncorrected bw gain secondary to decreased gravid uterine weights. 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). U.S. EPA/OPP/HED 2006a: Developmental NOAEL: <14 mg/kg/day Developmental LOAEL: 14 mg/kg/day based on slightly decreased fetal body weight. At 29 mg/kg/day, skeletal abnormalities observed. At 58 and 94 mg/kg/day, high incidence skeletal and visceral abnormalities, and mortality.	Heindel et al. 1992, 1994 Also as summarized in U.S. EPA/OPP/HED 2006a, p. 17 MRID 41725401 Acceptable/ Non-guideline **This study is used along with Price et al. 1996a by Allen et al. 1996 to derive the IRIS chronic RfD of 0.2 mg/kg bw/day (U.S. EPA/OPP/NCEA 2004).**

Species	Exposure	Response	Reference
Rats	Boric Acid Dietary Concentrations: 0, 0.025, 0.050, 0.075, 0.1, or 0.2% gestational days 0-20 Doses as Boric Acid: 18.6, 36.2, 55.1, 75.9, and 142.9 mg BA/kg/day Equivalent B doses: 3.3, 6.3, 9.6, 13.3, and 25 mg B/kg/ day)	Maternal toxicity: No maternal deaths or signs of toxicity in any boron treatment group. Only effect was Increased kidney weight in 0.2% group. NOAEL = 13.3 mg B/k/day. LOAEL = 25 mg B./kg /day U.S. EPA/OPP/HED 2005a reassessment Maternal NOAEL = 25 mg/kg/day LOAEL = not determined (slightly decreased gravid uterine weight considered secondary to fetal toxicity) 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 U.S. EPA/OPP/HED 2005a identical to above.	Price et al. 1996a [Open literature] Also summarized in U.S. EPA/OPP HED 2006a MRID 43340101 Acceptable/ Non-guideline **Working Note: The NOAEL of 9.6 mg B/kg bw used by Institute of Medicine 2001 to derive acceptable dose. UF of 30. Functional RfD of 0.3 mg B/kg bw/day. This study is also used along with Heindel et al. (1992) by Allen et al. 1996 to derive the IRIS chronic RfD of 0.2 mg/kg bw/day (U.S. EPA/OPP/NCEA 2004)**
Rats, Sprague-Dawley, 10 weeks old, 5 per dose	Boric Acid Initial Study Single Dose to females: 0, 350 and 500 mg BA/kg Equivalent Dose: 0, 61.25 and 87.5 mg B/kg bw Second Study Boric Acid Single Dose to females: 0, 40, 100, and 250 mg BA/kg bw Equivalent Dose: 0, 7, 17.5, and 43.75 mg B/kg bw.	No signs of toxicity or impact on body weights in dams. Delayed ossification and skeletal malformations. General and apparently dose-related decrease in fetal weights (5 to 23%). Increase in post-implantation losses. See Table 1 of study. Statistical significance not clear. Based on the % litters with malformations, effects appear to be significant at lowest dose and are clearly dose-related. Maternal: NOAEL: 87.5 mg B/kg bw/day. LOAEL: N.D. Fetal: NOAEL: N.D. LOAEL: 40 mg B/kg bw/day.	Wise and Winkelmann 2009

Species	Exposure	Response	Reference
Standard Reproduction			
Rats, Sprague-Dawley	Borax Dietary Concentrations: 0, 500, 1000, and 2000 ppm boron equivalents. Doses equivalent to: 45, 150 and 450 mg B/kg bw. Duration: 60 days	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. NOAEL = 45 mg B/kg/day LOAEL = 150 mg B/kg/day	Dixon et al. 1979 Working Note: Not reviewed in EPA/HED risk assessments. IPCS/WHO 1998 estimates the boron doses as 0, 25, 50, and 100 mg B/kg bw/day. The doses used in the current document are taken from Dixon et al. 1979, p. 54, column 2.

Species	Exposure	Response	Reference
Rats (albino)	Borax Dietary Concentrations: 0, 0.103, 0.308, and 1.030% in diet. B Equivalent Doses: Males: 0, 8.1, 25, and 82 mg B/kg bw. Females: 0, 9.2, 27, and 92 mg B/kg bw. Duration: 3 generations through the weaning of the second litter of the 3rd generation.	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. Maternal Effect: Evidence of decreased ovulation noted in females at highest dose. 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. U.S. EPA/OPP/HED 2006a assessment Parental/Systemic NOAEL = 25 mg/kg/day LOAEL = 82 mg/kg/day based on decreased body weight, testicular atrophy, decreased testes weight, decreased corpora lutea. Reproductive NOAEL = 25 mg/kg/day LOAEL = 82 mg/kg/day based on decreased fertility. Offspring NOAEL = 25 mg/kg/day LOAEL = 82 mg/kg/day based on decreased pup survival.	U.S. EPA/OPP/ HED 2006a, MRID 40692311 as summarized on p. 18. Appears to be same data as published in open literature by Wier and Fisher 1972, summarized below except for minor adjustments in estimated concentrations.
Rats	Borax and Boric Acid Dietary concentrations: 117, 350, and1170 ppm (boron equivalents) Duration: 14 weeks prior to mating. Diets continued through 3 generations.	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

Table A1-4: Skin Irritation and Sensitization Studies

Species	Exposure	Response	Reference
Skin Irritation			
Rabbit	Boric acid	1/6 erythema at 72 hours Category III	U.S. EPA/ OPP/HED 2006a, 2015a MRID 00106011
Rabbit and Guinea pig	Boric acid	Rabbit: Score of 1.7 Guinea Pig: 2.1 Scores <5: Not primary skin irritants	Roudabush et al. 1965
Rabbits (White New Zealand)	Borax Single dose of 0.5 g applied to shaved skin and occluded. Animals observed for 28, 52, and 76 hours after application.	No irritation. Working Note: U.S. EPA/OPP/HED 2006a, Table 4.1b, p. 15, and 2015a (Table 3.1b, p. 8) references this study as an eye irritation study. The citation to this study in the HED 2006a (p. 59) clearly indicates that the study involved dermal irritation.	Reagan 1985b MRID 43553203
Rabbit	Borax	Non-irritating Category IV	U.S. EPA/ OPP/HED 2006a, 2015a MRID 43553202
Rabbit and Guinea pig	Borax	Rabbit: Score of 2.0 Guinea Pig: 1.4 Scores <5: Not primary skin irritants	Roudabush et al. 1965
Skin Sensitization [1,2]			
Guinea pigs (10)	Borax (98%) 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

[1] U.S. EPA/OPP/HED 2006a (p. 15) indicates that a sensitization study for borax is not required.
[2] U.S. EPA/OPP/HED 2006a (p. 14) indicates that a sensitization study for boric acid is not required.

Table A1-5: Eye Irritation Studies

Species	Exposure	Response	Reference
Rabbits (6 White New Zealand)	Borax, 20 Mule Team 0.1 g 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
Rabbits	Borax	Corrosive. Category I	U.S. EPA/ OPP/HED 2006a, MRID 43553203 Working Note: The MRID cited by EPA (p. 15) is incorrect. As indicated on p. 59 of the EPA document, this MRID is a dermal study. The correct citation is MRID 43553202, summarized above.
Rabbits	Boric acid	Conjunctival irritation clearing by Day 4. Category III	U.S. EPA/ OPP/HED 2006 MRID 00064209

Table A1-6: Dermal Toxicity Studies

Species	Exposure	Response	Reference
Acute			
Rabbits (10 White New Zealand)	Borax Limit Dose: 2 g/kg Test substance removed after 2 hours. Animals observed for 15 days after application. No control group (normal for limit assay).	No mortalities. Clinical observations: anorexia, decreased activity, diarrhea, soft stools, and nasal discharge. Gross pathological examination revealed no significant findings.	Reagan 1985a MRID 43553200
Rabbit	Borax	LD_{50} >2 g/kg bw Category III	U.S. EPA/ OPP/HED 2006a, 2015a MRID 43553201 Working Note: This study identical to Reagan 1985a, summarized above, based on citation in HED 2006a, p. 58.
Rats (5M/5F)	Borax (100%) Limit Dose: 5000 mg/kg Exposure: 24 hours, shaved skin and occluded skin. Animals observed for 12 days after exposure. No control group (normal for limit assay).	No mortalities. LD_{50} > 5000 mg/kg bw. 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.	Wnorowski 1996 MRID 44048603
Rabbit	Boric acid	LD_{50} >2 g/kg bw Category III	U.S. EPA/ OPP/HED 2006a, 2015a MRID 00106011
Repeated Dose			
No studies identified			

Table A1-7: Inhalation Toxicity

Species	Exposure	Response	Reference
Acute			
Rats (5M/5F)	Borax Limit Exposure: 2 mg/L for 4 hours Measured concentration = 2.03 mg/L. Animals observed for 14 days after exposure.	No mortalities. 4-hour LC_{50} > 2.03 mg/L [>2,030 mg/m^3, >229 mg B/m^3]. 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. Category III	Wnorowski 1994a MRID 43500801 Also cited in U.S. EPA/ OPP/HED 2015a
Rats	Boric acid	LC_{50} >2.03 mg/L (no deaths) [>2,030 mg/m^3, >355 mg B/m^3] Category III	U.S. EPA/ OPP/HED 2015a MRID 43500701 Not cited in U.S. EPA/ OPP/HED 2006a
Rats	Boric acid	LC_{50}: >0.16 mg/L (no deaths) [>28 mg B/m^3] Category II	U.S. EPA/ OPP/HED 2006a MRID 00005592 Not cited in U.S. EPA/ OPP/HED 2015a
Human volunteers, exercising	Sodium borate dusts Sodium Borate: 0, 6.8, 10.3, 16, and 30.7 mg/m^3. B Equivalent concentrations: 0, 1.03, 1.56, 2.4, 4.6 mg B/m^3 Duration: Up to 47 minutes. Working Note: B equivalents at 0.151 per ATSDR 2010, p. 10.	Throat, nasal, and eye irritation. (Fig. 3C). See composite note concerning ATSDR (2010) analysis under Cain et al. 2008.	Cain et al. 2004

Species	Exposure	Response	Reference
Human volunteers, exercising, n=12	Boric acid Concentrations: 0, 2.5, 5, and 10 mg/m^3. B Equivalent concentrations: 0, 0.44, 0.875, and 1.75 mg B/m^3 Duration: Up to 47 minutes.	Throat, nasal, and eye irritation. (Fig. 2). Nasal irritation most pronounced followed by throat and eye irritation. ATSDR 2010 Assessment NOAEL: 0.8 mg B/m^3 [boric acid] LOAEL: 1.5 mg B/m^3 [as sodium borate] based on increased nasal secretions. Considered as minimal adverse effect. Working Note: Basis for ATSDR (2010, p. 13) acute (14 days or less) MRL of 0.3 mg/m^3 using an uncertainty factor of 3 for human variability. Note the rounding differences between this RA and ATSDR 2010. Incidental.	Cain et al. 2008
Longer-term			
Rats	Boron oxide (conversion factor of 0.155 from ATSDR 2010, p. 10) Concentration/Duration: 77 mg/ m^3 x 24 weeks 175 mg/m^3 x 12 weeks 470 mg/m^3 x 10 weeks Above from Table 1 of Wilding et al. 1959 All 6 hours/day, 5 days/week B equivalents: 11.6 mg/ m^3 x 24 weeks 26.4 mg/m^3 x 12 weeks 70.97 mg/m^3 x 10 weeks	No adverse systemic effects based on clinical chemistries and pathology. High Exposure Group: Slight red exudate from the nose. Singes of local irritation. Decreased body weight gain. Low Exposure: No effect on body weight. NOAEL: 12 mg B/m^3 for 24 weeks (ATSDR 2010, p. 28) LOAEL: 27 mg B/m^3 for 12 weeks Working Note: Very minor rounding differences with ATSDR 2010.	Wilding et al. 1959
Dogs	Boron oxide All exposures 6 hours/day, 5 days/week Concentration: 57 mg m^3 for 23 weeks B-equivalents: 8.6 mg/ m^3 x 24 weeks	No adverse systemic effects based on clinical chemistries and pathology.	Wilding et al. 1959

[1] U.S. EPA/OPP/HED 2006a (p. 15) indicates that an inhalation study for borax is not required.

Table A1-8: Mutagenicity Screening Studies

Species	Exposure	Response	Reference
Mouse *in vitro* lymphoma forward gene mutation assay	boric acid 1200-5000 µg/mL +/- S9 (liver microsomes)	Negative for induction of mutagenic response in two independently performed mouse L5178Y cell lymphoma forward mutation assays. Marginal cytotoxicity at 3500-5000 µg/mL	U.S. EPA/OPP/ HED 2006a MRID 42038902 Acceptable/ Guideline
Salmonella typhimurium reverse gene mutation assay	Boric Acid 10-2500 µg/plate	Negative for induction of mutagenic response in strains TA1535, TA1537, TA1538, TA98 or TA100 in the presence or absence of S9 up to 2500 µg/plate. No cytotoxicity was observed.	U.S. EPA/OPP/ HED 2006a MRID 42038901 Acceptable/ Guideline
Rat liver *in vitro* unscheduled DNA synthesis	Boric Acid 5-5000 µg/mL boric acid	Inconclusive study as presented in the report. Submission of the primary data (cytoplasmic and gross nuclear grain counts) may provide sufficient information to interpret results and allow upgrading of study to acceptable.	U.S. EPA/OPP/ HED 2006a MRID 42038903 Unacceptable/ Guideline (Upgradeable)

Appendix 2: Toxicity to birds

Table A2-1: Acute Oral/Gavage Toxicity to Birds 166
Table A2-2: Acute Dietary Toxicity to Birds 167
Table A2-3: Reproductive and Subchronic Toxicity to Birds 168

Table A2-1: Acute Oral/Gavage Toxicity to Birds

Species	Exposure	Response	Reference
Bobwhite quail, *Colinus virginianus*, 10 birds/treatment, age, 5 months.	Borax (sodium tetraborate decahyrate, 100% a.i.) Single oral doses (0, 398, 631, 1000, 1590, and 2510 mg/kg bw) Boron Equivalent Doses: 0, 45, 72, 113, 180, and 284 mg B/kg bw Observation Period: 14 days	LD_{50} > 2510 mg borax/kg (equivalent to > 284 mg B/kg). Death in one bird at 2510 mg borax/kg group (285 mg B/kg bw). 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 borax/kg treatment groups – i.e., 180 and 284 mg B/kg bw. NOAEL: 113 mg B/kg bw *Practically nontoxic* on a technical grade basis.	Fink et al. 1982a, MRID 00100657 Also summarized in U.S. EPA/ OPP/EFED 2015a. Acceptable Used in current Forest Service risk assessment as acute NOAEL.
Bobwhite quail, *Colinus virginianus*, 5 months, 10 birds/treatment	Disodium Octaborate Tetrahydrate ($Na_2B_8O_3 \cdot 4H_20$) 99.4% a.i. Oral, single dose	No mortalities observed 14-day LD_{50} >284 mg B/kg 14-day LD_{50} >2510 mg DOT/kg bw TGAI: *Practically nontoxic*	U.S. EPA/OPP/EFED 2015 MRID 00107904 Acceptable
Mallard duck, *Anas platyrhynchos*	Boric acid (H_3BO) 99.9% a.i. Oral, single dose	No mortalities observed LD_{50} >2150 BA/kg LD_{50} >376 B/kg *B*: *Moderately toxic* Technical: *Practically non-toxic*	U.S. EPA/OPP/EFED 2015a ACC 254367 Acceptable

Table A2-2: Acute Dietary Toxicity to Birds

Species	Exposure	Response	Reference
Standard Dietary			
Bobwhite quail , *Colinus virginianus* (10-15 days old)	Borax (sodium tetraborate decahyrate (100% a.i.) 5-Day dietary exposure. Borax: 0, 312.5, 625, 1250, 2500, 5000 ppm (mg Borax/kg diet). Boron Equivalents: 0, 35, 71, 141, 282, and 565 mg B/kg diet. Observation Period: 8 days (3 day recovery) Average body weight: 43 g Average food: consumption: 10.4 g/bird/day Working Note: Food factor: 0.24 [136 mg B/kg bw ÷ 565 mg B/kg food].	LC_{50} > 5000 ppm borax (equivalent to >565 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. NOAEL: 5000 ppm group: 565 mg B/kg food x 0.0104 kg food ÷ 0.043 kg bw ≈ 136 mg B/kg bw.	Reinart and Fletcher 1977 MRID 00149195 Working Note: This study is cited but not discussed or described in U.S. EPA/OPP/EFED 2015a.
LD_{50}/ft^2 studies			
Chicken (NOS), 20 birds/group	Boric acid (H_3BO) 100% a.i Litter treated with boric acid	No Mortalities 14-day LC_{50} >7.257 kg BA/ft^2 14-day LC_{50} >1.27 B kg/ft^2	U.S. EPA/OPP/EFED 2015a MRID 41017501 MRID 41086601
Turkey (NOS), 20 birds/group	Boric acid (H_3BO) 100% a.i Litter treated with boric acid	No Mortalities 14-day LC_{50} >7.257 kg BA/ft^2 14-day LC_{50} >1.27 kg B/ft^2	U.S. EPA/OPP/EFED 2015a MRID 41017501 MRID 41086601

[1] Additional assays on formulations containing borax and 2-chloro-N-(hydroxymethyl)acetamide are given in U.S. EPA/OPP/EFED 2015a, Table I16, but are not summarized above or relevant to current risk assessment.

Table A2-3: Reproductive and Subchronic Toxicity to Birds

Species	Exposure	Response	Reference[1]
Reproduction			
Bobwhite quail, *Colinus virginianus*, 20 weeks 4 days, 16 pairs/ dose level	Boric acid (H_3BO) 100% a.i.	NOAEL = 490 mg BA/kg diet LOAEL = 971 mg BA/kg diet NOAEL = 85.7 mg B/kg diet LOAEL = 170 mg B/kg diet Approximate mg/kg bw doses[1] NOAEL = 6 mg B/kg bw LOAEL = 12 mg B/kg bw Based on percent hatchlings/live embryos and male weight gain.	U.S. EPA/OPP/EFED 2015a MRID 49185901 Supplement/ Quantitative
Mallard duck, *Anas platyrhynchos*, 27-weeks-old, 16 pairs/dose level	Boric acid (H_3BO) 100% a.i. Working Note: Food factor of 0.085 [21.2 ÷ 249] is reasonably consistent with standard factor of 0.07 typically used in Forest Service risk assessments[1].	NOAEL = 249 mg BA/kg-diet LOAEL = 743 mg a.e./kg-diet ***(21.2 mg/kg bw daily dose estimated by EPA)*** NOAEL = 43.6 B/kg diet LOAEL = 130 B/kg diet Estimated mg/kg bw doses: NOAEL = 3.7 mg B/kg bw LOAEL = 11 mg B/kg diet based on food factor of 0.085. LOAEL Endpoints: Percent hatchlings/live embryos.	U.S. EPA/OPP/EFED 2015a MRID 49009801 Acceptable Working Note: Used by U.S. EPA/OPP/ EFED 2015a and current Forest Service risk assessment for risk characterization.
Mallard duck, *Anas platyrhynchos*	Boric acid Concentrations: 0, 30, 300 and 1000 ppm B Duration: 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 B. NOAEL = 300 ppm B LOAEL = 1000 ppm B <u>Adults</u> No effect of treatment on adult survival or egg fertility NOAEL >1000 ppm B Approximate Doses [1] : NOAEL: 21 mg B/kg bw LOAEL: 70 mg B/kg bw (hatchling growth and survival)	Smith and Anders 1989

Appendix 2: Toxicity to Birds (*continued*)

Species	Exposure	Response	Reference[1]
Broiler chickens	Borax Concentrations: 0 and 250 ppm B equivalents. Duration: 28 days (males and females) Approximate dose [1]: 17.5 mg B/kg bw	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 borax group. In exposed males, increase in number of damaged spermatozoa cells in boron-treated birds (approached statistical significance p<0.051)	Rossi et al. 1993
Other subchronic			
Mallard duck, *Anas platyrhynchos*, 1-day-old, 30/treatment group	Boron as boric acid powder (99% pure) mixed into commercial duck starter mash. Nominal boron concentrations: 0, 100, 400, or 1600 ppm. Measured Concentrations (based on boron): 13, 120, 430, or 1750 mg B/kg diet (reported on p. 336, top of column 2 of paper). Estimated Doses [1]: 0.9 (control), 8.4, 30, and 122 mg B/kg bw. Duration: 10 weeks	Highest dietary concentration (1600 ppm B) caused 10% mortality and decreased body weight in females (Table 1 of paper). Decreased hemoglobin at highest dose. Increase in hematocrit (F only) at highest dose. Increase (6%) in plasma calcium at highest dose. Increase in plasma triglycerides (21-42%, p<0.05) at all doses (Table 2 of paper). Increased B concentration in the brain to 25 times that of controls; elevated brain acetyl-cholinesterase activity and total ATPase activity (in males) and lowered protein concentration. No assay of depuration. Boron accumulated less in the liver than in brain, but caused an initial elevation of hepatic glutathione.	Hoffman et al. 1990

Appendix 2: Toxicity to Birds (*continued*)

Species	Exposure	Response	Reference[1]
Hens, Hyline Brown 98, 18-weeks-old, 32/treatment group	Boron Dietary Concentrations: 0, 5, 10, 50, 100, 200, or 400 mg B/kg diet Estimated doses: 0, 0.33, 0.67. 3.34, 6.7, 13, and 27 mg B/kg bw Duration: 8 weeks Working Note: Based on average body weight of 1700 g (Table 2 of paper) and average food consumption (Table 3), the average food factor (kg food/kg bw) is about 0.067. This is similar to food factors used for quail and mallards [1]. The dose conversions above are based on 0.067.	No differences in feed efficiency between groups observed. Egg shape index decreased ($p<0.05$) in all treatment groups at week 26. Average damaged egg ratio increased significantly ($p<0.01$) at 200 and 400 mg/kg B. Live weight ($p < 0:05$) and feed consumption ($p < 0:001$) were decreased significantly in the 400 mg/kg B supplemented group. Egg weight decreased significantly ($p < 0:001$), while egg production decreased slightly in the 400 mg/kg B supplemented group. NOAEL: 6.7 mg B/kg bw LOAEL: 13 mg B/kg bw based on damaged eggs.	Eren et al. 2004 [Turkey]
Hens, Lohmann Brown-Classic, 26-weeks-old, 4/treatment group	Basal diet supplemented with Boron Boric Acid Doses: 0, 60, 120, or 240 mg/kg food. Boron Equivalents: 0, 10.5, 21, and 42 mg B/kg food. Duration: 16 weeks Approximate dose [1]: 0, 0.74, 1.5, and 2.9 mg B/kg bw	No significant effects on specific gravity, eggshell breaking strength, eggshell weight and frequency of damaged eggs.	Olgun et al. 2012
Hens, Hyline Brown, 60-weeks-old	Basal diet supplemented with boric acid (H_3BO_3) 99.995% pure Boric Acid Doses: 0, 25, 50, or 100 mg/kg Boron Equivalents: 0, 4.3, 8.7, or 17.5 mg B/kg food. Duration: 75 days Approximate dose [1]: 0, 0.3, 0.6, and 1.2 mg B/kg bw	No significant effects on feed efficiency and egg production ($p>0.05$) BA supplemented diets resulted in better feed consumption, egg weight, decreased percentage of cracked eggs, and eggshell quality (i.e., thickness and breaking strength), relative to controls. BA supplemented diets also significantly ($p<0.01$) increased serum Mg levels.	Yeslibag and Eren 2008 [Turkey]

Appendix 2: Toxicity to Birds (*continued*)

Species	Exposure	Response	Reference[1]
Chickens, Ross-308 broiler, 1-day-old, males, 6/treatment group	Diluted boric acid (17.5% boron) used as a source of boron. Standard diet supplemented with 60 mg BA/kg diet [10.5 mg B/kg] during different rearing periods: T_1 – during 1st and 3rd weeks T_2 – during 3rd and 6th weeks T_3 – during whole experimental period Duration: 42 days	No negative effects on growth performance, serum cholesterol concentrations, or carcass characteristics; however, there was a significant ($p<0.001$) increase in calcium and phosphorus deposits in the tibia bone ash, especially in birds *supplemented for the finishing period*.	Yildiz et al. 2013 [Turkey]

[1] Dietary concentrations (ppm) converted to mg/kg bw doses using food consumption rates of 0.07 kg food/kg bw for reproduction studies in quail and mallards taken from SERA (2007b).

Appendix 3: Toxicity to Terrestrial Invertebrates.

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Table A3-1: Toxicity Studies in Bees

Species	Exposure	Response	Reference
Oral			
Apis mellifera, honey bee [Hymenoptera: Apidae]	Boric acid Concentration: 8.75 and 17.5 mg B/L syrup.	No effect on survival at lower dose. Fatal to about 50% at higher dose.	Eisler 1990 citing unpublished report from U.S. Borax and Chemical Corp.
Apis mellifera, honey bee worker, 1st instar larvae [Hymenoptera: Apidae]	Agent: Boric acid powder (Merck) incorporated into food. Concentrations in food: 1.0, 2.5, or 7.5 mg/g Duration: 6 days	Concentration-related decrease in median survival times: 3 days at 1 mg/g 2 days at 2.5 mg/g 1 day at 7.5 mg/g Treatment induced cell death in the midgut epithelium, which *probably leads to starvation*.	da Silva Cruz et al. 2010
Scaptotrigona postica, stingless bee Newly emerged workers (4-days-old) 25/group, 3 replicates [Hymenoptera: Apidae]	Agent: Boric acid Dietary Exposure: 0.75 µg boric acid/bee/day Duration: 10 days	Significant decrease in survival ($p<0.0001$), compared with controls, and 100% mortality in treated bees by day 10. Time to 50% mortality of about 7 days (Figure 1 of paper). Behavioral changes in treated bees included wing flapping and accelerated movement, compared with controls. Working Note: Taking the body weight of 30 mg for this species of bee (Thompson 2015), the estimated dose is 0.025 µg BA/mg bw or 25 mg BA/kg bw or 4.375 mg B/kg bw.	Ferreira et al. 2013
Contact (µg/organism)			
Apis mellifera, honey bee [Hymenoptera: Apidae]	Agent: Boric acid, NOS	No mortality LD_{50} >362.58 µg boric acid/bee (or 63 µg B/bee) Practically nontoxic Working Note: Taking a body weight of 116 mg for this species (Winston 1987, p. 54), the toxicity value is 0.543 µg/mg or 540 mg B/kg bw.	Atkins 1987 MRID 40269201 Acceptable U.S. EPA/OPP/ EFED 2015a

Note: ng/mg = µg/g = mg/kg

Table A3-2: Toxicity Studies in Other Insects

Species [Order: Family]	Exposure	Response	Reference
Blattodea			
Blattella germanica, German cockroach, adults, 10 colonies/treatment [Blattodea: Blattellidae]	Agent: Boric acid Concentration: 0.01, 0.1, or 0.2% in water. Reported concentrations equivalent to 100, 1000, and 2000 mg/L. Duration: 2 weeks	Sub-lethal concentration induced significantly elevated levels of a cockroach allergen as measured in excreted fecal pellets, compared with controls;	Zhang et al. 2005
lncisitermes snyderi and *Cryptotermes brevis*, drywood termites [Blattodea, Isoptera: Kalotermitidae]	Agent: Disodium octaborate tetrahydrate (DOT) Aqueous concentration: 100,000 a.i. mg/L Dust concentration: 980,000 a.i. ppm Duration: 4 or 8 weeks	None of the aqueous treatments yielded mortality or fecal pellet production that was significantly different from controls. Only 98% dust caused higher mortality than observed in controls at 8 weeks. Study indicates that DOT applied over an 8-week exposure duration is below toxicity thresholds and that DOT generally has a low toxicity to drywood termites.	Scheffrahn et al. 1997
Coleoptera			
Poecilus cupreus, carabid beetle, 3 males and 3 females/replicate [Coleoptera: Carabidae]	Agent: Boric acid, 99.8% LUFA 2.2 soil (organic matter=3.9%, texture=6% clay; 17% silt; 77% sand) Concentration: 3.16, 10.0, 31.6, 100, 316, 1000, or 3162 mg a.i./kg Duration: 21 days	No altered behavior, relative to controls, among adult beetles exposed to six lowest concentrations. Beetles exposed to 3162 mg /kg soil moved slower and were less coordinated on days 17 and 21, relative to controls. 21-day LC_{50} could not be determined but is assumed to be close to the highest concentration tested. 21-day EC_{50} = 1342 mg/kg soil (dw) for food uptake	Becker et al. 2011
Diptera			
Anastrepha suspensa, Caribbean fruit fly, 10-day-old males [Diptera: Tephritidae]	Agent: Sodium tetraborate (purity not given) Acute dietary study Duration: 48 hours	48-h LC_{50}: 2060 (580- 2540) mg B/kg-diet Slope 6.13 ± 1.9	U.S. EPA/OPP/ EFED 2015a MRID 45356601
Musca domestica, houseflies [Diptera: Muscidae]	Agent: Boric acid Concentration: 250-5000 mg B/kg diet	Inhibits reproduction	Eisler 1990

Appendix 3: Toxicity to Terrestrial Invertebrates (*continued*)

Species [Order: Family]	Exposure	Response	Reference
Musca domestica, houseflies, adults (3- to 7-days-old), 30 mated females [Diptera: Muscidae]	Agent: Disodium octaborate tetrahydrate (DOT), mixed with granulated sucrose Concentration: 2, 4, 7, or 10% (dry wt) Duration: 48 hours	48-hour LC_{50} = 5.7% (57,000 mg/kg) In choice tests, flies rejected treated sugar at levels ≥4%, (i.e., levels that were acutely toxic to them).	Mullens and Rodriguez 1992
Musca domestica, houseflies, adults, 100 mated flies [Diptera: Muscidae	Agent: Disodium octaborate tetrahydrate (DOT), mixed with granulated sucrose Concentration: 0, 1, 02% (dry wt) Duration: 8 days	Reduced egg hatch apparent after day1 of diet and greatest (<10% egg hatch) after day 2, with partial rebound in egg hatch after 3 to 4 days on treated diet. No effect of treatment on sperm motility in females. Fertile eggs place on treated poultry manure did not hatch, which indicated embryonic death.	Mullens and Rodriguez 1992
Fannia canicularis, lesser houseflies, adults (3- to 7-days-old), 30 mated females [Diptera: Fanniidae]	Agent: Disodium octaborate tetrahydrate (DOT), mixed with granulated sucrose Concentration: 0.3, 0.7, 1.5, or 3.0% (dry wt) Duration: 48 hours	48-hour LC_{50} = 1% (10,000 mg/kg diet)	Mullens and Rodriguez 1992

Appendix 3: Toxicity to Terrestrial Invertebrates (*continued*)

Species [Order: Family]	Exposure	Response	Reference
Lepidoptera			
Galleria mellonella, greater wax moth, larvae, 20 test concentration [Lepidoptera: Pyralidae]	Agent: Boric acid, NOS Concentration; 0, 156, 620, 1250, or 2500 mg/kg diet Duration: not specified	Significant concentration dependent mortality at all test concentrations LC_{50} = 160 ppm LOEC (LC_1) = 1.346 ppm Sublethal effects included increased lipid peroxidation and altered activity of catalase, superoxide dismutase, glutathione S-transferase, and glutathione peroxidase	Buyukguzel et al. 2013
Galleria mellonella, greater wax moth, larvae, 20 test concentration, 4 replicates [Lepidoptera: Pyralidae]	Agent: Borax, 99% Dietary concentration: 0.005, 0.1, 0.2, or 0.3 % borax in diet `Working Note: Concentrations equivalent to 50, 1000, 2000, and 3000 mg/kg diet.`	Survival: Two highest concentrations significantly decreased larval survival to the 7th instar. Development: Highest concentration decreased pupa and adult yields by 12.5% and prolonged development by 5 days. Adult longevity was not significantly affected by treatment. Fecundity: significant decreases in fecundity and egg viability, completely inhibiting oviposition of survivors at the highest concentration.	Durmus and Buyukguze 2008 [Turkey]
Galleria mellonella, greater wax moth, larvae, 7th instar (100-150 mg) and newly emerged pupae (90-100 mg) [Lepidoptera: Pyralidae]	Agent: Boric acid (crystal form 99.9% H_3BO_3) Dietary concentration: 156, 620, 1250, or 2500 mg/kg diet	Lowest concentration extended adult longevity, decreased developmental time to adulthood, and slightly increased survival of pupae and adults. The 1250- and 2500-ppm concentrations led to significantly increased larval and pupal mortality and prolonged development. Boric acid toxicity believed to be related in part to oxidative stress.	Hyrsl et al. 2007 [Turkey]

Appendix 3: Toxicity to Terrestrial Invertebrates (*continued*)

Species [Order: Family]	Exposure	Response	Reference
Lymantria dispar, gypsy moth, larvae [Lepidoptera: Erebidae]	Agent: Boric acid Concentration: 0.25% boric acid solution (436 mg B/L), 0.5%, or 1% boric acid	Effect on NPV activity: No effect at 436 mg B/L 2x enhancement at 0.5% boric acid 11x enhancement at 1% boric acid	Eisler 1990

Table A3-3: Efficacy Studies in Insects

<table>
<tr><th>Species [Order: Family]</th><th>Exposure</th><th>Response</th><th>Reference</th></tr>
<tr><td>Blattodea</td><td></td><td></td><td></td></tr>
<tr><td>Blattella germanica, German cockroach [Blattodea: Blattellidae]</td><td>Agent: Boric Acid
Concentration: baits containing 25% boric acid plus honey
Duration: 9 months</td><td>Population reduction of 50% in about 5 days, 80% in 4 weeks, and 98% in 6 to 9 months</td><td>Eisler 1990</td></tr>
<tr><td>Blattella germanica, German cockroach [Blattodea: Blattellidae]</td><td>Agent: Boric acid
Concentration: 11, 25, 50 or 100% boric acid
Duration: 72 hours</td><td>72-Hour Exposure<table><tr><th>Boric acid</th><th>Mortality</th></tr><tr><td>11%</td><td>44%</td></tr><tr><td>25%</td><td>79%</td></tr><tr><td>50%</td><td>80%</td></tr><tr><td>100%</td><td>91%</td></tr></table></td><td>Eisler 1990</td></tr>
<tr><td>Blattella germanica, German cockroach [Blattodea: Blattellidae]</td><td>Agent: Boric acid baits
Concentration: 20% boric acid
Duration 12 weeks</td><td>Boric Acid (20%)<table><tr><th>Population Reduction</th><th>Weeks</th></tr><tr><td>88%</td><td>2</td></tr><tr><td>92-95%</td><td>4-12</td></tr></table></td><td>Eisler 1990</td></tr>
<tr><td>Blattella germanica, German cockroach, 25 adult males [Dictyoptera: Blattellidae]</td><td>Agent: Boric acid in 50% (wt:wt) bait
Concentration in wet and dry-mixed bait: 6.25, 12.5, 25.0, or 50%</td><td>Effective control with use of dry-mixed baits that kill with contact activity and with use of liquid baits that kill by disruption of water regulation.

Toxicity of Boric Acid with Water Solutions<table><tr><th>Test</th><th>3-day LC_{50}</th></tr><tr><td>Nonchoice</td><td>0.72%</td></tr><tr><td>Choice</td><td>0.90%</td></tr></table>N=300</td><td>Strong et al. 1993</td></tr>
<tr><td>Blattella germanica, German cockroach, 25 adult males [Dictyoptera: Blattellidae]</td><td>Agent: Disodium octaborate tetrahydrate (DOT) in 50% (wt:wt) bait
Concentration in wet and dry-mixed bait: 6.25, 12.5, 25.0, or 50%</td><td>Effective control with use of dry-mixed baits that kill with contact activity and with use of liquid baits that kill by disruption of water regulation

Toxicity of DOT with Water Solutions<table><tr><th>Test</th><th>3-day LC_{50}</th></tr><tr><td>Nonchoice</td><td>0.59%</td></tr><tr><td>Choice</td><td>1.29%</td></tr></table>N=300</td><td>Strong et al. 1993</td></tr>
<tr><td>Periplaneta americana, American cockroach [Blattodea: Blattellidae]</td><td>Agent: Boric acid
Concentration: baits containing 1.5% boric acid</td><td>100% mortality in 6 days</td><td>Eisler 1990</td></tr>
</table>

Appendix 3: Toxicity to Terrestrial Invertebrates (*continued*)

Species [Order: Family]	Exposure	Response	Reference
Reticulitermes flavipes, eastern subterranean termite [Blattodea: Rhinotermitidae]	Agent: Disodium octaborate tetrahydrate (DOT) Treated wood (slash pine) concentration: 0.02, 0.10, 0.15, 0.30, or 0.54% boric acid equivalent Duration: 4 weeks	Concentrations of 0.10 and 0.30% boric acid equivalent protected wood	Maudlin and Kard 1996
Coptotermes formasanus, Formosan subterranean termite [Blattodea: Rhinotermitidae]	Agent: Disodium octaborate tetrahydrate (DOT) Treated wood (slash pine) concentration: 0.02, 0.10, 0.15, 0.30, or 0.54% boric acid equivalent Duration: 4 weeks	Concentrations of 0.10 and 0.30% boric acid equivalent protected wood In choice test between treated and non-treated wood, 0.54% boric acid equivalent not was effective.	Maudlin and Kard 1996
Coptotermes formasanus, Formosan subterranean termite, 150 workers/test [Blattodea: Rhinotermitidae]	Agents: Boric acid, Borax, Zinc borate, and Sodium perborate tetrahydrate. Concentration: 1, 1.5, 2, or 2.5% based on dry fiber weight in medium density fiberboard. Duration: 3 weeks	Treated fiberboard was highly resistant to termite attacks, compared with control samples. Concentration of 1.5% of all boron compounds provided 100% mortality by the end of exposure time (3 weeks) Highest mortality rates determined for borax and boric acid.	Usta et al. 2009 [Turkey]
Coleoptera			
Anobium punctatum, Common house borer, NOS [Coleoptera: Abobiidae]	Agent: Boric acid Concentration: 430 mg boric acid/m^3 wood	Adequate wood protection	Eisler 1990
Hemicolelus gibbicollis, larvae [Coleoptera: Anobiidae]	Agent: Disodium octaborate tetrahydrate (DOT) dust Concentration: 5% or 10% a.i. (average boron retention of 0.07 and 15% in Douglas-fir test blocks) Duration:	Decreased number of larvae by >95% Treatment had no effect on oviposition of females; however, treatment prevented larval emergence and penetration into timbers.	Suomi and Akre 1992
Diptera			
Anastrepha ludens, Mexican fruit fly [Diptera: Tephritidae]	Agent: Borax baits containing cottonseed hydrolysate and borax (NOS)	Reduced infestation in oranges by 68%, and in mangoes by 98%	Eisler 1990

Appendix 3: Toxicity to Terrestrial Invertebrates (*continued*)

Species [Order: Family]	Exposure	Response	Reference
Aedes albopictus, (Asian) tiger mosquito, adults [Diptera: Culicidae]	Agent: Boric acid 1% a.i. in sugar bait applied to Egyptian star cluster plant, *Pentas lanceolate* Duration: 14 days	Mortality =100% at 7 days and 92% at 14 days	Naranjo et al. 2013
Aedes albopictus, (Asian) tiger mosquito, adults [Diptera: Culicidae]	Agent: Boric acid 1% a.i. in sugar bait in field application conducted in residential backyards in St. Augustine Florida Duration: 21 days	Significant reduction in populations, as determined by BG trap and ovitrap collections, up to 21days. Significant reduction in oviposition on days 7 and 14 post application, which may suggest negative impact of toxin on females prior to possible blood feeding or ovipositioning.	Naranjo et al. 2013
Anopheles gambiae sensu stricto, pyrethroid susceptible mosquito originally from Kenya [Diptera: Culicidae] *Anopheles. arabiensis*, pyrethroid-resistant, F1 generation of mosquitoes collected from Lower Moshi, Tanzania [Diptera: Culicidae] *Culex quinquefasciatus* Masimbani strain, pyrethroid resistant, originally collected in Muheza, Tanzania. [Diptera: Culicidae]	Agent: Boric acid (99.5%) Concentration: 2% w/v mixed in guava juice-based bait a.k.a Attractive Toxic Sugar Bait (ATSB) Duration: 16 nights	Bait treatments resulted in >90% mortality in all three species of mosquitos.	Stewart et al. 2013

Appendix 3: Toxicity to Terrestrial Invertebrates (*continued*)

Species [Order: Family]	Exposure	Response	Reference
Aedes aegypti, mosquito [Diptera: Culicidae] *Ochlerotatus taeniorhynchus*. black saltmarsh mosquito [Diptera: Culicidae]	Agent: Boric acid Concentration:1% boric (and 10% sucrose) Bait stations: cylindrical basket with cup containing saturated cotton balls Duration: 48-hours	Overall, not effective In screened cages outdoors, bait stations significantly reduced the landing rate of mosquitos on human forearm. In the field study conducted in residential yards with natural populations of mosquitos, bait stations were relatively ineffective at reducing landing rates of mosquitos on human forearm or decreasing mosquito populations.	Xue et al. 2008
Aedes albopictus, Asian) tiger mosquito, females, 5- to 7-days old [Diptera: Culicidae	Agent: Boric acid spray Concentration: 0.25, 0.5, 0.75, or 1% (in 5% sucrose-water solution) Bait station: outdoor screened enclosure with plants in bed surrounded by turf. Sugar bait solutions were applied to plants surfaces Duration: up to 14 days	Concentration of 1% boric acid in sugar bait solution significantly decreased the landing rates of mosquitos on a human forearm as well as the number of females in mechanical traps Toxicity of 1% boric acid sugar bait persisted for 14 days under laboratory conditions; however under field-like conditions, toxicity persisted only 7 days (investigators assume difference is due to degradation of sucrose)	Xue et al. 2011
Musca domestica, houseflies [Diptera: Muscidae]	Agent: Isobornyl thiocyanoacetate Concentration: >2% aerosols	50% knockdown in 6 minutes	Eisler 1990
Phlebotomus papatasi, Turkish strain of sand flies, 10 males and 10 females [Diptera: Psychodidae]	Agent: Boric acid added to sucrose bait solutions Concentration: 1-100 g/L Duration: 48 hours	Concentrations as high as 40 g/liter of boric acid in sugar bait solution did not achieve complete control of sand flies; moreover, concentrations >40 g/liter were found to be repellent to the sand flies.	Mascari and Foil 2010
Hymenoptera			
Atta sexdens rubropilosa, leafcutter ant, 70 adult workers [Hymenoptera: Formicidae]	Agent: Boric acid Concentration: 0.2 or 0.5% added to artificial diet (baits) Duration: 48 hours	Significant decreases in survival, regardless of concentration. Treatment led to progressive, dose-dependent and time-dependent morphological changes in the midgut.	Sumida et al. 2010

Appendix 3: Toxicity to Terrestrial Invertebrates (*continued*)

<table>
<tr><th>Species [Order: Family]</th><th>Exposure</th><th>Response</th><th>Reference</th></tr>
<tr><td>Camponotus mus, carpenter ant
Linepithema humile, Argentine ants
[Hymenoptera: Formicidae]</td><td>Agent: Baits containing either boric acid (5% wt:vol) or borax (5% wt:vol)
Duration: 14 days</td><td>Asymmetrical response to toxicants.
C. mus more readily accepted the borax baits, while L. humile more readily accepted the boric acid baits.</td><td>Sola et al. 2013</td></tr>
<tr><td>Linepithema humile, Argentine ant, starved (24 or 48 hours) worker ants (300) and queen ants (100)
[Hymenoptera: Formicidae]</td><td>Agent: Boric acid (Exterm-an-Ant bait)
Concentration: 8% boric acid and 5.6% sodium borate
Duration: 21 days</td><td>Efficacy strongly influenced by starvation
Bait considered effective.</td><td>Mathieson et al. 2012</td></tr>
<tr><td>Linepithema micans, Argentine ants, colonies, each containing approximately 10 queens and several pupae and workers.
[Hymenoptera: Formicidae]</td><td>Agent: Boric acid, liquid bait
Concentration: 0.5, 1.0, or 12%
Duration: 15 weeks (1st experiment), 7 weeks (2nd experiment), and 13 weeks (3rd experiment)</td><td>Not effective</td><td>Nondillo et al. 2014</td></tr>
<tr><td>Linepithema micans, Argentine ants, [Hymenoptera: Formicidae]</td><td>Agent: Boric acid (Orthoboric acid, 99% tech) dissolved in 1 to 2 mL ethanol or acetone and added to 25% sucrose solution.
Concentration: 0.0, 0.125, 0.25, 0.5, 1.0, 2.0, or 5.0%
Duration: 14 days</td><td>Boric acid was not repellent to ants.

Average No. Dead Workers Exposed to Boric Acid
<table>
<tr><th>Conc (%)</th><th>Day 1</th><th>Day 7</th><th>Day 14</th></tr>
<tr><td>1.0</td><td>16.7</td><td>76.0</td><td>262.0</td></tr>
<tr><td>0.5</td><td>13.3</td><td>46.7</td><td>161.0[a]</td></tr>
</table>
[a]Colonies started with 300 workers and 5 queens.
Boric acid concentrations necessary to produce an LT_{50} within 1-4 days were 3.63 to 0.55%</td><td>Rust et al. 2004</td></tr>
<tr><td>Paratrechina longicornis, black crazy ant
[Hymenoptera: Formicidae]</td><td>Agent: Boric acid (99.5% a.i.)
Bait: 1% boric acid in 25% sugar water</td><td>Relatively effective: boric acid and sugar water was among the most attractive of seven baits to foragers.</td><td>Stanley and Robinson 2007</td></tr>
</table>

Appendix 3: Toxicity to Terrestrial Invertebrates (*continued*)

Species [Order: Family]	Exposure	Response	Reference
Zygentoma			
Thermobia domestica, firebrat [Zygentoma: Lepismatidae]	Agent: MotherEarth Granular Scatter Bait (5% orthoboric acid); InTice Granular Bait (5% orthoboric acid); Niban FG Bait (5% orthoboric acid) Duration: 21 days	No effective control: no differences between the choice and no choice LT_{50} values. All treatments resulted in <10% mortality during 21-day study.	Sims and Appel 2012
Lepisma saccharina, silverfish [Zygentoma: Lepismatidae]	Agent: MotherEarth Granular Scatter Bait (5% orthoboric acid); InTice Granular Bait (5% orthoboric acid); Niban FG Bait (5% orthoboric acid Duration: 21 days	No effective control: there were no differences between the choice and no choice LT_{50} values. All treatments resulted in <10% mortality during 21-day study.	Sims and Appel 2012

Table A3-4: Toxicity Studies on Soil Arthropods

Species [Order: Family]	Exposure	Response	Reference
Folsomia candida, springtail, 14-days-old, 20/replicate [Entomobryomorpha: Isotomidae]	Agent: Boric acid, 99.8% LUFA 2.2 soil (organic matter=3.9%, texture=6% clay; 17% silt; 77% sand) Concentration: 200, 400. 800, 1600, or 3200 mg a.i./kg Duration: 48 hours	48-hour EC_{50} = 1441 mg/kg soil (dw) for avoidance behavior.	Becker et al. 2011
Oppia nitens, oribatid mite [Sarcoptiformes: Oppiidae]	Agent: Boric acid, 99% purity OECD formulated soil (70% sand, 20% kaolin clay, 10% sphagnum peat by dry weight) Concentration: 0, 100, 200, 400, 800, 1600, or 3200 mg/kg Duration: 1, 2, or 5 days	No avoidance Survival: LC_{50} = 1468 mg/kg soil Reproduction: EC_{50} = 314 mg/kg soil Avoidance: EC_{50} = 2454 mg/kg soil Boric acid not a good reference chemical for avoidance in mites	Owojori et al. 2011, 2014
Hypoaspis aculeifer, predatory mite, protnymphs [Mesostigmata: Laelapidae]	Agent: Boric acid, analytical grade in spiked LUFA 2.1 soil Duration: 16days	Round robin reproduction study involving 16 different tests: NOECs = 10 to 316 BA/kg dw soil Repro EC_{50} values = 70.8 to 402.4 BA/kg dw soil See Table 4 of study for details.	Smit et al. 2012

Appendix 3: Toxicity to Terrestrial Invertebrates (*continued*)

<table>
<tr><th>Species [Order: Family]</th><th>Exposure</th><th>Response</th><th>Reference</th></tr>
<tr>
<td>Oppia nitens, oribatid mite, adults, 10/group in peat amended soil, 20/group in non-amended soil
[Sarcoptiformes: Oppiidae]</td>
<td>Agent: Boric acid (NOS)
Concentration for peat amended soil: 0, 60, 100, 160, 256, 410, 655, or 1050 mg boric acid/kg oven dry soil (mg/kg)
Concentration for non-amended soil: 0, 30, 60, 100, 160, 256, 410, or 655 mg/kg
Duration: 28 days</td>
<td>Adult Survival
<table>
<tr><th>Soil</th><th>LC_{50} (mg/kg)</th></tr>
<tr><td>Peat amended</td><td>530</td></tr>
<tr><td>Non-amended</td><td>250</td></tr>
</table>
Reproduction
<table>
<tr><th>Soil</th><th>EC_{50} (mg/kg)</th></tr>
<tr><td>Peat amended</td><td>96</td></tr>
<tr><td>Non-amended</td><td>78</td></tr>
</table>
Adult Survival in Peat Amended Soil
<table>
<tr><th>Culture</th><th>LC_{50} (mg/kg)</th></tr>
<tr><td>Age Synchronized</td><td>847</td></tr>
<tr><td>Non-Synchronized</td><td>530</td></tr>
</table>
Reproduction in Peat Amended Soil
<table>
<tr><th>Culture</th><th>EC_{50} (mg/kg)</th></tr>
<tr><td>Age Synchronized</td><td>118</td></tr>
<tr><td>Age Synchronized</td><td>96</td></tr>
</table>
</td>
<td>Princz et al. 2010</td>
</tr>
</table>

Table A3-5: Earthworms and Other Non-arthropods

Species [Order: Family]	Exposure	Response	Reference
Enchytraeus albidus, white worm [Haplotaxida: Enchytraeidae]	Agent: Boric acid, 99.8% LUFA 2.2 soil (organic matter=3.9%, texture=6% clay; 17% silt; 77% sand) Concentration: 200, 380, 630, 1125, or 2000 mg a.i./kg Duration: 48 hours	No avoidance 48-hour $EC_{50\ (avoidance)}$ >2000 mg/kg	Amorim et al. 2008
Caenorhabditis elegans, roundworm, juveniles (1st larval stage), 200-300 µm [Rhabditida: Rhabditidae]	Agent: Boric acid ≥99.5% purity Artificial soil (69.6% quartz sand, 20% kaolin clay, 10% sphagnum-peat, and 0.4% calcium carbonate) Concentration: 0, 10.0, 31.6, 56.2, 75.0, 100, 237, 562, or 1000 mg/kg soil (dw) Duration: 4 days	4-day EC_{50} = 747 mg/kg soil (dw)	Becker et al. 2011
Enchytraeus crypticus, worm, adults with clitellum and containing eggs [Haplotaxida: Enchytraeidae]	Agent: Boric acid ≥99.5% purity Artificial soil (69.6% quartz sand, 20% kaolin clay, 10% sphagnum-peat, and 0.4% calcium carbonate) Concentration: 0, 1.00, 10.0, 31.6, 100, 133, 178, 237, 316, 422, 562, 750, or 1000 mg/kg soil (dw) Duration: 28 days	Adult mortality could not be determined. 28-day EC_{50} = 220 mg/kg soil (dw) for juvenile production	Becker et al. 2011
Enchytraeus luxuriosus, white worm, adults with clitellum and containing eggs [Haplotaxida: Enchytraeidae]	Agent: Boric acid ≥99.5% purity Artificial soil (69.6% quartz sand, 20% kaolin clay, 10% sphagnum-peat, and 0.4% calcium carbonate) Concentration: 0, 10.0, 31.6, 56.2, 75.0, 100, 133, 178, 237, 316, 422, 562, or 1000 mg/kg soil (dw) Duration: 28 days	Adult mortality could not be determined. 28-day EC_{50} = 228 mg/kg soil (dw) for mean number of juveniles produced	Becker et al. 2011

Appendix 3: Toxicity to Terrestrial Invertebrates (*continued*)

Species [Order: Family]	Exposure	Response	Reference
Eisenia fetida (Lumbricidae), earthworms, adults with clitellum, 2-months- to ≤1-year-old, fresh weight: 300-600 mg [Haplotaxida: Lumbricidae]	Agent: Boric acid ≥99.5% purity Artificial soil (69.6% quartz sand, 20% kaolin clay, 10% sphagnum-peat, and 0.4% calcium carbonate) Concentration: 0, 75.0, 100, 133, 178, 237, 316, 422, 562, 750, or 1000 mg/kg soil (dw) Duration: 56 days	Mean adult biomass increased by 6-18% at ≤316 mg/kg soil (dw), relative to controls; at 1000 mg/kg soil (dw), weight gain was 35% lower than controls. 56-day EC_{50} = 484 mg /kg soil (dw) for number of juveniles produced.	Becker et al. 2011
Enchytraeus crypticus, worm, 5 replicates/ treatment [Haplotaxida: Enchytraeidae]	Agent: Boric acid, 99.8% pure LUFA 2.2 natural soil Concentration: 0, 200, 350, 630, 1125, o4 2000 mg/kg soil (dw) Duration: 48 hours	**Non-avoidance behavior**: 48-hour EC_{10} = 249 mg/kg soil (dw) 48-hour EC_{20} = 342 mg/kg soil (dw) 48-hour EC_{50} = 527 mg/kg soil (dw) 48-hour EC_{90} = 699 mg/kg soil (dw)	Bicho et al. 2015
Lumbricus terrestris, earthworm [Haplotaxida: Lumbricidae] *Lumbricus castaneus*, earthworm [Haplotaxida: Lumbricidae] *Allolobophora chlorotica*, green worm [Haplotaxida: Lumbricidae] Several additional species.	Boric acid powder (≥99.8% purity) Single application rate; 187 or 750 kg/ha (low dose corresponding to 14-day LC_{50} for *Lumbricus terrestris* in laboratory tests) Test site was a grassland site in Hessian highlands, Germany not previously treated with chemical fertilizers or pesticide Duration: 4 weeks	Treatment had a significant impact (>50% reduction) on abundance and biomass of earthworms. Not clear whether boric acid affected the worms directly or indirectly, given the influence of boric acid on soil pH. No residue analysis was performed.	Stegger et al. 2011
Efficacy			
Zachrysia provisoria, Cuban brown snail, n=5, 4 replicates [Stylommatophora: Camaenidae]	Agent: Orthoboric acid (Niban Granular Bait) Concentration: 0.25 g Duration: 14 days	Boric acid-based bait (Niban) required 12 days for the induction of significant levels of mortality and clearly disrupted snail feeding and growth.	Capinera 2013

Appendix 4: Toxicity to Terrestrial Plants

Table A4-1: Vegetative Vigor 187
Table A4-2: Seedling Emergence 188
Table A4-3: Other Toxicity Studies..... 189

Table A4-1: Vegetative Vigor

Species	Exposure	Response	Reference [1]
Monocots			
Corn, *Zea mays* Onion, *Allium cepa* Ryegrass, *Lolium perenne* Oat, *Avena sativa*	Boric acid (TGAI) 0.2 lb a.e./acre	EC_{25} > 0.2 lb a.e./acre NOAEL > 0.2 lb BA./acre EC_{25} > 0.03 lb B/acre NOAEL > 0.03 lb B/acre Most sensitive monocot could not be determined	U.S. EPA/OPP/EFED 2015a MRID 48885401 Supplemental/Quantitative
Dicots			
Common bean, *Phaseolus vulgaris* Cucumber, *Cucumis sativus* Oilseed rape, *Brassica napus* Radish, *Raphanus sativus* Soybean, *Glycine max* Tomato, *Lycopersicon esculentum*	Boric acid (TGAI) 0.2 lb a.e./acre	EC_{25} > 0.2 lb BA/acre NOAEL > 0.2 lb a.e./acre EC_{25} > 0.03 lb B/acre NOAEL > 0.03 lb B/acre Most sensitive dicot could not be determined	U.S. EPA/OPP/EFED 2015a MRID 48885401 Supplemental/Quantitative

Table A4-2: Seedling Emergence

Species	Exposure	Response	Reference [1]
Monocots			
Corn, *Zea mays* Onion, *Allium cepa* Ryegrass, *Lolium perenne* Oat, *Avena sativa*	Boric acid (TGAI) 5.0 lb a.e./acre	EC_{25} > 5.0 lb BA./acre NOAEL > 5.0 lb a.e./acre EC_{25} > 0.87 lb B/acre NOAEL > 0.87 lb B/acre Most sensitive monocot could not be determined	U.S. EPA/OPP/EFED 2015a MRID 48885402 Supplemental/Quantitative
Dicots			
Common bean, *Phaseolus vulgaris* Cucumber, *Cucumis sativus* Oilseed rape, *Brassica napus* Radish, *Raphanus sativus* Soybean, *Glycine max* Tomato, *Lycopersicon esculentum*	Boric acid (TGAI) 5.0 lb a.e./acre	EC_{25} > 5.0 lb BA/acre NOAEL = 0.65 lb BA/acre (based on significant reduction of 9.9% in shoot length at 1.4 lb a.e./acre ($p<0.5$). EC_{25} > 0.87 lb B/acre NOAEL = 0.11 lb B/acre Most sensitive dicot: Oilseed rape	U.S. EPA/OPP/EFED 2015a MRID 48885402 Supplemental/Quantitative

Table A4-3: Other Toxicity Studies

Species	Exposure	Response	Reference [1]
Soil Exposures			
Potatoes, winter wheat, and sugar beet	Boric acid (concentration ranges 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 sugar beet: 20 - 35 mg B/kg soil Higher NOAECs observed in "heavy" soils (NOS).	Kluge 1990, as cited in ECETOC 1997
Poppy (*Papaver somniferum*)	Borax Concentrations: 1 to 32 mg B/kg 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 Concentrations of 1, 10, 100 and 1000 mg/kg dry soil (added prior to planting) Greenhouse study.	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
Northern wheatgrass (*Elymus lanceolatus*)	Boric acid 0, 17.8, 34, 67, 134, 268, or 536 mg/kg soil Duration: 21-day early seedling growth test	Phytotoxicity of boric acid in cryosols much greater than is commonly observed in other soils. Also, in addition to high sensitivity, there was great variability among the test results, which was not explained by soil properties. IC_{20} = 55 mg/kg soil for emergence and shoot length in Ekati C horizon soil IC_{20} = 554 mg/kg soil for emergence in Ekati O horizon soil. IC_{20} = 402 mg/kg soil for emergence in Truelove soil (calculated based on means from single-point dosing).	Anaka et al. 2008

Species	Exposure	Response	Reference [1]
Oilseed rape, *Brassica napus* and Oat, *Avena sativa*, 10 each undressed seeds	Boric acid (H_3BO_3) ≥99.5% pure 0.0 (control), 31.3, 62.5, 125, 250, or 500 mg/kg soil Duration: harvested 14 days after emergence to determine shoot fresh weight and shoot length	Oat, *Avena sativa*: EC_{50} = 182 mg boric acid/kg soil (dw) for shoot fresh weight EC_{50} = 308 mg boric acid/kg soil (dw) for above ground shoot length Oilseed rape, *Brassica napus*: EC_{50} = 175 mg boric acid/kg soil (dw) for shoot fresh weight EC_{50} = 357 mg boric acid/kg soil (dw) for above ground shoot length	Becker et al. 2010
Liquid Exposures			
Jack pine (*Pinus banksiana*) seedlings, dormant, 1-year-old	Boron (H_3BO_3) 0.5, 1, or 2 mM B in a conifer nutrient solution. Equivalent to: about 5.4, 10.8, 21.4 mg B/L. Duration: treatment applied for 6 weeks	No significant effects on survival and measured growth traits. Boron significantly increased needle electrolyte leakage and caused needle tip necrosis in jack pine seedlings and inhibited stomatal conductance and root water flow, which did not appear to affect nutrient uptake and distribution. The concentration of boron in the needles of plants treated with 2 mM B was three times higher than the concentration of boron in the roots.	Apostol and Zwiazek 2004

Species	Exposure	Response						Reference [1]
Lettuce (*Lactuca sativa*) Alfalfa (*Medicago sativa*) Carrot (*Daucus carota*) Petri dish assay for seedling emergence.	Boric acid 40, 80, 160, 320, or 640 mg/L. Duration: 5 days for lettuce and alfalfa; 7 days for carrot. Working Note: Boric acid used as positive control in assays of antibiotics. Applied as spray. Cannot get application rates. Use only to assess relative sensitivity.	**Species**	**EC_{50} (mg/L)**	**EC_{25} (mg/L)**	**EC_{10} (mg/L)**	**LOEC (mg/L)**		Hillis et al. 2011
		Germin-ation						
		Carrot T_1	>640	>640	>640	NSD		
		Carrot T_2	>640	>640	>640	NSD		
		Carrot T_3	>640	>640	>640	NSD		
		Lettuce T_1	>640	>640	>640	NSD		
		Lettuce T_2	>640	>640	>640	NSD		
		Lettuce T_3	>640	>640	>640	NSD		
		Alfalfa T_1	>640	>640	>640	NSD		
		Alfalfa T_2	>640	>640	>640	NSD		
		Alfalfa T_3	>640	>640	>640	NSD		
		Total Length						
		Carrot T_1	55	7.4	2.2	160		
		Carrot T_2	76	8.7	2.4	320		
		Carrot T_3	106	10	2.5	160		
		Lettuce T_1	>640	63	5.3	640		
		Lettuce T_2	>640	89	6.0	NSD		
		Lettuce T_3	>640	27	3.7	640		
		Alfalfa T_1	>640	281	9.5	640		
		Alfalfa T_2	>640	370	149	640		
		Alfalfa T_3	>640	309	81	320		
		Root Length						
		Carrot T_1	38	6.2	2.1	320		
		Carrot T_2	64	8.0	2.3	320		
		Carrot T_3	112	11	2.6	160		
		Lettuce T_1	>640	30	3.9	NSD		
		Lettuce T_2	>640	44	4.5	NSD		
		Lettuce T_3	180	14	2.8	640		
		Alfalfa T_1	>640	>640	>640	NSD		
		Alfalfa T_2	>640	>640	>640	NSD		
		Alfalfa T_3	>640	>640	>640	NSD		
		Shoot Length						
		Carrot T_1	76	8.7	2.4	160		
		Carrot T_2	75	8.6	2.4	160		
		Carrot T_3	90	9.5	2.5	160		
		Lettuce T_1	>640	272	101	640		
		Lettuce T_2	>640	255	86	640		
		Lettuce T_3	>640	213	92	640		
		Alfalfa T_1	>640	216	70	320		
		Alfalfa T_2	>640	284	119	640		
		Alfalfa T_3	>640	184	67	320		

Appendix 5: Toxicity to fish.

Table A5-1: Acute Toxicity 192
Table A5-2: Early Life-stage Assays (Chronic) 195

Table A5-1: Acute Toxicity

Species	Exposure	Response	Reference
Bluegill sunfish, *Lepomis macrochirus*, average 0.77 g, TL 40 mm	Boric acid, 100% a.i. Static exposure Duration: 96 hours	96-hour LC_{50} = 1021 mg a.e./L 96-hour LC_{50} = 178 mg B/L (based on measured concentrations) Practically non-toxic on both a.e. and B basis	U.S. EPA/OPP/EFED 2015a MRID 40594602 Acceptable
Bonytail, *Gila elegans* (T&E species)	Boric acid Duration: 96 hours	96-hr LC_{50}: for swim-up fry = 280 mg B/L small juvenile = 552 mg B/L larger juvenile = 337 B mg /L	Hamilton 1995
Colorado squawfish, *Ptychocheilus lucius* (T&E species)	Boric acid Duration: 96 hours	Colorado squawfish 96-hr LC_{50}: swim-up fry = 279 mg B mg/L small juvenile > 100 mg B mg/L larger juvenile = 527 mg B/L	Hamilton 1995
Fathead minnow, *Pimephales promelas*	Boric acid, 99.9% a.i.	96-hour LC_{50} = 404 mg a.e./L 96-hour LC_{50} = 70.6 mg B/L Slightly toxic on B basis and Practically non-toxic on a.e. basis	U.S. EPA/OPP/EFED 2015a Acceptable MRID number not specified. **Used by EFED 2015a (Table 5.2, p. 39) for acute risks to fish. Used in current risk assessment for sensitive species.**
Fathead minnow, *Pimephales promelas*, 0.12 g, 19.8 mm	Boric acid, 99.9% a.i. Static exposure	96-hour LC_{50} = 578 mg a.e./L 96-hour LC_{50} = 101 mg B/L (based on measured concentrations) Practically non-toxic on both a.e. and B basis	U.S. EPA/OPP/EFED 2015a Acceptable
Japanese flounder, *Paralichthys olivaceus*, 0.05g (tested up to 70g, but lowest wt. most sensitive)	Boric acid (NOS) Semi-static exposure	96-hour LC_{50} = 618 mg a.e./L 96-hour LC_{50}= 108 mg B/L (based on measured concentrations) Toxicity of boron increased linearly with increasing water temperature (see table 4, p 360 of study) Slightly toxic on B basis and Practically non-toxic on a.e. basis	Furuta et al. 2007 U.S. EPA/OPP/EFED 2015a Supplemental/Quanti-tative ECOTOX ID: E166696

Appendix 5: Toxicity to fish *(continued)*

Species	Exposure	Response	Reference
Rainbow trout, *Oncorhynchus mykiss*	Borax, concentration range not reported	**Duration (Hours)** / **LC_{50} (mg B/L)** 24 / 602.0 48 / 387.0 Working Note: Cannot verify in Alabaster (1969) paper.	Alabaster 1969, as cited in Hovatter and Ross 1995
Rainbow trout, *Oncorhynchus mykiss*, 1.06 g	Boric acid, 100% a.i. Static exposure	0% mortality (0/20 fish) 96-hour LC_{50} >1100 mg a.e./L 96-hour LC_{50} >192 mg B/L (based on measured concentrations). No mortality. Practically non-toxic on both a.e. and B basis	U.S. EPA/OPP/EFED 2015a MRID 40594601 Acceptable Used in current risk assessment in dose-response for tolerant species
Rainbow trout, *Oncorhynchus mykiss*, average 2.32 g, 58.6 mm	Boric acid, 99.9% a.i. Static exposure	0% mortality (0/10 fish) 96-hour LC_{50} >800 mg a.e./L (based on nominal concentrations) 96-hour LC_{50} >140 mg B/L Practically non-toxic on both a.e. and B basis	U.S. EPA/OPP/EFED 2015a, TN 2751 (TN 2860)/ Supplemental
Razorback sucker , *Xyrauchen texanus* (E&T)	Boric acid Duration: 96 hours	96-hr LC_{50}: swim-up fry = 233 mg B/L small juvenile = 279 mg B/L larger juvenile > 100 mg B/L	Hamilton 1995
Red sea bream, *Pagrus major*, 0.4g (tested up to 20.3g, but lowest wt. most sensitive)	Boric acid (NOS) Semi-static exposure	96-hour LC_{50} = 555 mg a.e./L 96-hour LC_{50}= 97 mg B/L (based on measured concentrations) Toxicity of boron increased linearly with increasing water temperature; however the relationship was not significant (see table 4, p 360 of study) Slightly toxic on B basis and Practically non-toxic on a.e. basis	Furuta et al. 2007 U.S. EPA/OPP/EFED 2015a Supplemental/Quanti-tative ECOTOX ID: E166696
Western mosquitofish, *Gambusia affinis*	Borax Duration: 96 hours	**Duration (Hours)** / **LC_{50} (mg B/L)** 24 / 1361 48 / 930 96 / 408	Wallen et al,. 1957, as cited in Hovatter and Ross 1995

Appendix 5: Toxicity to fish *(continued)*

<table>
<tr><th>Species</th><th>Exposure</th><th>Response</th><th>Reference</th></tr>
<tr><td>Young salmon fry, Chinook (Oncorhynchus tshawytscha) and Coho (O. kisutch)</td><td>Boric Acid
Duration: 96 hours</td><td>Chinook
<table><tr><th>Duration (Hours)</th><th>LC_{50} (mg B/L)</th></tr><tr><td>24</td><td>>1000</td></tr><tr><td>96</td><td>600</td></tr></table>For eyed egg and alevin, 24- and 96 hr LC50 >1000 mg B/L

Coho
<table><tr><th>Duration (Hours)</th><th>LC_{50} (mg B/L)</th></tr><tr><td>24</td><td>>1000</td></tr><tr><td>96</td><td>447</td></tr></table></td><td>Hamilton and Buhl 1990</td></tr>
</table>

WORKING NOTE for Table A5-1: Some formulations containing borates are much more toxic than the formulations of borax or DOT summarized in this table. See U.S. EPA/OPP/EFED (2015a) for details. None of the more toxic formulations consist of borax or DOT as the primary ingredients.

Table A5-2: Early Life-stage Assays (Chronic)

Species	Exposure	Response	Reference
Channel catfish, *Ictalurus punctatus* Early life-stage (eggs to alevins/yolk-fry) Working Note: LC_1 values in Table 24 and LC_{50} values in Table 25. Note that all toxicity values in report are specified as boron equivalents (p. 3 of report)	Boric acid and Borax Concentrations: 0.001 to 300 ppm boron Duration: 9 days (fertilization to 4 days post-hatch) Working Note: Only post-hatched (cumulative) toxicity values are summarized here. Report gives both hatchling and post-hatchling values.	Boric acid **Water** / **LC_1 (mg B/L)** / **LC_{50} (mg B/L)** Soft / 0.5 / 155 Hard / 0.2 / 22 Borax **Water** / **LC_1 (mg B/L)** / **LC_{50} (mg B/L)** Soft / 5.5 / 155 Hard / 1.7 / 71	Birge and Black 1977
Goldfish, *Carassius auratus* Early life-stage (eggs to alevins/yolk-fry) Working Note: LC_1 values in Table 24 and LC_{50} values in Table 25. Note that all toxicity values in report are specified as boron equivalents (p. 3 of report).	Boric acid and Borax Concentrations: 0.001 to 300 ppm boron Duration: fertilization to 4 days post-hatch. Working Note: Only post-hatched (cumulative) toxicity values are summarized here. Report gives both hatchling and post-hatchling values.	Boric acid **Water** / **LC_1 (mg B/L)** / **LC_{50} (mg B/L)** Soft / 0.6 / 46 Hard / 0.2 / 75 Borax **Water** / **LC_1 (mg B/L)** / **LC_{50} (mg B/L)** Soft / 1.4 / 65 Hard / 0.9 / 69	Birge and Black 1977
Rainbow trout, *Oncorhynchus mykiss* Early life-stage (eggs to alevins/yolk-fry) Working Note: LC_1 values in Table 24 and LC_{50} values in Table 25. Note that all toxicity values in report are specified as boron equivalents (p. 3 of report)	Boric acid and Borax Concentrations: 0.001 to 300 ppm boron Duration: 28 days. Soft water ($CaCl_2$ 50 ppm) Hard water ($CaCl_2$ 200 ppm) Working Note: Only post-hatched (cumulative) toxicity values are summarized here. Report gives both hatchling and post-hatchling values.	Boric acid **Water** / **LC_1 (mg B/L)** / **LC_{50} (mg B/L)** Soft / 0.1 / 100 Hard / 0.001 / 79 Borax **Water** / **LC_1 (mg B/L)** / **LC_{50} (mg B/L)** Soft / 0.07 / 27 Hard / 0.07 / 54	Birge and Black 1977

Appendix 5: Toxicity to fish *(continued)*

Species	Exposure	Response	Reference
Fathead minnow, *Pimephales promelas*, 7-hour post-fertilized eggs	Boric acid 99.7% Flow-through exposure Duration: 32 days	Most sensitive endpoint was total length; post-hatch survival and dry weight was significantly reduced at140 mg a.e./L (28 mg B/L) NOAEC = 42 mg a.e./L LOAEC = 74 mg a.e./L (based on measured concentrations) NOAEC = 7.4 mg B/L LOAEC = 13 mg B/L	U.S. EPA/OPP/EFED 2015a MRID 48914601 Acceptable **Used by EFED 2015a (Table 5.2, p. 39) for chronic risks to fish.**
Fathead minnow, *Pimephales promelas*, <24-hour-old fertilized embryos	Boric acid 99.7% Flow-through exposure	*Control mortality exceeded acceptable levels, and was attributed to handling issues and two of the control replicates were not included in the statistical analysis. If there were handling issues with the controls, effects in other treatments may also be impacted and not separable from treatment related impacts. Source of water was dechlorinated (carbon filtered) Traverse, MI tap water, LEC, 60-90% control mortality in two replicates* (Taken from Table I8 of EPA/OPP/EFED 2015a)	U.S. EPA/OPP/EFED 2015a Classified by EPA as *Unacceptable.*
Zebra fish, *Danio rerio*, embryo to larval stage	Boric acid, 99.5% a.i. Static renewal exposure	96-hour LC_{50} >74.4mg a.e./L 96-hour NOAEC ≥74.4mg a.e./L 96-hour LC_{50} >13.0 mg B/L 96-hour NOAEC ≥13.0 mg B/L At most slightly toxic on both a.e. and B basis.	U.S. EPA/OPP/EFED 2015a Supplemental/ Quantitative ECOTOX ID: E105984 Rowe et al. 1998

Appendix 5: Toxicity to fish *(continued)*

Species	Exposure	Response	Reference
Zebra fish, *Danio rerio*, eggs, 6-8 hours post-fertilization.	Boric acid 5-days post-fertilization Working Note: Basically, the investigators just used a 4-parameter Hill Equation rather than a probit or logistic model. These results are not consistent with the bioassays by Selderslaghs et al. 2012 and Teixido et al. 2013. See entries in this table.	Summary from paper: AC_{50}: 60.6850 µM 0.656 mg B/L EFED 2015a Summary Developmental EC_{50} = 0.656 mg a.e./L Developmental EC_{50} = 3.75 mg B/L EPA Note: Footnote indicates: *This is not an LC50 but a type of EC50 (median effects concentration) that authors refer to as a developmental effect index, a half-maximal activity concentration (AC50).*	Padilla et al. 2012 Also cited in U.S. EPA/OPP/EFED 2015a Supplemental/ Quantitative ECOTOX ID: E161191 **Working Note: Cannot verify the EC50 of 3.75 mg B/L from EPA report.**
Zebrafish, *Danio rerio*, embryos	Boric acid in incubator under static conditions 0.63 to 80.86 mM Duration: 144 hours post-fertilization (hpf) [≈6 days]	24-hpf LC_{50} = no value calculated 24-hpf EC_{50} = 63.54 mM 48-hpf LC_{50} = 63.17 mM 48-hpf EC_{50} = 25.24 mM 72-hpf LC_{50} = 42.20 mM 72-hpf EC_{50} = 23.45 mM 144-hpf LC_{50} = 23.55 mM 144-hpf EC_{50} = 5.85 mM **Working Note: The lowest EC50 is about 60 mg B/L [5.85 mM x 10.811 mg/mM = 60.32 mg/L].**	Selderslaghs et al. 2012
Zebrafish, *Danio rerio*, embryos, n=10	Boric acid in incubator under semi-static conditions 7 to 35.5 mM Duration: 52 hours post-fertilization (hpf) [≈2 days]	Adverse effects of treatment included mostly tail malformation and pericardial and yolk sac edema. 52-hpf LC_{50} = 53.4 mM [≈577 mg B/L] 52-hpf $EC_{50\ teratogenic}$ = 18.3 mM [≈197 mg B/L]	Teixido et al. 2013

Appendix 6: Toxicity to amphibians.

Table A6-1: Acute Toxicity to Amphibians 198
Table A6-2: Chronic toxicity to Amphibians 199

Table A6-1: Acute Toxicity to Amphibians

Species	Exposure	Response	Reference
African clawed frog, *Xenopus laevis*, NOS	Boron, NOS	96-hour LC_{50} = 73.4 to 239 mg B/L Working Note: This appears to be a summary of studies but details are not provided.	U.S. EPA/OPP/EFED 2015a, p. 120
African clawed frog, *Xenopus laevis*, larvae	Boric acid Concentrations: not reported Duration: 96 hours Results given for composite of 3 laboratories (Table 13 of paper). Individual laboratory data in Table 2 of paper.	LC_{50}: 978 mg BA/L or 171 mg B/L EC_{50} (malformations): 348 mg BA/L or 60.9 mg B/L [reduced eyes and some abnormal gut coiling. More severe effects at higher concentrations.] LOAEL (Growth inhibition): 239 mg BA/L or 41.8 mg B/L Working Note: Slightly lower values for assays with liver microsomes not included above.	Bantle et al. 1999
African clawed frog, *Xenopus laevis*, embryos, 96-hours-old	Boric acid (>95% pure) Concentrations: 1, 2, 3, 4, 5, 10, 50, 100, 1000, or 5000 µg/B/L Duration: 4 days Working Note: This is an assay of boron deficiency.	<u>PHASE I (Acute)</u> Boron concentrations ≤3 µg B/L caused a statistically significant ($p<0.05$) increase in malformations that was not observed at higher concentrations. Observations included abnormal development of the gut, craniofacial region and eye, visceral edema, and kinking of the tail musculature (abnormal myotome development) due to low levels of boron. NOAEL: 5000 µg B/L (5 mg B/L) Working Note: See Table A6-2 for Phase II (longer-term) portion of study.	Fort et al. 1998
African clawed frog, *Xenopus laevis*, oocytes	Boron (NOS)	No effect on germinal vesicle breakdown at concentrations of 100 mg B/L.	Fort et al. 2002

Table A6-2: Chronic toxicity to Amphibians

<table>
<tr><th>Species</th><th>Exposure</th><th>Response</th><th>Reference</th></tr>
<tr>
<td>Fowler's Toad, Anaxyrus fowleri (Bufo fowleri)
Early life-stages
Working Note: LC_1 values in Table 24 and LC_{50} values in Table 25. Note that all toxicity values in report are specified as boron equivalents (p. 3 of report)</td>
<td>Boric acid and Borax
Concentrations: 0.001 to 300 ppm B
Duration: 7.5 days, fertilization to 4 days post-hatch
Soft water ($CaCl_2$ 50 ppm)
Hard water ($CaCl_2$ 200 ppm)</td>
<td>Boric acid
<table>
<tr><th>Water</th><th>LC_1 (mg B/L)</th><th>LC_{50} (mg B/L)</th></tr>
<tr><td>Soft</td><td>25</td><td>145</td></tr>
<tr><td>Hard</td><td>5</td><td>123</td></tr>
</table>
Borax
<table>
<tr><th>Water</th><th>LC_1 (mg B/L)</th><th>LC_{50} (mg B/L)</th></tr>
<tr><td>Soft</td><td>5.5</td><td>N/A</td></tr>
<tr><td>Hard</td><td>1.7</td><td>N/A</td></tr>
</table></td>
<td>Birge and Black 1977</td>
</tr>
<tr>
<td>Leopard Frog, Lithobates pipiens
Early life-stages
Working Note: LC_1 values in Table 24 and LC_{50} values in Table 25. Note that all toxicity values in report are specified as boron equivalents (p. 3 of report)</td>
<td>Boric acid and Borax
Concentrations: 0.001 to 300 ppm B
Duration: 7.5 days, fertilization to 4 days post-hatch
Soft water ($CaCl_2$ 50 ppm)
Hard water ($CaCl_2$ 200 ppm)</td>
<td>Boric acid
<table>
<tr><th>Water</th><th>LC_1 (mg B/L)</th><th>LC_{50} (mg B/L)</th></tr>
<tr><td>Soft</td><td>13</td><td>130</td></tr>
<tr><td>Hard</td><td>22</td><td>135</td></tr>
</table>
Borax
<table>
<tr><th>Water</th><th>LC_1 (mg B/L)</th><th>LC_{50} (mg B/L)</th></tr>
<tr><td>Soft</td><td>5</td><td>47</td></tr>
<tr><td>Hard</td><td>5</td><td>54</td></tr>
</table></td>
<td>Birge and Black 1977</td>
</tr>
<tr>
<td>African clawed frog, Xenopus laevis, adults, separate group of four males and four females prior to mating.</td>
<td>Boric acid (>95% pure)
Low boron diet: 62 µg B/kg
Boric acid supplemented diet: 1851 µg B/kg
Duration: 28 days

Working Note: This is an assay of boron deficiency.</td>
<td><u>PHASE II</u>
Mortality of embryos from adult frogs fed low boron diet was approximately 50%, compared with 5% mortality among embryos from adults fed boric acid supplemented diet.
Incidence of malformations was also greater in embryos from adults fed low boron diet and maintained on culture media containing ≤ 5 µg B/kg. The malformations observed were similar to those observed in Phase I of the study.
No evidence of malformations among embryos from adult frogs fed boric acid supplemented diet.

Working Note: See entry in Table A6-1 for Phase I (acute) study.</td>
<td>Fort et al. 1998</td>
</tr>
</table>

Appendix 6: Toxicity to Amphibians *(continued)*

Species	Exposure	Response	Reference
African clawed frog, *Xenopus laevis*, adults, n=4 for reproductive endpoint evaluation and n=4 for breeding response.	Boric acid (99%) Concentrations: 0.0, 1.0, 10.0, 50.0, 100.0, 500.0, or 1000.0 mg BA/L Duration: 30 days prior to evaluation	No statistically significant increases in mortality observed. Significant increase ($p<0.05$) in abnormal development in fertilized embryos from females exposed to 100 or 500 mg BA/L for 30 days and cultured in FETAX for 4 days. Malformations due to female exposure to 500 mg BA/L included abnormal development of the craniofacial region, gut, kinking of the notochord and microencephaly. Male exposure to ≥50.0 mg BA/L significantly ($p<0.05$) reduced testis weight, significantly reduced sperm count and increased the rate of sperm dysmorphology. Exposure to 1000 mg BA/L resulted in necrosis of the testes and rate of sperm dysmorphology was 18.3 ± 1.2%. There were no effects on breeding response and no significant reduction in fertilization rates or embryonic viability at 96 hours. NOAEC: 10 mg BA/L or 1.75 mg B/L	Fort et al. 2001
Wood Frog, *Rana sylvatica* (a.k.a. *Lithobates sylvaticus* Eggs, collect in wild, 5 replicates of 15 eggs/replicate per concentration.	Borax Concentrations: 0, 49.5, or 102.24 mg B/L Duration: Days 13-23 (until hatch)	Dose-dependent increase ($p<0.001$) in proportion of deformed larvae (crescent shaped bodies). No effect of boron exposure on proportion of eggs hatching. See Table 1 of paper. Hatching: NOAEL: 102.24 mg B/L LOAEL: not determined Deformities: NOAEL: not determined LOAEL: 49.5 mg B/L	Lapsota and Dunson 1998

Appendix 6: Toxicity to Amphibians *(continued)*

Species	Exposure	Response	Reference
Jefferson salamander, *Ambystoma jeffersonianum* Eggs, collect in wild, 5 replicates of 15 eggs/replicate per concentration.	Borax Concentrations: 0, 49.5, or 102.24 mg B/L Duration: Days 17-35 (until hatch)	Dose-dependent increase in proportion of deformed larvae (crescent shaped bodies). No effect of boron exposure on proportion of eggs hatching. See Table 1 of paper. Hatching: NOAEL: 102.24 mg B/L LOAEL: not determined Deformities: NOAEL: not determined LOAEL: 49.5 mg B/L	Lapsota and Dunson 1998
Spotted salamander, *Ambystoma maculatum* Eggs, collect in wild, 5 replicates of 15 eggs/replicate per concentration.	Borax Concentrations: 0, 49.5, or 102.24 mg B/L Duration: Days 38-44 (until hatch)	Dose-dependent increase in proportion of deformed larvae (crescent shaped bodies). No effect of boron exposure on proportion of eggs hatching. See Table 1 of paper. Hatching: NOAEL: 102.24 mg B/L LOAEL: not determined Deformities: NOAEL: not determined LOAEL: 49.5 mg B/L	Lapsota and Dunson 1998
American toad, *Bufo americanus* (currently named as *Anaxyrus americanus*), Eggs, collect in wild	Borax Concentrations: 0, 49.5, or 102.24 mg B/L Duration: Days 15-23 (until hatch)	Dose-related decrease in proportion of eggs hatching in boron treatment groups. No indication of deformities. Hatching: NOAEL: not determined LOAEL: 49.5 mg B/L	Lapsota and Dunson 1998

Appendix 7: Toxicity to aquatic invertebrates

Table A7-1: Acute Toxicity to Aquatic Invertebrates 202
Table A7-2: Chronic toxicity to Aquatic Invertebrates 207

Table A7-1: Acute Toxicity to Aquatic Invertebrates

<table>
<tr><th>Species</th><th>Exposure</th><th>Response</th><th>Reference</th></tr>
<tr><td>Ceriodaphnia dubia</td><td></td><td></td><td></td></tr>
<tr><td>Ceriodaphnia dubia<24-hours-old, 5/treatment, 4 replicates
[Cladocera: Daphniidae]</td><td>Agent: Boric acid
Static
Duration:48 hours</td><td>48-hour LC_{50} concentrations in natural water samples from three field sites were all greater than LC_{50} concentrations in laboratory waters reconstituted to match the natural waters except for dissolved organic carbon, which the investigators suggest may have mitigated the toxicity of boron to the daphnids.
<table>
<tr><th>Site water treatments</th><th>Measured LC_{50} (mg B/L)</th></tr>
<tr><td>Poudre River Site</td><td>114.8</td></tr>
<tr><td>Poudre River Match</td><td>82.7</td></tr>
<tr><td>Desjardins Canal Site</td><td>160.9</td></tr>
<tr><td>Desjardins Canal Match</td><td>107.8</td></tr>
<tr><td>Clark Fork River Site</td><td>154.3</td></tr>
<tr><td>Clark Fork River Match</td><td>84.6</td></tr>
</table>
48 hour LC_{50} values using reconstituted water range from 45.4 mg B/L to 134.1 mg B/L. See Table 1 of paper for details.</td><td>Dethloff et al. 2009</td></tr>
<tr><td>Ceriodaphnia dubia, daphnid, <24-hours-old
[Cladocera: Daphniidae]</td><td>Agent: Boric acid
Static exposure
Duration: 48 hours

Working Note: The ECOTOX reference specified by EPA corresponds to Dethloff et al. (2009) which is summarized in the previous row. The EPA does select the lowest toxicity value for risk assessment.</td><td>pH = 8.1
Water hardness = 96
<u>Temperature = 20°C</u>
48-hour EC_{50} = 260 mg a.e./L
48-hour EC_{50} = 45.5 mg B/L

pH = not reported
Water hardness = 168
<u>Temperature = 20°C</u>
48-hour EC_{50} = 289 mg a.e./L
48-hour EC_{50} = 50.6 mg B/L

Practically nontoxic on a.e. basis, Slightly toxic on B basis</td><td>U.S. EPA/OPP/EFED 2015a
Supplemental/ Quantitative
ECOTOX ID E118810 (Dethloff et al. 2009)
The 260 mg a.e./L value is used by U.S. EPA/OPP/EFED 2015a for risk characterization.</td></tr>
</table>

Appendix 7: Toxicity to Aquatic Invertebrates *(continued)*

Species	Exposure	Response	Reference
Ceriodaphnia dubia, daphnid, <24-hours-old [Cladocera: Daphniidae]	Agent: Boric acid, ≥99.5% Flow-through exposure Duration: 48 hours	48-hour EC_{50} = 440 mg a.e./L (measured) 48-hour EC_{50} = 76.9 mg B/L (measured) Practically non-toxic on a.e. basis; Slightly toxic on B basis	U.S. EPA/OPP/EFED 2015a Acceptable
Ceriodaphnia dubia, neonates 10/concentration [Cladocera: Daphniidae]	Agent: Boron (H_3B0_3, AR grade) Duration: 24 hours	24-hour EC_{50} = 180.6 g/m^3 (mg/L) 24-hour EC_{10} = 130.4 g/m^3 (mg/L)	Hickey 1989 See matched study on *Daphnia magna* below.
Daphnia magna			
Daphnia magna, <24-hours-old, 10/dose group [Cladocera: Daphniidae]	Agent: Boric acid, % not reported Static exposure Concentrations: 54, 91, 151, 252, 420, or 700 mg/L as boron Duration: 48 hours	48-hour EC_{50} = 761 mg a.e./L (nominal) 48-hour EC_{50} = 133 mg B/L (nominal) Practically non-toxic on both a.e. and B basis	Gersich 1984 U.S. EPA/OPP/EFED 2015a Supplemental/ Quantitative
Daphnia magna, water flea, <24-hours-old [Cladocera: Daphniidae]	Agent: Boric acid, 99.6% Static exposure Duration: 48 hours	48-hour EC_{50} = 777 mg a.e./L (nominal) 48-hour EC_{50} = 136 mg B/L (nominal) Practically non-toxic on both a.e. and B basis	U.S. EPA/OPP/EFED 2015a Acceptable
Daphnia magna, water flea, neonates [Cladocera: Daphniidae]	Agent: Boron Duration: 48 hours	48-hour LC_{50} = 141 mg B/L	Maier and Knight 1991
Daphnia magna [Cladocera: Daphniidae]	Agent: disodium tetraborate (anhydrous borax) in tap water free of chlorine Static exposure Duration: 24 hours	24-hour LC_{50} = 340 mg disodium tetraborate (anhydrous borax) 24-hour LC_{50} = 73 mg B/L 24-hour LC_0 = 61 mg disodium tetraborate (anhydrous borax) 24-hour LC_0 = 13 mg B/L 24-hour LC_{100} = 1930 mg disodium tetraborate (anhydrous borax) 24-hour LC_{100} = 415 mg B/L	Bringmann and Kuhn 1977, as cited in WHO 1998a and Hovatter and Ross 1995
Daphnia magna, water flea, <24-hours-old, 5/test concentration [Cladocera: Daphniidae]	Agent: Boric acid, analytical grade Static exposure Concentrations: not reported Duration: 48 hours	No kill concentration <200 mg B/L 48-hour LC_{50} = 1293 mg a.e./L (nominal) 48-hour LC_{50} = 226 mg B/L (nominal) Practically non-toxic on both a.e. and B basis	Lewis and Valentine 1981 U.S. EPA/OPP/EFED 2015a Supplemental/ Quantitative

Appendix 7: Toxicity to Aquatic Invertebrates *(continued)*

Species	Exposure	Response	Reference
Daphnia magna, water flea, neonates 10/concentration [Cladocera: Daphniidae]	Agent: Boron (H_3B0_3, AR grade) Concentrations: not reported Duration: 24 hours	24-hour EC_{50} = 319.8 g/m^3 (mg/L) 24-hour EC_{10} = 250.0 g/m^3 (mg/L)	Hickey 1989
Diptera			
Chironomus decorus, midge, 4th instar larvae [Diptera: Chironomidae]	Agent: Boron Concentrations: Duration: 96 hours	48-hr LC_{50} = 1376 mg B/L 96-hour NOAEC (for decreased growth) 10 mg B/L 96-hour LOAEC (significantly decreased growth) 20 mg B/L No 96-hour LC_{50} reported	Maier and Knight 1991
Ostracoda			
Cypris subglobosa (freshwater ostracod) [Ostracoda: Cyprididae]	Agent: Borax (Na2B4O7. 10H2O) reagent grade (>98-99.9% purity) Concentrations: not specified Duration: 48 hours	48-hour EC_{50} = 1645 mg B/L	Khangarot and Das 2009

<table>
<tr><th>Species</th><th>Exposure</th><th>Response</th><th>Reference</th></tr>
<tr><td>Decopoda</td><td></td><td></td><td></td></tr>
<tr><td>Litopenaeus vannamei (saltwater shrimp) [Decopoda: Penaeidae]</td><td>Agent: Boric acid (H_3BO_3, special grade, Fuchen Chemical Reagent Industry, Tianjin City, China)
Static renewal exposure
Concentrations at 3% salinity: 0, 20, 40, 80, 160, 320, or 640 mg/L
Concentrations at 20% salinity: 0, 30, 60, 120, 240, 480, or 960 mg/L
Duration: 96 hours

Working Note: The paper seems to indicate that boric acid was used to prepare the solutions but the exposures and reported toxicity values are given in unit of boron rather than boric acid. The EPA, however, appears to have interpreted the exposures and toxicity values in unit of boric acid rather than boron. The EPA interpretation may be correct. The paper is not unequivocally clear.</td><td>L. vannamei more sensitive to ambient boron toxicity at low salinity. LC_{50} values at 3.0% salinity significantly lower at 48 hours (p=0.013), 72 hours (p=0.000), and 96 hours (p=0.000), relative to toxicity values measured at 20% salinity.

3.0% salinity
<table><tr><th>Duration (Hours)</th><th>Mean LC_{50} (mg a.e./L)</th></tr><tr><td>24</td><td>552.55</td></tr><tr><td>48</td><td>153.35</td></tr><tr><td>72</td><td>50.14</td></tr><tr><td>96</td><td>25.05</td></tr></table>
20.0% salinity
<table><tr><th>Duration (Hours)</th><th>Mean LC_{50} (mg a.e./L)</th></tr><tr><td>24</td><td>598.13</td></tr><tr><td>48</td><td>219.52</td></tr><tr><td>72</td><td>147.80</td></tr><tr><td>96</td><td>80.06</td></tr></table>
EPA/OPP/EFED (2015a) reports the mean 96-hour LC_{50} values for 20% salinity only:
96-hour LC_{50} = 80.1 mg a.e./L
96-hour LC_{50} = 14.0 mg B/L
Slightly toxic on both a.e. and B basis.</td><td>Li et al. 2008
U.S. EPA/OPP/EFED 2015
Supplemental/ Quantitative
ECOTOX ID E111738

The 80.1 mg a.e./L value is used by U.S. EPA/OPP/EFED 2015a for risk characterization for estuarine/marine organisms.</td></tr>
<tr><td>Bivalves [Bivalvia]</td><td></td><td></td><td></td></tr>
<tr><td>Lampsilis siliquoidea, fatmucket clam, <5-days-old, juveniles [Unionoida: Unionidae]</td><td>Agent: Boric acid 99.6%
Static exposure
Duration: 96 hours</td><td>96-hour EC_{50} =784 mg a.e./L (measured)
96-hour EC_{50} =137 mg B/L (measured)
Practically non-toxic on both a.e. and B basis</td><td>U.S. EPA/OPP/EFED 2015a
Acceptable

Internal EPA study</td></tr>
<tr><td>Megalonaias nervosa, washboard mussel, <5-days-old, juveniles [Unionoida: Unionidae]</td><td>Agent: Boric acid 99.6%
Static exposure
Duration: 96 hours</td><td>Control <0.02 mg B/L
96-hour EC_{50} >3169 mg a.e./L (measured)
96-hour EC_{50} >544 mg B/L (measured)
Practically non-toxic on both a.e. and B basis</td><td>U.S. EPA/OPP/EFED 2015a
Acceptable

Internal EPA study</td></tr>
</table>

Appendix 7: Toxicity to Aquatic Invertebrates *(continued)*

Species	Exposure	Response	Reference
Ligumia recta, black sandshell mussel <5-days-old, juveniles [Unionoida: Unionidae]	Agent: Boric acid 99.6% Static exposure Duration: 96 hours	Control <0.02 mg B/L 96-hour EC_{50} =841 mg a.e./L (measured) 96-hour EC_{50} =147 mg B/L (measured) Practically non-toxic on both a.e. and B basis	U.S. EPA/OPP/EFED 2015a Acceptable Internal EPA study

Table A7-2: Chronic toxicity to Aquatic Invertebrates

Species	Exposure	Response	Reference
Daphnids			
Ceriodaphnia dubia, neonates 10/concentration [Cladocera: Daphniidae]	Agent: Boron (H_3B0_3, AR grade) Concentrations: not reported Duration: 14 days	LOEC = 18.0 g/m^3 (mg/L) NOEC = 10.0 g/m^3 (mg/L) See Table 3 for comparison of acute/chronic ratios	Hickey 1989
Daphnia magna, water flea, neonates [Cladocera: Daphniidae]	Agent: Boric acid, analytical grade Static renewal exposure Mean boron concentrations: control, 6, 13, 27, 53, or 106 Duration: 21 days	21-day LC_{50} = 53.2 mg B/L (based on adult mortality) **Endpoint** / **NOAEC (mg B/L)** / **LOAEC (mg B/L)** Length / 27 / 53 Brood size / 6 / 13 Number of young produced / 6 / 13 Most sensitive endpoints: brood size and total number of young produced	Lewis and Valentine 1981 U.S. EPA/OPP/EFED 2015a Supplemental/ Quantitative (Open literature study submitted by registrant conducted using acceptable protocol; however, due to lack of raw data and GLP compliance verification, EPA classifies study as supplemental data usable quantitatively.
Daphnia magna, water flea, <24-hours-old, 20/concentration [Cladocera: Daphniidae]	Agent: NOS Nominal concentrations: 0, 7, 14, 28, or 56, or 105 mg B/L Mean analyzed concentrations: 0, 6.4, 13. 6, 29.4, or 59.3 mg B/L Duration: 21 days Working Note: All toxicity values in the column to the right are given as mean measured concentrations.	21-day LC_{50} = 52.2 mg B/L (based on adult mortality) NOAEC = 37 mg a.e./L LOAEC = 77.8 mg a.e./L NOAEC (for reproductive parameters) = 6.4 mg B/L LOAEC (for reproductive parameters) = 13.6 mg B/L Sensitive endpoints: mean number of broods/daphnid; mean total young/daphnid; mean brood size/daphnid; and mean length. See Table 1 of paper. No adults survived to reproductive age at highest test concentration (105 mg B/L); however, survival was reduced significantly at 59.3 mg B/L No effects observed on time to first reproduction at concentrations ≤59.3 mg/L	Gersich 1984 U.S. EPA/OPP/EFED 2015a Supplemental/ Quantitative Open literature study submitted by registrant conducted using acceptable protocol; however, due to lack of raw data and GLP compliance verification, EPA classifies study as supplemental data usable quantitatively

Species	Exposure	Response	Reference
Daphnia magna, water flea, 1st instar [Cladocera: Daphniidae]	Agent: Boric acid 99.9% Static renewal exposure Concentrations: not reported Duration: 21 days	Most sensitive endpoint: number of young produced/ surviving female Adult survival significantly reduced at 320 mg a.e./L (56 mg B/L) NOAEC = 57 mg a.e./L LOAEC = 103 mg a.e./L NOAEC = 10 mg B/L (measured) LOAEC = 18 mg B/L (measured)	U.S. EPA/OPP/EFED 2015a MRID 48507004 Supplemental *Time to first brood release and growth of young were not assessed in the study.*
Daphnia magna, water flea, neonates 10/concentration [Cladocera: Daphniidae]	Agent: Boron (H_3B0_3, AR grade) Concentrations: not reported Duration: 14 days	LOEC = 32.0 g/m^3 (mg/L) NOEC = 18.0 g/m^3 (mg/L)	Hickey 1989
Bivalves [Bivalvia]			
Lampsilis siliquoidea, freshwater clam [Unionoida: Unionidae]	Agent: Boron Duration: 21 days	**Survival: (21 days)** **Whole-sediment (mg B/kg sediment dry weight)** *IC_{25}* / *NOEC* / *LOEC* 363.1 / 254.8 / 452.4 **Pore water (mg B/L)** *IC_{25}* / *NOEC* / *LOEC* 45.0 / 31.6 / 56.1 **Water only (mg B/L)** *IC_{25}* / *NOEC* / *LOEC* 38.4 / 31.6 / 56.1 **Growth: (21 days)** **Whole-sediment (mg B/kg sediment dry weight)** *IC_{25}* / *NOEC* / *LOEC* 310.6 / 80.6[a] / 143.4[a] **Pore water (mg B/L)** *IC_{25}* / *NOEC* / *LOEC* 38.5 / 10[a] / 10[a] **Water only (mg B/L)** *IC_{25}* / *NOEC* / *LOEC* 34.6 / 10[a] / 10[a] [a] Values markedly lower than the IC_{25} value due to low variability of this end point. Shell growth % coefficient of variation values ranged from 4.1 to 13.5 % in the three lowest boron exposures	Hall et al. 2014

Appendix 7: Toxicity to Aquatic Invertebrates *(continued)*

Species	Exposure	Response	Reference
Aquatic worms			
Lumbriculus variegatus (California blackworm) [Lumbriculida: Lumbriculidae]	Agent: Boron Duration: 28 days	**Survival: (28 days)** **Whole-sediment (B/kg sediment dry weight)** ***IC_{25}*** ***NOEC*** ***LOEC*** (61.7-171.6) 100.8 100.8 **Pore water (B/L)** ***IC_{25}*** ***NOEC*** ***LOEC*** 12.7 12.5 12.5 **Growth: (28 days)** **Whole-sediment (B/kg sediment dry weight)** ***IC_{25}*** ***NOEC*** ***LOEC*** 235.5 201.6 403.2 **Pore water (B/L)** ***IC_{25}*** ***NOEC*** ***LOEC*** 25.9 25.0 50.0	Hall et al. 2014

Appendix 8: Toxicity to Aquatic Plants

Table A8-1: Algae 210
Table A8-2: Macrophytes 212

Table A8-1: Algae

Species	Exposure	Response	Reference
Anabaena flosaquae, blue-green algae inoculum culture 3-days-old	Agent: Boric acid 99.7% Static exposure Concentration: not reported Duration: 96 hours	96-hour EC_{50} = 81.3 mg a.e./L NOAEC = 9.2 mg a.e./L LOAEC = 20 mg a.e./L 96-hour EC_{50} = 14.2 mg B/L NOAEC = 1.6 mg B/L LOAEC = 3.5 mg B/L (measured) Most sensitive endpoint was area under the growth curve. A supplemental component of the study suggested that boric acid is algistatic rather than algicidal.	U.S. EPA/OPP/EFED 2015a MRID 48820801 Acceptable **Note: Used by EFED in risk characterization for non-vascular aquatic plants. EC50 for non-listed and NOAEC for listed.**
Microcytsis aeruginosa, blue-green alga	Agent: NOS Duration: 72 hours	72-hour EC_3 = 20.3 mg B/L	Bringmann and Kuhn 1978, from German literature as cited in ECETOC 1997
Navicula pelliculosa, freshwater diatom, inoculum culture 3-days-old	Agent: Boric acid 99.7% Static exposure Concentration: not reported Duration: 96 hours	96-hour EC_{50} = 585 mg a.e./L NOAEC = 260 mg a.e./L LOAEC = 540 mg a.e./L 96-hour EC_{50} = 102 mg B/L NOAEC = 45.4 mg B/L LOAEC = 94.3 mg B/L (measured) Most sensitive endpoint was biomass	U.S. EPA/OPP/EFED 2015a MRID 48851201 Acceptable
Pseudokirchneriella subcapitata, green algae	Agent: Boric acid 99.9% Static exposure Concentration: not reported Duration: 74.5 hours	74.5-hour EC_{50} = 230 mg a.e./L NOAEC = 100 mg a.e./L LOAEC = 181 mg a.e./L 74.5-hour EC_{50} = 40.2 mg B/L NOAEC = 17.5 mg B/L LOAEC = 31.6 mg B/L (nominal but confirmed with selected measurements) Most sensitive endpoint was area under the growth curve.	U.S. EPA/OPP/EFED 2015a MRID 48507003 Supplemental/Quanti-tative *Study redone as MRID 48820804*

Appendix 8: Toxicity to Aquatic Plants *(continued)*

Species	Exposure	Response	Reference
Pseudokirchneriella subcapitata, green algae, inoculum culture 3-days-old	Agent: Boric acid 99.7% Static exposure Concentration: not reported Duration: 96 hours	96-hour EC_{50} = 124 mg a.e./L NOAEC = 66 mg a.e./L LOAEC = 150 mg a.e./L 96-hour EC_{50} = 21.7 mg B/L NOAEC = 11.5 mg B/L LOAEC = 26.2 mg B/L (measured) Most sensitive endpoint was cell density and area under the growth curve. *Boric acid has an algistatic, rather than algicidal effect (at test termination cells from 1000 mg a.e./L were exposed to 66 mg a.e./L for 4 days—961 fold increase).*	U.S. EPA/OPP/EFED 2015a MRID 48820804 Acceptable
Scenedesmus quadricauda, green alga	Agent: NOS Duration: 72 hours	72 h-EC_3= 16 mg B/L	Bringmann and Kuhn 1978, from German literature as cited in ECETOC 1997
Scenedesmus subspicatus, green algae	Agent: NOS Duration: 72 hours	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, from German literature as cited in ECETOC 1997
Skeletonema costatum, marine diatom, inoculum culture 8-days-old	Agent: Boric acid 99.7% Static exposure Concentration: not reported Duration: 96 hours	96-hour EC_{50} = 388 mg a.e./L NOAEC = 270 mg a.e./L LOAEC = 510 mg a.e./L 96-hour EC_{50} = 67.8 mg B/L NOAEC = 47.1 mg B/L LOAEC = 89.1 mg B/L (measured) Most sensitive endpoint was area under the growth curve. *Boric acid has an algistatic, rather than algicidal effect (at test termination cells from 1000 mg a.e./L were exposed to 250 mg a.e./L for 9 days—6.16 fold increase).*	U.S. EPA/OPP/EFED 2015a MRID 48820803 Supplemental/Quantitative *Final control density slightly below test standard causing uncertainty as to whether cells were in optimum logarithmic growth phase.*

See macrophytes on next page.

Table A8-2: Macrophytes

Species	Exposure	Response	Reference
Duckweed (*Lemna gibba* G3), inoculum culture 2-days-old	Agent: Boric acid, 99.7% Static-renewal exposure Concentrations: not reported Duration: 7 days	7-day EC_{50} = 163 mg a.e./L NOAEC = 60 mg a.e./L LOAEC = 130 mg a.e./L (based on reduced final biomass) 7-day EC_{50} = 28.5 mg B/L (measured) NOAEC = 11 mg B/L LOAEC = 22 mg B/L (based on reduced final biomass) Most sensitive endpoint was biomass based on dry weight.	U.S. EPA/OPP/EFED 2015a MRID 48820802 Acceptable **Note: Used by EFED in risk characterization for vascular aquatic plants. EC50 for non-listed and NOAEC for listed.**
Duckweed (*Lemna minor*)	Agent: Boric acid Concentrations: 0.017 (background), 20, 50, 100, and 200 mg B/L at pH 7 Concentrations: 0.017 (background), 1, 5, 10, 20, and 50 mg B/L at pH 5. Duration: 6 days	pH 7 (Table 2 of paper). NOAEC: 20 mg B/L 50 mg B/L: slight increase in growth rate LOAEC: 100 mg B/L based in reduced growth rate. Reduced growth reversible when plants were transferred to control media. 200 mg B/L: mortality in all plants. pH 5 (Table 1 of paper). No significant impact on growth	Brick 1985
Elodea sp., waterweed	Agent: Boric acid Concentrations: 0, 1, 2, 5, 10 and 250 mg B/L Duration: 21 days	21-day EC_{50} for decreased photosynthesis= 5 mg B/L	Nobel 1981, from German literature as cited in IPCS/WHO 1998
Myriophyllum sp., watermilfoil	Agent: Boric acid Concentrations: 0, 1, 2, 10 mg B/L Duration: 21 days	21-day EC_{50} for decreased photosynthesis = 5 mg B/L	Nobel 1981, from German literature as cited in IPCS/WHO 1998
Phragmites australis, common reed	Agent: Boric acid Concentrations: 1. 0.5, 1.0, 2.0, 4.0, 8.0, 16.0 mg B/L Duration: 2-3 months or 2 years Working Note: This is a container study in which water concentrations maintained at 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	IPCS/WHO 1998 and ECETOC 1997 citing Bergmann et al. 1995 from the German literature.

Appendix 8: Toxicity to Aquatic Plants *(continued)*

Species	Exposure	Response	Reference
Ranunculus sp, water buttercup	Agent: Boric acid Concentrations: 0, 1, 2, 10 mg B/L Duration: 21 days	21-day EC_{50} for decreased photosynthesis = 10 mg B/L	Nobel 1981, from German literature as cited in IPCS/WHO 1998

Working Note: ECETOX 1997, Table 14, summarizes additional older literature on macrophytes, including some field studies. Some of these are not well described relative to EPA studies and are not included in the above table.

Table A9-1: Effective Off-site Application Rate (lb/acre)

Site	Clay	Loam	Sand
Dry and Warm Location	0.019 (0 - 0.122)	0.00107 (0 - 0.033)	0 (0 - 0.0047)
Dry and Temperate Location	0.0218 (0.000263 - 0.148)	0.00226 (0 - 0.04)	0 (0 - 0.00315)
Dry and Cold Location	0.012 (0.00171 - 0.036)	0.00049 (0 - 0.0057)	0 (0 - 0)
Average Rainfall and Warm Location	0.187 (0.09 - 0.298)	0.052 (0.0153 - 0.124)	0.00241 (0.000048 - 0.0156)
Average Rainfall and Temperate Location	0.166 (0.057 - 0.276)	0.042 (0.0094 - 0.135)	0.00125 (0.000035 - 0.0187)
Average Rainfall and Cool Location	0.09 (0.033 - 0.183)	0.0208 (0.0024 - 0.083)	0.000199 (2.14E-07 - 0.0052)
Wet and Warm Location	0.152 (0.071 - 0.277)	0.035 (0.0093 - 0.103)	0.00092 (2.75E-05 - 0.0075)
Wet and Temperate Location	0.118 (0.048 - 0.236)	0.0226 (0.006 - 0.07)	0.000234 (2.48E-05 - 0.0085)
Wet and Cool Location	0.34 (0.193 - 0.49)	0.102 (0.048 - 0.196)	0.0053 (0.00032 - 0.0201)
Average of Central Values:	0.123	0.0309	0.00115
25th Percentile:	0.0218	0.00226	0
Maximum:	0.49	0.196	0.0201
Summary:	0.123 (0.0218 - 0.49)	0.0309 (0.00226 - 0.196)	0.00115 (0 - 0.0201)

Table A9-2: Concentration in Top 12 Inches of Soil (ppm)

Site	Clay	Loam	Sand
Dry and Warm Location	0.52 (0.5 - 0.52)	0.46 (0.45 - 0.46)	0.46 (0.45 - 0.46)
Dry and Temperate Location	0.52 (0.5 - 0.52)	0.46 (0.45 - 0.46)	0.46 (0.43 - 0.46)
Dry and Cold Location	0.52 (0.51 - 0.52)	0.46 (0.46 - 0.46)	0.46 (0.45 - 0.46)
Average Rainfall and Warm Location	0.48 (0.44 - 0.51)	0.44 (0.36 - 0.45)	0.39 (0.248 - 0.45)
Average Rainfall and Temperate Location	0.49 (0.44 - 0.51)	0.44 (0.36 - 0.46)	0.39 (0.248 - 0.45)
Average Rainfall and Cool Location	0.5 (0.43 - 0.51)	0.45 (0.34 - 0.46)	0.37 (0.25 - 0.43)
Wet and Warm Location	0.45 (0.287 - 0.48)	0.35 (0.241 - 0.43)	0.241 (0.231 - 0.301)
Wet and Temperate Location	0.44 (0.272 - 0.48)	0.35 (0.233 - 0.42)	0.236 (0.231 - 0.294)
Wet and Cool Location	0.43 (0.277 - 0.47)	0.37 (0.228 - 0.42)	0.248 (0.23 - 0.307)
Average of Central Values:	0.48	0.42	0.36
25th Percentile:	0.45	0.37	0.248
Maximum:	0.52	0.46	0.46
Summary:	0.48 (0.45 - 0.52)	0.42 (0.37 - 0.46)	0.36 (0.248 - 0.46)

Table A9-3: Concentration in Top 36 Inches of Soil (ppm)

Site	Clay	Loam	Sand
Dry and Warm Location	0.172 (0.166 - 0.173)	0.152 (0.151 - 0.153)	0.152 (0.152 - 0.152)
Dry and Temperate Location	0.172 (0.165 - 0.174)	0.153 (0.151 - 0.153)	0.153 (0.153 - 0.153)
Dry and Cold Location	0.174 (0.172 - 0.174)	0.154 (0.154 - 0.154)	0.154 (0.154 - 0.154)
Average Rainfall and Warm Location	0.164 (0.152 - 0.17)	0.15 (0.145 - 0.152)	0.152 (0.135 - 0.152)
Average Rainfall and Temperate Location	0.166 (0.153 - 0.171)	0.151 (0.147 - 0.153)	0.153 (0.136 - 0.153)
Average Rainfall and Cool Location	0.17 (0.163 - 0.173)	0.153 (0.15 - 0.153)	0.153 (0.139 - 0.153)
Wet and Warm Location	0.164 (0.153 - 0.169)	0.15 (0.132 - 0.151)	0.131 (0.078 - 0.15)
Wet and Temperate Location	0.167 (0.148 - 0.171)	0.151 (0.115 - 0.153)	0.124 (0.078 - 0.151)
Wet and Cool Location	0.154 (0.138 - 0.169)	0.147 (0.118 - 0.152)	0.139 (0.078 - 0.151)
Average of Central Values:	0.167	0.151	0.146
25th Percentile:	0.164	0.15	0.139
Maximum:	0.174	0.154	0.154
Summary:	0.167 (0.164 - 0.174)	0.151 (0.15 - 0.154)	0.146 (0.139 - 0.154)

Table A9-4: Maximum Penetration into Soil Column (inches)

Site	Clay	Loam	Sand
Dry and Warm Location	18 (8 - 24)	18 (4 - 30)	18 (8 - 36)
Dry and Temperate Location	18 (12 - 30)	18 (8 - 36)	30 (8 - 36)
Dry and Cold Location	18 (18 - 30)	18 (18 - 30)	30 (24 - 36)
Average Rainfall and Warm Location	30 (24 - 36)	36 (30 - 36)	36 (36 - 36)
Average Rainfall and Temperate Location	30 (24 - 36)	36 (30 - 36)	36 (36 - 36)
Average Rainfall and Cool Location	30 (24 - 36)	36 (30 - 36)	36 (36 - 36)
Wet and Warm Location	36 (36 - 36)	36 (36 - 36)	36 (36 - 36)
Wet and Temperate Location	36 (36 - 36)	36 (36 - 36)	36 (36 - 36)
Wet and Cool Location	36 (36 - 36)	36 (36 - 36)	36 (36 - 36)
Average of Central Values:	28	30	32.7
25th Percentile:	18	18	30
Maximum:	36	36	36
Summary:	28 (18 - 36)	30 (18 - 36)	32.7 (30 - 36)

Table A9-5: Stream, Maximum Peak Concentration in Surface Water (ug/L or ppb)

Site	Clay	Loam	Sand
Dry and Warm Location	22.4 (0 - 150)	1.81 (0 - 58)	0 (0 - 6.5)
Dry and Temperate Location	20.3 (0.5 - 133)	4 (0 - 32)	0 (0 - 3.9)
Dry and Cold Location	13.3 (2.9 - 34)	0.9 (0 - 7.9)	2.9E-06 (0 - 0.025)
Average Rainfall and Warm Location	78 (27.5 - 205)	30.4 (7.1 - 100)	9.2 (0.6 - 122)
Average Rainfall and Temperate Location	74 (19.6 - 285)	25.3 (6.7 - 128)	5.8 (0.4 - 82)
Average Rainfall and Cool Location	51 (11.6 - 124)	15.7 (1.67 - 71)	5.1 (0.18 - 72)
Wet and Warm Location	60 (19.2 - 203)	22.7 (7.9 - 90)	69 (23.6 - 169)
Wet and Temperate Location	43 (14.4 - 143)	18.7 (4.6 - 63)	63 (19.5 - 146)
Wet and Cool Location	92 (47 - 235)	37 (13.9 - 98)	51 (18.5 - 134)
Average of Central Values:	50.4	17.4	22.6
25th Percentile:	22.4	4	2.90E-06
Maximum:	285	128	169
Summary:	50.4 (22.4 - 285)	17.4 (4 - 128)	22.6 (2.90E-06 - 169)

Table A9-6: Stream, Annual Average Concentration in Surface Water (ug/L or ppb)

Site	Clay	Loam	Sand
Dry and Warm Location	0.24 (0 - 1.3)	0.013 (0 - 0.4)	0 (0 - 0.05)
Dry and Temperate Location	0.26 (0.004 - 1.52)	0.029 (0 - 0.5)	0 (0 - 0.03)
Dry and Cold Location	0.15 (0.027 - 0.5)	0.007 (0 - 0.07)	2.4E-08 (0 - 0.0007)
Average Rainfall and Warm Location	1.41 (0.7 - 2.58)	0.5 (0.16 - 1)	0.17 (0.008 - 5.3)
Average Rainfall and Temperate Location	1.29 (0.5 - 2.45)	0.3 (0.09 - 1.11)	0.13 (0.007 - 6.2)
Average Rainfall and Cool Location	0.8 (0.26 - 1.73)	0.19 (0.025 - 1.01)	0.17 (0.007 - 5.4)
Wet and Warm Location	1.26 (0.6 - 4.2)	0.6 (0.23 - 7.6)	6.2 (1.92 - 12.3)
Wet and Temperate Location	1.1 (0.5 - 5.2)	0.5 (0.12 - 8)	6.7 (1.55 - 11.2)
Wet and Cool Location	1.65 (0.9 - 3.05)	0.6 (0.4 - 6.7)	4.8 (1.41 - 12.6)
Average of Central Values:	0.91	0.304	2.02
25th Percentile:	0.26	0.029	2.40E-08
Maximum:	5.2	8	12.6
Summary:	0.91 (0.26 - 5.2)	0.304 (0.029 - 8)	2.02 (2.40E-08 - 12.6)

Table A9-7: Pond, Maximum Peak Concentration in Surface Water (ug/L or ppb)

Site	Clay	Loam	Sand
Dry and Warm Location	12.8 (0 - 85)	0.7 (0 - 23.1)	0 (0 - 3.11)
Dry and Temperate Location	14.5 (0.17 - 82)	1.48 (0 - 26.2)	0 (0 - 1.62)
Dry and Cold Location	7.9 (1.13 - 24.3)	0.3 (0 - 3.8)	1.2E-06 (0 - 0.031)
Average Rainfall and Warm Location	134 (61 - 228)	37 (11 - 90)	11.9 (0.7 - 340)
Average Rainfall and Temperate Location	117 (37 - 211)	28.9 (6.2 - 95)	10.5 (0.5 - 380)
Average Rainfall and Cool Location	62 (22.9 - 129)	15.2 (1.78 - 74)	11.3 (0.4 - 307)
Wet and Warm Location	68 (29 - 167)	24.2 (11.2 - 193)	176 (36 - 430)
Wet and Temperate Location	40 (14.8 - 131)	14.2 (3.9 - 211)	119 (23.2 - 282)
Wet and Cool Location	41 (19.3 - 107)	19.7 (6.4 - 192)	143 (41 - 308)
Average of Central Values:	55.2	15.7	52.4
25th Percentile:	14.5	1.48	1.20E-06
Maximum:	228	211	430
Summary:	55.2 (14.5 - 228)	15.7 (1.48 - 211)	52.4 (1.20E-06 - 430)

Table A9-8: Pond, Annual Average Concentration in Surface Water (ug/L or ppb)

Site	Clay	Loam	Sand
Dry and Warm Location	6.1 (0 - 47)	0.4 (0 - 11.2)	0 (0 - 2.44)
Dry and Temperate Location	7.3 (0.11 - 52)	0.5 (0 - 16)	0 (0 - 1.06)
Dry and Cold Location	4.1 (0.6 - 17.9)	0.17 (0 - 2.09)	6.0E-07 (0 - 0.011)
Average Rainfall and Warm Location	74 (31.4 - 150)	21.1 (6.1 - 58)	4.8 (0.4 - 172)
Average Rainfall and Temperate Location	65 (24.5 - 149)	16.6 (2.67 - 50)	4.5 (0.14 - 135)
Average Rainfall and Cool Location	35 (12.1 - 86)	8.7 (0.9 - 38)	3.7 (0.06 - 105)
Wet and Warm Location	23.3 (8.2 - 58)	8.5 (3.2 - 72)	70 (12.2 - 229)
Wet and Temperate Location	12 (3.3 - 46)	4.4 (1 - 80)	54 (10.5 - 125)
Wet and Cool Location	20.2 (8.1 - 54)	7.7 (2.95 - 48)	32 (8.9 - 131)
Average of Central Values:	27.4	7.56	18.8
25th Percentile:	7.3	0.5	6.00E-07
Maximum:	150	80	229
Summary:	27.4 (7.3 - 150)	7.56 (0.5 - 80)	18.8 (6.00E-07 - 229)