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Environmental Health Criteria 204

BORON

First draft prepared by Ms C. Smallwood, US Environmental Protection Agency, Cincinnati, Ohio, USA

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World Health Organization
Geneva, 1998
The International Programme on Chemical Safety (IPCS), established in 1980, is a joint venture of the United Nations Environment Programme (UNEP), the International Labour Organisation (ILO), and the World Health Organization (WHO). The overall objectives of the IPCS are to establish the scientific basis for assessment of the risk to human health and the environment from exposure to chemicals, through international peer review processes, as a prerequisite for the promotion of chemical safety, and to provide technical assistance in strengthening national capacities for the sound management of chemicals.

The Inter-Organization Programme for the Sound Management of Chemicals (IOMC) was established in 1995 by UNEP, ILO, the Food and Agriculture Organization of the United Nations, WHO, the United Nations Industrial Development Organization and the Organisation for Economic Cooperation and Development (Participating Organizations), following recommendations made by the 1992 UN Conference on Environment and Development to strengthen cooperation and increase coordination in the field of chemical safety. The purpose of the IOMC is to promote coordination of the policies and activities pursued by the Participating Organizations, jointly or separately, to achieve the sound management of chemicals in relation to human health and the environment.

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NOTE TO READERS OF THE CRITERIA MONOGRAPHS

Every effort has been made to present information in the criteria monographs as accurately as possible without unduly delaying their publication. In the interest of all users of the Environmental Health Criteria monographs, readers are requested to communicate any errors that may have occurred to the Director of the International Programme on Chemical Safety, World Health Organization, Geneva, Switzerland, in order that they may be included in corrigenda.

* * *

A detailed data profile and a legal file can be obtained from the International Register of Potentially Toxic Chemicals, Case postale 356, 1219 Châtelaine, Geneva, Switzerland (telephone no. + 41 22 - 9799111, fax no. + 41 22 - 7973460, E-mail irptc@unep.ch).
Environmental Health Criteria

P R E A M B L E

Objectives

In 1973, the WHO Environmental Health Criteria Programme was initiated with the following objectives:

(i) to assess information on the relationship between exposure to environmental pollutants and human health, and to provide guidelines for setting exposure limits;

(ii) to identify new or potential pollutants;

(iii) to identify gaps in knowledge concerning the health effects of pollutants;

(iv) to promote the harmonization of toxicological and epidemiological methods in order to have internationally comparable results.

The first Environmental Health Criteria (EHC) monograph, on mercury, was published in 1976, and since that time an ever-increasing number of assessments of chemicals and of physical effects have been produced. In addition, many EHC monographs have been devoted to evaluating toxicological methodology, e.g. for genetic, neurotoxic, teratogenic, and nephrotoxic effects. Other publications have been concerned with epidemiological guidelines, evaluation of short-term tests for carcinogens, biomarkers, effects on the elderly, and so forth.

Since its inauguration, the EHC Programme has widened its scope, and the importance of environmental effects, in addition to health effects, has been increasingly emphasized in the total evaluation of chemicals.

The original impetus for the Programme came from World Health Assembly resolutions and the recommendations of the 1972 UN Conference on the Human Environment. Subsequently, the work became an integral part of the International Programme on Chemical Safety (IPCS), a cooperative programme of UNEP, ILO, and WHO. In this manner, with the strong support of the new partners, the importance of occupational health and environmental effects was fully
recognized. The EHC monographs have become widely established, used, and recognized throughout the world.

The recommendations of the 1992 UN Conference on Environment and Development and the subsequent establishment of the Intergovernmental Forum on Chemical Safety with the priorities for action in the six programme areas of Chapter 19, Agenda 21, all lend further weight to the need for EHC assessments of the risks of chemicals.

Scope

The criteria monographs are intended to provide critical reviews on the effects on human health and the environment of chemicals and of combinations of chemicals and physical and biological agents. As such, they include and review studies that are of direct relevance for the evaluation. However, they do not describe every study carried out. Worldwide data are used and are quoted from original studies, not from abstracts or reviews. Both published and unpublished reports are considered, and it is incumbent on the authors to assess all the articles cited in the references. Preference is always given to published data. Unpublished data are used only when relevant published data are absent or when they are pivotal to the risk assessment. A detailed policy statement is available that describes the procedures used for unpublished proprietary data so that this information can be used in the evaluation without compromising its confidential nature (WHO (1990) Revised Guidelines for the Preparation of Environmental Health Criteria Monographs. PCS/90.69, Geneva, World Health Organization).

In the evaluation of human health risks, sound human data, whenever available, are preferred to animal data. Animal and in vitro studies provide support and are used mainly to supply evidence missing from human studies. It is mandatory that research on human subjects is conducted in full accord with ethical principles, including the provisions of the Helsinki Declaration.

The EHC monographs are intended to assist national and international authorities in making risk assessments and subsequent risk management decisions. They represent a thorough evaluation of risks and are not, in any sense, recommendations for regulation or
standard setting. These latter are the exclusive purview of national and regional governments.

Content

The layout of EHC monographs for chemicals is outlined below.

- **Summary** — a review of the salient facts and the risk evaluation of the chemical
- **Identity** — physical and chemical properties, analytical methods
- **Sources of exposure**
- **Environmental transport, distribution, and transformation**
- **Environmental levels and human exposure**
- **Kinetics and metabolism in laboratory animals and humans**
- **Effects on laboratory mammals and *in vitro* test systems**
- **Effects on humans**
- **Effects on other organisms in the laboratory and field**
- **Evaluation of human health risks and effects on the environment**
- **Conclusions and recommendations for protection of human health and the environment**
- **Further research**
- **Previous evaluations by international bodies, e.g. IARC, JECFA, JMPR**

Selection of chemicals

Since the inception of the EHC Programme, the IPCS has organized meetings of scientists to establish lists of priority chemicals for subsequent evaluation. Such meetings have been held in: Ispra, Italy, 1980; Oxford, United Kingdom, 1984; Berlin, Germany, 1987; and North Carolina, USA, 1995. The selection of chemicals has been based on the following criteria: the existence of scientific evidence that the substance presents a hazard to human health and/or the environment; the possible use, persistence, accumulation, or degradation of the substance shows that there may be significant human or environmental exposure; the size and nature of populations at risk (both human and other species) and risks for the environment; international concern, i.e. the substance is of major interest to several countries; adequate data on the hazards are available.
If an EHC monograph is proposed for a chemical not on the priority list, the IPCS Secretariat consults with the cooperating organizations and all the Participating Institutions before embarking on the preparation of the monograph.

**Procedures**

The order of procedures that result in the publication of an EHC monograph is shown in the flow chart. A designated staff member of IPCS, responsible for the scientific quality of the document, serves as Responsible Officer (RO). The IPCS Editor is responsible for layout and language. The first draft, prepared by consultants or, more usually, staff from an IPCS Participating Institution, is based initially on data provided from the International Register of Potentially Toxic Chemicals and from reference databases such as Medline and Toxline.

The draft document, when received by the RO, may require an initial review by a small panel of experts to determine its scientific quality and objectivity. Once the RO finds the document acceptable as a first draft, it is distributed, in its unedited form, to well over 150 EHC contact points throughout the world who are asked to comment on its completeness and accuracy and, where necessary, provide additional material. The contact points, usually designated by governments, may be Participating Institutions, IPCS Focal Points, or individual scientists known for their particular expertise. Generally, some four months are allowed before the comments are considered by the RO and author(s). A second draft incorporating comments received and approved by the Director, IPCS, is then distributed to Task Group members, who carry out the peer review, at least six weeks before their meeting.

The Task Group members serve as individual scientists, not as representatives of any organization, government, or industry. Their function is to evaluate the accuracy, significance, and relevance of the information in the document and to assess the health and environmental risks from exposure to the chemical. A summary and recommendations for further research and improved safety aspects are also required. The composition of the Task Group is dictated by the range of expertise required for the subject of the meeting and by the need for a balanced geographical distribution.
The three cooperating organizations of the IPCS recognize the important role played by nongovernmental organizations. Representatives from relevant national and international associations may be invited to join the Task Group as observers. While observers may provide a valuable contribution to the process, they can speak only at the invitation of the Chairperson. Observers do not participate in the final evaluation of the chemical; this is the sole responsibility of the Task Group members. When the Task Group considers it to be appropriate, it may meet in camera.

All individuals who as authors, consultants, or advisers participate in the preparation of the EHC monograph must, in addition to serving in their personal capacity as scientists, inform the RO if at any time a conflict of interest, whether actual or potential, could be perceived in their work. They are required to sign a conflict of interest statement. Such a procedure ensures the transparency and probity of the process.

When the Task Group has completed its review and the RO is satisfied as to the scientific correctness and completeness of the document, the document then goes for language editing, reference checking, and preparation of camera-ready copy. After approval by the Director, IPCS, the monograph is submitted to the WHO Office of Publications for printing. At this time, a copy of the final draft is sent to the Chairperson and Rapporteur of the Task Group to check for any errors.

It is accepted that the following criteria should initiate the updating of an EHC monograph: new data are available that would substantially change the evaluation; there is public concern for health or environmental effects of the agent because of greater exposure; an appreciable time period has elapsed since the last evaluation.

All Participating Institutions are informed, through the EHC progress report, of the authors and institutions proposed for the drafting of the documents. A comprehensive file of all comments received on drafts of each EHC monograph is maintained and is available on request. The Chairpersons of Task Groups are briefed before each meeting on their role and responsibility in ensuring that these rules are followed.
WHO TASK GROUP ON ENVIRONMENTAL HEALTH CRITERIA FOR BORON

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IPCS TASK GROUP ON ENVIRONMENTAL HEALTH CRITERIA FOR BORON

A WHO Task Group on Environmental Health Criteria for Boron met in Washington, DC, USA, from 18 to 22 November 1996. The meeting was organized by the WHO Regional Office for the Americas (AMRO) on behalf of the IPCS. Dr H. Otterstetter, WHO AMRO, opened the meeting and welcomed the participants. Dr B.H. Chen, IPCS, welcomed the participants on behalf of the Director of IPCS and the three IPCS cooperating organizations (UNEP/ILO/WHO). The Task Group reviewed and revised the draft criteria monograph and made an evaluation of the risks for human health and the environment from exposure to boron.

The first draft of this monograph was prepared by Ms C. Smallwood of the US EPA in Cincinnati. The second draft was also prepared by Ms Smallwood, incorporating comments received following the circulation of the first draft to the IPCS Contact Points for Environmental Health Criteria monographs. Dr R. Goyer, Chairman of the Task Group, contributed significantly to the final text of the EHC for Boron.

Dr B.H. Chen, member of the IPCS Central Unit, and Ms M. Sheffer, Scientific Editor, Ottawa, Canada, were responsible for the overall scientific content and linguistic editing, respectively.

The efforts of all who helped in the preparation and finalization of the document are gratefully acknowledged.

Financial support for this Task Group meeting was provided by the US EPA.
ABBREVIATIONS

BMD Benchmark dose
CAS Chemical Abstracts Service
CL Confidence limit
CNS Central nervous system
EPA Environmental Protection Agency (USA)
FDA Food and Drug Administration (USA)
FSH Follicle stimulating hormone
GLP Good Laboratory Practices
HSDB Hazardous Substances Data Bank
ICP Inductively coupled plasma
ICP-AES Inductively coupled plasma atomic emission spectroscopy
ICP-MS Inductively coupled plasma mass spectroscopy
LH Luteinizing hormone
LOAEL Lowest-observed-adverse-effect level (human and animal toxicity)
LOEC Lowest-observed-effect concentration (environmental effects)
MATC Maximum acceptable toxicant concentration (environmental effects)
MMAD Median mass aerodynamic diameter
NADPH Reduced nicotinamide adenine dinucleotide phosphate
NIOSH National Institute for Occupational Safety and Health
NOAEL No-observed-adverse-effect level (human and animal toxicity)
NOEC No-observed-effect concentration (environmental effects)
NOHS National Occupational Hazard Survey
RR Rate ratio (or Relative risk)
RTECS Registry of Toxic Effects of Chemical Substances
SBR Standardized birth ratio
SGOT Serum glutamic-oxaloacetic transaminase
SGPT Serum glutamic-pyruvic transaminase
TI Tolerable intake
TLV Threshold limit value
TRI Toxic Release Inventory (US EPA)
1. SUMMARY, CONCLUSIONS, AND RECOMMENDATIONS

1.1 Summary

1.1.1 Identity, natural occurrence, and analytical methods

Boron is a naturally occurring element that is found in the form of borates in the oceans, sedimentary rocks, coal, shale, and some soils. It is widely distributed in nature, with concentrations of about 10 mg/kg in the Earth's crust (range: 5 mg/kg in basalts to 100 mg/kg in shales) and about 4.5 mg/litre in the ocean.

The most important commercial borate products and minerals are borax pentahydrate, borax, sodium perborate, boric acid, colemanite, and ulexite. At the low concentrations and near-neutral pH found in most biological fluids, monomeric $\text{B(OH)}_3$ will be the predominant species present (with some $\text{B(OH)}_4^-$), 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). Sodium perborate hydrolyses to give hydrogen peroxide plus metaborate; consequently, it may exhibit chemical and toxicological properties that are somewhat different from those of the other borates.

Inductively coupled plasma (ICP) methods are preferred for the analysis of the low levels of boron found in biological and environmental samples; colorimetric methods must be used with caution.

1.1.2 Production, uses, environmental fate, and sources of exposure

Economic borate deposits are rare, occurring in arid regions of Turkey, the USA, Argentina, Chile, Russia, China, and Peru. Total world production of boron minerals — mainly colemanite, ulexite, tincal, and kernite — was approximately 2 750 000 tonnes in 1994. About 800 000 tonnes of commercial borate products, expressed as $\text{B}_2\text{O}_3$, were manufactured from the boron minerals.

Major end uses for borate include insulation- and textile-grade fibreglass, laundry bleach (sodium perborate), borosilicate glass, fire
retardants, agricultural fertilizers and herbicides (as a trace element), and enamels, frits, and ceramic glazes, as well as a myriad of miscellaneous applications.

Boron enters the environment mainly through the weathering of rocks, boric acid volatilization from seawater, and volcanic activity. Boron is also released from anthropogenic sources to a lesser extent. Anthropogenic sources include agricultural, refuse, and fuel wood burning, power generation using coal and oil, glass product manufacture, use of borates/perborates in the home and industry, borate mining/processing, leaching of treated wood/paper, and sewage/sludge disposal. Many of these sources are difficult to quantify.

Atmospheric emissions of borates and boric acid in particulate and vapour form occur as a result of volatilization from the sea, volcanic activity, and, to a lesser extent, mining operations, glass and ceramics manufacturing, the application of agricultural chemicals, and coal-fired power plants. Boron is not present in the atmosphere at significant levels; however, the total amount present in the atmosphere at any one time is significant owing to the huge volume of the atmosphere. Based on their water solubility, borates would not be expected to persist to a significant degree in the atmosphere.

Boron can be released into water and soil water through weathering processes and, to a much smaller extent, through anthropogenic discharges such as sewage outfalls. Adsorption–desorption reactions are expected to be the only significant mechanism influencing the fate of boron in water. The extent of boron adsorption depends on the pH of the water and the concentration of boron in solution.

Boron is adsorbed onto soil particles, with the degree of adsorption depending on the type of soil, pH, salinity, organic matter content, iron and aluminium oxide content, iron- and aluminium-hydroxy content, and clay content. Boron adsorption can vary from being fully reversible to irreversible, depending on the soil type and condition.
Borate ions present in aqueous solution are essentially in their fully oxidized state. No aerobic processes are likely to affect their speciation, and no biotransformation processes are reported. Therefore, there are unlikely to be any differences in boron species due to biotransformation.

The octanol/water partition coefficient of boric acid has been measured as 0.175, indicating a low bioaccumulation potential. Laboratory experiments with aquatic organisms have confirmed this potential. Plants accumulate boron; however, uptake is affected by the pH of the soil solution, temperature, light intensity, and the concentration of other elements (e.g. calcium and potassium). The results of studies of boron accumulation in plants, insects, and fish have shown that boron bioaccumulates in plants but does not biomagnify in aquatic food-chains.

Boron occurs in soils at concentrations ranging from 10 to 300 mg/kg (average 30 mg/kg), depending on the type of soil, amount of organic matter, and amount of rainfall. Concentrations of boron in surface water are dependent on such factors as the geochemical nature of the drainage area, proximity to marine coastal regions, and inputs from industrial and municipal effluent discharges. Concentrations of boron in surface water range widely, from 0.001 to as much as 360 mg/litre. However, mean boron concentrations for waters of Europe, Pakistan, Russia, and Turkey are typically well below 0.6 mg/litre. Concentrations of boron in water in Japan, South Africa, and South America are generally below 0.3 mg/litre. Typical boron concentrations in North American waters are below 0.1 mg/litre, with about 90% at or below 0.4 mg/litre.

Boron accumulates in aquatic and terrestrial plants but does not magnify through the food-chain. Concentrations of boron have been shown to range between 26 and 382 mg/kg in submerged aquatic freshwater plants, from 11.3 to 57 mg/kg in freshwater emergent vegetation, and from 2.3 to 94.7 mg/kg dry weight in terrestrial plants. Based on wet weights, boron concentrations in marine invertebrates and fish are similar to the levels found in the exposure media, between 0.5 and 4 mg/kg. The biocccentration factor for two freshwater fish species was found to be 0.3.
Boron concentrations in ambient air range from <0.5 to approximately 80 ng/m³, with an average over the continents of 20 ng/m³.

Close similarity of boron concentrations in groundwater, fresh surface water, and drinking-water indicates that boron is not removed in the treatment of groundwater and fresh surface water used for drinking-water.

Intakes of boron for humans are expected to be 0.44 µg/day from ambient air, 0.2–0.6 mg/day from drinking-water, and 1.2 mg/day from the diet. Average boron intake from the soil is considered to be 0.5 µg/day. A reasonable estimate of boron exposure from consumer products is 0.1 mg/day.

1.1.3 Kinetics and biological monitoring

The pharmacokinetics of boron appear to be quite similar across species in the following respects:

a) Absorption of borates is essentially complete (approximately 95% in humans and rats), and boron appears rapidly in the blood and body tissues of several mammalian species following ingestion.

b) Distribution of boron in mammals appears to occur by passive diffusion throughout the body fluids. In contrast to soft tissues and blood, bone shows selective uptake of boron (≥4 times higher than serum) and significantly longer retention times.

c) Metabolism of boric acid is thermodynamically unfavourable in biological systems. Thus, the ionic species in systemic circulation are expected to be equivalent across mammals. This eliminates a major source of potential uncertainty for risk extrapolation, as interspecies differences in enzymatic pathways and/or metabolic rates do not need to be taken into consideration.

d) Elimination kinetics (especially route of elimination and terminal half-life) also appear to be similar for humans and rats.
The similarities in pharmacokinetic parameters between humans and rats, the species defining the no-observed-adverse-effect level (NOAEL) for laboratory studies, reduce the uncertainty for risk extrapolation between these two species.

1.1.4 Effects on experimental animals and humans

The data regarding developmental and reproductive toxicity show that lower fetal body weight in rats is the critical effect. The NOAEL for lower fetal body weight is 9.6 mg boron/kg body weight per day. The lowest-observed-adverse-effect level (LOAEL), at which rats show slight (~5%) fetal body weight differences and rib anomalies, is about 13 mg boron/kg body weight per day. As dose level increases, the effects that are seen (and the doses at which they are seen) are:

a) further rib effects and testicular pathology in the rat (~25 mg boron/kg body weight per day);

b) decreased fetal body weight and increased fetal cardiovascular malformations in the rabbit, and severe testicular pathology in the rat (~40 mg boron/kg body weight per day);

c) testicular atrophy and sterility in the rat (~55 mg boron/kg body weight per day); and

d) reduced fetal body weight in the mouse (~80 mg boron/kg body weight per day).

Animal studies on mice and rats showed no evidence of carcinogenicity of boric acid. Based on the lack of human data and the limited animal data, boron is not classifiable as to its human carcinogenicity.

Only a few human studies have been conducted to assess health effects associated with exposure to boron compounds. The available data show that exposure is associated with short-term irritant effects on the upper respiratory tract, nasopharynx, and eye. These effects, however, appear to be short-term and reversible. The sole long-term (7-year) follow-up study failed to identify any long-term health effects, although a healthy worker effect cannot be entirely ruled out.
given the rate of attrition (47%). Two descriptive studies assessed fertility and secondary sex ratios in relation to exposure. Neither study reported a detrimental effect on demonstrated fertility for its select sample. Although an excess percentage of female births has been suggested, the absence of statistical significance and attention to other co-variates known to affect sex ratios warrants careful interpretation of this finding. No studies have been identified that assess the spectrum of reproductive outcomes, such as time-to-pregnancy, conception delays, spontaneous abortions, and sperm analyses in males. The role of other lifestyle or behavioural factors in relation to health and fertility requires further study to identify potentially sensitive populations and to evaluate reproductive effects more fully.

1.1.5 Effects on organisms in the environment

Bacteria are relatively tolerant towards boron. Acute and chronic effect concentrations range between 8 and 340 mg boron/litre, with most values greater than 18 mg boron/litre. More sensitive are protozoa. Tests with *Entosiphon* and *Paramecium* yielded 72-h no-observed-effect concentrations (NOECs) and EC₃ values between 0.3 and 18 mg boron/litre.

Boron is an essential micronutrient for cyanobacteria and diatoms. Standard chronic tests with freshwater green algae resulted in no-effect concentrations between 10 and 24 mg boron/litre. Blue-green algae appear to be similar in sensitivity, with an 8-day EC₃ of 20 mg boron/litre.

Based on acute toxicity values, invertebrates are less sensitive to boron than microorganisms. For several species, 24- to 48-h EC₅₀ values ranged from 95 to 1376 mg boron/litre, with most values in the 100–200 mg boron/litre range. Chronic toxicity studies with *Daphnia magna* gave NOECs ranging between 6 and 10 mg boron/litre. Slightly lower NOEC values were obtained from laboratory and field biocenosis studies. The 28-day laboratory study consisting of six trophic stages yielded a NOEC of 2.5 mg boron/litre. Long-term outdoor pond and field studies (not including fish) yielded NOECs up to 1.52 mg boron/litre.
Acute tests with several fish species yielded toxicity values ranging from about 10 to nearly 300 mg boron/litre. Rainbow trout (*Oncorhynchus mykiss*) and zebra fish (*Brachydanio rerio*) were the most sensitive, providing values around 10 mg boron/litre.

The toxicity of boron to early life stages of fish has been documented for several species in reconstituted water. Embryonic and early larval stages of rainbow trout, largemouth bass (*Micropterus salmoides*), channel catfish (*Ictalurus punctatus*), and goldfish (*Carassius auratus*) were exposed to boron, as boric acid or borax, from fertilization up to 8 days post-hatch in soft or hard water. Neither water hardness nor the form of boron consistently affected embryo-larval survival of fish. Rainbow trout was the most sensitive species. The NOECs for rainbow trout ranged from 0.009 to 0.103 mg boron/litre.

The effect of natural dilution water on boron toxicity was determined by using surface waters collected from three locations, with boron concentrations of 0.023, 0.091, and 0.75 mg/litre. No adverse effects were determined up to 0.75 mg boron/litre. Lowest-observed-effect concentrations (LOECs) ranged from 1.1 to 1.73 mg boron/litre. One test using deep (600 m) well-water, typically used for aquatic toxicity tests, from a contract laboratory located in Wareham, Massachusetts, USA, yielded a NOEC of >18.0 mg boron/litre. Hence, reconstituted water exposures appeared to overestimate the toxicity determined in natural waters, possibly as a result of nutrient deficiency in the former.

Boron has been known since the 1920s to be an essential micronutrient for higher plants, with interspecies differences in the levels required for optimum growth. Boron plays a role in cell division, metabolism, and membrane structure and function. Boron in the form of borates occurs naturally in fruits, nuts, and vegetables. There is a small range between deficiency and excess uptake (toxicity) in plants. Boron deficiencies in terrestrial plants have been reported in many countries. Boron deficiency is more likely to occur in light-textured, acid soils in humid regions because of boron’s susceptibility to leaching. Boron excesses usually occur in soil solutions from geologically young deposits, arid soils, soils derived from marine
sediments, and soils contaminated by pollutant sources, such as releases from coal-fired power plants and mining operations. Irrigation water is one of the main sources of high boron levels resulting in toxicity in the field.

Mallard (Anas platyrhynchos) duckling growth was adversely affected at dietary levels of 30 and 300 mg boron/kg, and survival was reduced at 1000 mg/kg.

1.2 Conclusions

Boron is a naturally occurring element that is found in nature in the form of borates in the oceans, sedimentary rocks, coal, shale, and some soils. Natural sources of borates released into the environment are the oceans, geothermal steam, and natural weathering of clay-rich sedimentary rocks. Boron is also released from anthropogenic sources to a lesser extent.

Boron is an essential micronutrient for higher plants, with interspecies differences in the levels required for optimum growth. Boron deficiency in terrestrial plants has been observed in many countries throughout the world. There is a small range between deficiency and toxicity in some plants.

Comparison of the environmental no-effect concentration (1 mg/litre) with the general ambient environmental levels of boron indicates that the risk of adverse effects of boron on the aquatic ecosystem is low. In a few boron-rich environments, natural levels will be higher. It is reasonable to assume that aquatic organisms in such habitats may be adapted to the local conditions.

For humans, boron exposure occurs primarily through the diet and drinking-water. The mean global boron concentration in drinking-water was considered to be between 0.1 and 0.3 mg boron/litre.

For the general population, the greatest boron exposure comes from the oral intake of food. The mean daily intake of boron in the diet is about 1.2 mg.
In humans and animals, boric acid and borate are absorbed from the gastrointestinal and respiratory tracts. More than 90% of administered doses of these compounds are absorbed, as evidenced by excretion in the urine, which is rapid, occurring over a few to several days.

Animal experiments have shown that boron in the form of boric acid and borate demonstrates reproductive and developmental toxicity at levels that are approximately 100- to 1000-fold greater than normal exposure levels. There is a lack of sufficient toxicity data on humans. The tolerable intake (TI) of boron was set as 0.4 mg/kg body weight per day. The allocation of the TI in various media should be based on the exposure data of individual countries.

1.3 Recommendations

a) Water and food guideline values should be based on the TI provided by this document.

b) The TI should be applied with the understanding that boron may provide a physiological benefit for human health.

c) It should be recognized in applying standards that boron is essential for some constituents of the environment (e.g. boron is an essential micronutrient for higher plants).

d) Dietary supplements that exceed the TI should be avoided.
2. IDENTIFY, PHYSICAL AND CHEMICAL PROPERTIES, AND ANALYTICAL METHODS

This chapter deals with the identity and physical and chemical properties of the inorganic borates of importance in commerce, as well as the analytical methods used to determine boron concentrations in various media.

2.1 Identity

Elemental boron (B) is a member of Group IIIIB of the periodic table, along with aluminium, gallium, indium, and thallium. It has an atomic number of 5 and a relative atomic mass of 10.81. Boron is never found in the elemental form in nature. Its chemistry is complex and resembles that of silicon (Cotton & Wilkinson, 1988). The Chemical Abstracts Service (CAS), National Institute for Occupational Safety and Health (NIOSH) Registry of Toxic Effects of Chemical Substances (RTECS), and Hazardous Substances Data Bank (HSDB) numbers for boron are 7440-42-8, ED7350000, and 4482, respectively.

The borates used most widely in commerce are listed in approximate decreasing order of usage in Table 1, along with their formulae and CAS numbers. Elemental boron is included, even though its production is quite small. Throughout this document, the term "borax" refers to disodium tetraborate decahydrate (see Table 1).

2.2 Physical and chemical properties

Elemental boron exists as a solid at room temperature, either as black monoclinic crystals or as a yellow or brown amorphous powder when impure. The amorphous and crystalline forms of boron have specific gravities of 2.37 and 2.34, respectively. Boron exists as a mixture of the $^{10}$B (19.78%) and $^{11}$B (80.22%) isotopes (Budavari et al., 1989). Boron is a relatively inert metalloid except when in contact with strong oxidizing agents. Boron dust exposed to air is flammable and an explosion hazard. It also reacts violently when ground with lead fluoride and silver fluoride (Lewis, 1992). Physical and chemical properties of elemental boron and the most important borates in commerce are provided in Table 2.
Table 1. Boron compounds of commerce in approximate decreasing order of usage

<table>
<thead>
<tr>
<th>Substance</th>
<th>Formula</th>
<th>CAS No.</th>
</tr>
</thead>
<tbody>
<tr>
<td>Borax pentahydrate (disodium tetraborate</td>
<td>( \text{Na}_2[\text{B}_4\text{O}_5(\text{OH})_4]\cdot3\text{H}_2\text{O} )  &amp; 3754418</td>
<td></td>
</tr>
<tr>
<td>tetraborate pentahydrate)</td>
<td>(( \text{Na}_2\text{B}_4\text{O}_7\cdot5\text{H}_2\text{O} ))</td>
<td></td>
</tr>
<tr>
<td>Borax (disodium tetraborate decahydrate)</td>
<td>( \text{Na}_2[\text{B}_4\text{O}_5(\text{OH})_4]\cdot8\text{H}_2\text{O} )  &amp; 1303-96-4</td>
<td></td>
</tr>
<tr>
<td></td>
<td>(( \text{Na}_2\text{B}_4\text{O}_7\cdot10\text{H}_2\text{O} ))</td>
<td></td>
</tr>
<tr>
<td>Ulexite</td>
<td>( \text{NaCa}[\text{B}_5\text{O}_6(\text{OH})_6]\cdot5\text{H}_2\text{O} )  &amp; 1319-33-1</td>
<td></td>
</tr>
<tr>
<td></td>
<td>(( \text{Na}_2\text{O}\cdot2\text{CaO}\cdot3\text{B}_2\text{O}_3\cdot16\text{H}_2\text{O} ))</td>
<td></td>
</tr>
<tr>
<td>Colemanite</td>
<td>( \text{Ca}[\text{B}_3\text{O}_4(\text{OH})_3]\cdot\text{H}_2\text{O} )    &amp; 1318-33-8</td>
<td></td>
</tr>
<tr>
<td></td>
<td>(( 2\text{CaO}\cdot3\text{B}_2\text{O}_3\cdot5\text{H}_2\text{O} ))</td>
<td></td>
</tr>
<tr>
<td>Sodium perborate tetrahydrate</td>
<td>( \text{Na}_2[\text{B}_2\text{O}_4(\text{OH})_4]\cdot6\text{H}_2\text{O} )  &amp; 10486-00-7</td>
<td></td>
</tr>
<tr>
<td></td>
<td>(( \text{NaBO}_3\cdot4\text{H}_2\text{O} ))</td>
<td></td>
</tr>
<tr>
<td>Sodium perborate monohydrate</td>
<td>( \text{Na}_2[\text{B}_2\text{O}_4(\text{OH})_4] )                         &amp; 10332-33-9</td>
<td></td>
</tr>
<tr>
<td></td>
<td>(( \text{NaBO}_3\cdot\text{H}_2\text{O} ))</td>
<td></td>
</tr>
<tr>
<td>Boric acid</td>
<td>( \text{B(OH)}_3 )                                                             &amp; 10043-35-3</td>
<td></td>
</tr>
<tr>
<td></td>
<td>(( \text{H}_3\text{BO}_3 ))</td>
<td></td>
</tr>
<tr>
<td>Anhydrous borax (disodium tetraborate)</td>
<td>( \text{Na}_2\text{B}_2\text{O}_7 ) (amorphous)                           &amp; 1330-43-4</td>
<td></td>
</tr>
<tr>
<td>Boron oxide</td>
<td>( \text{B}_2\text{O}_3 ) (amorphous)                                 &amp; 1303-86-2</td>
<td></td>
</tr>
<tr>
<td>Boron(^b)</td>
<td>( \text{B} )                                                                 &amp; 7440-42-8</td>
<td></td>
</tr>
</tbody>
</table>

\(^a\) US EPA (1991); ATSDR (1992); Culver et al. (1994b).

\(^b\) Produced in small quantities.

Sodium perborates are persalts that are hydrolytically unstable because they contain characteristic boron–oxygen–oxygen bonds that react with water to form hydrogen peroxide and stable sodium metaborate (\( \text{NaBO}_2\cdot\text{nH}_2\text{O} \)). This hydrolysis reaction is the basis of the use of perborates as bleaches in detergents at high (70–100 °C) temperature. At lower washing temperatures (25–70 °C), activators are needed; these react with peroxide to give peracids, which are stronger oxidants and give bleaching effects at lower temperatures.
<table>
<thead>
<tr>
<th>Substance</th>
<th>Relative molecular mass</th>
<th>Colour</th>
<th>% boron</th>
<th>Relative density</th>
<th>Water solubility</th>
<th>Melting point (°C)</th>
<th>Boiling point (°C)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Borax pentahydrate</td>
<td>291.35</td>
<td>White</td>
<td>14.85</td>
<td>1.81</td>
<td>3.6 g/100 g @ 20 °C</td>
<td>742</td>
<td>—</td>
</tr>
<tr>
<td>Borax</td>
<td>381.37</td>
<td>Colourless</td>
<td>11.34</td>
<td>1.73</td>
<td>5.92 g/100 g @ 25 °C</td>
<td>75, decomposes</td>
<td>—</td>
</tr>
<tr>
<td>Ulexite</td>
<td>810.6</td>
<td>White</td>
<td>13.33</td>
<td>1.62</td>
<td>Slightly soluble</td>
<td>Decomposes</td>
<td>—</td>
</tr>
<tr>
<td>Colemanite</td>
<td>411.1</td>
<td>White</td>
<td>15.78</td>
<td>2.42</td>
<td>Slightly soluble</td>
<td>Decomposes</td>
<td>—</td>
</tr>
<tr>
<td>Sodium perborate</td>
<td>153.9</td>
<td>White</td>
<td>7.03</td>
<td>1.73</td>
<td>23 g/litre @ 20 °C</td>
<td>Decomposes</td>
<td>—</td>
</tr>
<tr>
<td>Sodium perborate</td>
<td>99.8</td>
<td>White</td>
<td>10.83</td>
<td>—</td>
<td>15 g/litre @ 20 °C</td>
<td>Decomposes</td>
<td>—</td>
</tr>
<tr>
<td>monohydrate</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Boric acid</td>
<td>61.84</td>
<td>Colourless</td>
<td>17.48</td>
<td>1.435 @ 15 °C</td>
<td>63.5 g/litre @ 30 °C</td>
<td>169</td>
<td>—</td>
</tr>
<tr>
<td>Anhydrous borax</td>
<td>201.22</td>
<td>White</td>
<td>21.49</td>
<td>2.367</td>
<td>2.5556 g/100 g @ 25 °C</td>
<td>741</td>
<td>1575</td>
</tr>
<tr>
<td>Boron oxide</td>
<td>69.62</td>
<td>Colourless</td>
<td>31.06</td>
<td>2.46</td>
<td>Slightly soluble</td>
<td>450</td>
<td>1860</td>
</tr>
<tr>
<td>Boron</td>
<td>10.81</td>
<td>Black crystal or yellow-brown amorphous</td>
<td>100</td>
<td>2.3</td>
<td>Insoluble</td>
<td>2300</td>
<td>~3500</td>
</tr>
</tbody>
</table>

* Muetterties (1967); Windholz et al. (1983); Weast et al. (1985); ACGIH (1991); ATSDR (1992); Lewis (1993); US NLM (1993); Culver et al. (1994b).
Boric acid is a very weak acid, with a pKₐ of 9.15, and therefore boric acid and the sodium borates exist predominantly as undissociated boric acid \([\text{B(OH)}_3]\) in dilute aqueous solution below pH 7; above pH 10, the metaborate anion \(\text{B(OH)}_4^-\) becomes the main species in solution. Between pH 6 and pH 11 and at high concentration (>0.025 mol/litre), highly water soluble polyborate ions such as \(\text{B}_3\text{O}_3(\text{OH})_4^-\), \(\text{B}_4\text{O}_5(\text{OH})_4^{2-}\), and \(\text{B}_5\text{O}_6(\text{OH})_4^{-}\) are formed.

The chemical and toxicological properties of borax pentahydrate, borax, boric acid, and other borates are expected to be similar on a mol boron/litre equivalent basis when dissolved in water or biological fluids at the same pH and low concentration. Boric oxide will exhibit properties identical to those of boric acid, as it is an anhydride that will hydrolyse to give boric acid. Sodium perborate monohydrate and tetrahydrate hydrolyse to give hydrogen peroxide and borate. Thus, they are oxidants and may have chemical and toxicological properties that are different from those of the other borates.

The chemical properties of sodium metaborate differ from those of the other sodium borates, in that the metaborate has a much higher solubility and alkalinity in aqueous solution. Thus, the solubility in water at 20 °C is 41.9 parts sodium metaborate octahydrate (compared with 4.7 for borax) per hundred parts saturated solution by weight. The pH of an aqueous solution of the metaborate at 20 °C ranges from 10.5 at 0.1% w/w to 12.0 at 18% w/w (compared with pH 9.24 for borax over a wide range of concentrations).

### 2.3 Conversion factors

#### 2.3.1 Conversion factors of ppm and mg/m³ for boron

\[
\begin{align*}
1 \text{ ppm} &= 0.4421 \text{ mg/m}^3 \\
1 \text{ mg/m}^3 &= 2.262 \text{ ppm}
\end{align*}
\]

#### 2.3.2 Conversion factors for boron compounds to boron

- dose of boric acid \(\times 0.175 = \) equivalent dose of boron
- dose of borax \(\times 0.113 = \) equivalent dose of boron
- dose of anhydrous borax \(\times 0.215 = \) equivalent dose of boron
dose of sodium perborate tetrahydrate × 0.070 = equivalent dose of boron

dose of sodium perborate monohydrate × 0.108 = equivalent dose of boron

dose of metaboric acid × 0.247 = equivalent dose of boron

2.4 Analytical methods

Analyses of environmental and biological samples for boron content utilize a variety of preparative methods (see Table 3).

<table>
<thead>
<tr>
<th>Media</th>
<th>Extraction method</th>
<th>Reference</th>
</tr>
</thead>
<tbody>
<tr>
<td>Biological</td>
<td>Acid digestion with:</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Microwave</td>
<td>Pennington et al. (1991)</td>
</tr>
<tr>
<td></td>
<td>Dry ashing</td>
<td>Wilkner (1986)</td>
</tr>
<tr>
<td></td>
<td>Wet ashing</td>
<td>Kowalenko (1979)</td>
</tr>
<tr>
<td></td>
<td>Low temperature, wet ashing</td>
<td>Banuelos et al. (1992)</td>
</tr>
<tr>
<td></td>
<td>Freeze drying</td>
<td>Iyengar et al. (1990)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Smith et al. (1991)</td>
</tr>
<tr>
<td>Soil</td>
<td>Hot water solubility</td>
<td>Odom (1980)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Cumakov (1991)</td>
</tr>
<tr>
<td>Water</td>
<td>Liquid–liquid extraction from acidified solutions into chloroform</td>
<td>Aznarez et al. (1985)</td>
</tr>
<tr>
<td></td>
<td>Ion exchange column</td>
<td>Sekerka &amp; Lechner (1990)</td>
</tr>
</tbody>
</table>

The preferred method for analysis of boron in bone, plasma, and food is inductively coupled plasma atomic emission spectroscopy (ICP-AES) (Hunt, 1989). It is also used for tumour, blood, liver, skin, and cell suspensions (Barth et al., 1991). It also has been used for wastewater (Huber, 1982) and fish tissues (Hamilton & Wiedmeyer, 1990). Detection limits range from 0.005 to 0.05 mg boron/litre in the solution analysed.
Inductively coupled plasma mass spectroscopy (ICP-MS) is used to measure boron concentrations in plant, rat, and human samples. Isotope ratios ($^{10}\text{B}/^{11}\text{B}$) can be measured accurately (Vanderpool et al., 1994). Using direct nebulization, ICP-MS can give a detection limit of 1 ng/g in human blood, human serum, orchard leaves, and total diet (Smith et al., 1991).

ICP-MS is the most widely used non-spectrophotometric method for analysis of boron, as it uses small volumes of sample, is fast, and applies to a wide range of materials (fresh and saline water, sewage wastewater, soils, and plant samples, as well as the biological materials mentioned above). Interferences are minimal or can be removed (Gregoire, 1990). ICP-MS can detect boron down to 0.15 µg/litre.

The ability to measure the boron isotope ratio accurately allows studies starting with pure $^{10}\text{B}$ compounds and following the isotopic dilution in biological systems. This is particularly useful, as no stable radioactive boron isotopes usable as tracers exist. A number of boron compounds made with nearly isotopically pure $^{10}\text{B}$ are available for such studies.

When expensive ICP equipment is not available, colorimetric/spectrophotometric methods can be utilized. However, many of these methods are subject to interference and should be used with caution; they should also preferably be calibrated against an ICP method.

Azomethine-H has been used to analyse boron in environmental water samples and is very sensitive, with a detection limit of 0.02 mg/litre (Lopez et al., 1993). The well-known curcumin method is subject to interference by nitrate, chloride, and fluoride but is claimed to be applicable to samples with 0.1–1 mg boron/litre (Black et al., 1993).

A simple, sensitive spectrophotometric method for determination of boron in soils, plant materials, and water uses Alizarin Red S but is also subject to interference (Garcia-Campana et al., 1992). Flow injection analysis utilizing the sorbitol/borate complex and Methyl Orange indicator for eye lotion samples has a detection limit of 0.02 mg/litre (Nose & Zenki, 1991).
Another method of analysis of boron uses neutron activation and mass spectrometric analysis. Mass spectrometric assay of $^3$He from decay of tritium produced by thermal neutron irradiation of boron to give $^4$He has been described by Clarke et al. (1987a). The method, useful for trace levels of boron in blood and other biological samples, can detect $10^{-8}$ g boron/g of sample (Clarke et al., 1987b). Iyengar et al. (1990) used this method to determine boron in citrus leaves, human erythrocytes, and food items, all with freeze-dried samples.
3. SOURCES OF HUMAN AND ENVIRONMENTAL EXPOSURE

3.1 Natural occurrence

Boron, in the form of various inorganic borates, is widely distributed in low concentrations throughout nature. It constitutes about 10 mg/kg of the Earth’s crust, ranging from 5 mg/kg in basalts to 100 mg/kg in shales (Woods, 1994). The majority of the boron resides in the ocean, at an average concentration of about 4.5 mg/litre (Weast et al., 1985). Economic deposits of borate minerals are rare and are usually found in arid desert regions with a geological history of volcanic and/or hydrothermal activity (Mellor, 1980). Major world deposits are found in Turkey, the USA, Argentina, Russia, Chile, China, and Peru (Culver et al., 1994b).

The most abundant boron mineral is tourmaline, an aluminium borosilicate that contains about 3.1% boron (Muetteertites, 1967). It is not a practicable source of usable boron, as it is widely distributed as a minor component of rocks. Economic borate minerals include tincal, kernite, colemanite, and ulexite.

Natural sources of borate released to air are the oceans (largest), volcanoes, and geothermal steam (Graedel, 1978). Natural weathering of clay-rich sedimentary rocks on land surfaces accounts for a large proportion of the boron mobilized into soils and the aquatic environment, amounting to some 360 000 tonnes of boron annually (Bertine & Goldberg, 1971). Although few data are available for quantifying boron released from industrial sources, natural weathering and seawater evaporation are considered greater sources than industrial emissions (see chapter 4).

3.2 Mining and production

The total world production of boron minerals in 1994 was approximately 2 750 000 tonnes (Lyday, 1996). The main commercial borate minerals are colemanite, kernite, ulexite, and tincal. Approximately 800 000 tonnes of commercial borate products, expressed as $\text{B}_2\text{O}_3$, were manufactured from boron minerals in 1994. The two
largest producers are the USA and Turkey. Further mining and production facilities exist in Argentina, Bolivia, China, Chile, Peru, and Russia (Lyday, 1996). Most US production of borates occurs in California, where colemanite, ulexite, tincal, kernite, and brines are processed. These minerals are also processed elsewhere in the world, as are ascharite, hydroboracite, datolite, etc.

Disodium tetraborate (borax) containing 5 or 10 molecules of water is produced mainly from sodium-containing borate ores. The mined ore is crushed and ground before dissolution in a hot recycled aqueous solution containing some borax. Insoluble gangue (clay particles) present in the hot slurry is separated off to produce a clear concentrated borax solution. Evaporative cooling of this solution to selected temperatures results in crystallization of the desired products, which are then separated from the residual liquor and dried (personal communication from Borax US to the IPCS, 1995).

Boric acid is produced mainly from sodium- or calcium-containing borate ores. The mined ore is crushed and ground before being reacted with sulfuric acid in the presence of a hot aqueous recycled liquor containing some boric acid. The resultant slurry contains insoluble gangue and either calcium or sodium sulfate by-product. After separation of unwanted insoluble gangue, recovery of the boric acid product is similar to that for borax (personal communication from Borax US to the IPCS, 1995).

### 3.3 Uses and release

The end uses of boron minerals and of borate products are diverse. Estimated amounts of borate consumed in the USA for the major end uses in 1992 are listed in Table 4 (Lyday, 1993). Partial data for Europe are also included (ECETOC, 1997). It should be noted that vitreous products such as fibreglass, borosilicate glass, and enamels, frits, and glazes are not significant sources of potential human exposure, because the boron is tied up tightly in the glassy structure. All of the boron from the sodium perborate contained in detergents ultimately enters the wastewater stream.
Sources of Human and Environmental Exposure

Table 4. Estimated amount consumed (as $B_2O_3$) for boric acid, borates, and boron minerals in the USA in 1992$^a$ and in Europe in 1993$^b$

<table>
<thead>
<tr>
<th>Use</th>
<th>Consumption (tonnes)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>USA</td>
</tr>
<tr>
<td>Insulation-grade fibreglass</td>
<td>129 000</td>
</tr>
<tr>
<td>Textile-grade fibreglass</td>
<td>78 500</td>
</tr>
<tr>
<td>Soaps and detergents</td>
<td>38 600</td>
</tr>
<tr>
<td>Borosilicate glass</td>
<td>34 400</td>
</tr>
<tr>
<td>Fire retardants</td>
<td>13 400</td>
</tr>
<tr>
<td>Agriculture</td>
<td>11 100</td>
</tr>
<tr>
<td>Enamels, frits, and ceramic glazes</td>
<td>9 300</td>
</tr>
<tr>
<td>Metallurgy</td>
<td>3 700</td>
</tr>
<tr>
<td>Nuclear applications</td>
<td>900</td>
</tr>
</tbody>
</table>

$^b$ ECETOC (1997).
$^c$ Does not include minerals.
$^d$ No data.

The average market shares for the USA, Europe, and Japan in 1992 were about 23% (fibreglass), 17% (detergents), 11% (enamels/glazes), and 11% (glass) for major end uses (personal communication from Borax US to the IPCS, 1995).

Other minor uses include cosmetics and pharmaceuticals (as a pH buffer), boron neutron capture therapy (for cancer treatment), and pesticides (personal communication from Borax US to the IPCS, 1995). The cancer treatment application utilizes a boron compound made with all $^{10}$B isotope, which preferentially accumulates in tumour versus normal tissue (Barth & Soloway, 1994). Subsequent irradiation of the patient with thermal neutrons produces $^7$Li plus alpha particles. The latter have a destructive path length of about the diameter of a cell, thereby selectively destroying the cancer. Research in this field is being pursued in Japan and, to a lesser extent, in the USA.

Boron enters the environment mainly through the weathering of rocks, volatilization from seawater, agricultural, refuse, and fuel wood burning, power generators (coal and oil combustion), the manufacture of glass products and other boron-containing compounds, the industrial and household use of boron-containing products (including
soaps and detergents), borax mining and processing, leaching from treated wood and paper, geothermal releases, chemical plants, and sewage and sludge disposal (Versar, Inc., 1975; Larsen, 1988; ATSDR, 1992; Anderson et al., 1994a). Boron is not present in the atmosphere at significant levels because of its low volatility, but the total amount in the air is very significant owing to the huge volume of the atmosphere (see chapter 4).

Boron releases to water occur from municipal sewage containing perborates from detergents and also in runoff from areas using boron-containing herbicides or fertilizers (Waggott, 1969; Nolte, 1988; Butterwick et al., 1989). Boron levels in sewage sludge from 23 cities in the USA ranged from 7.1 to 53.3 mg/kg (Mumma et al., 1984). It has been estimated that 11,800 tonnes of boron are released yearly in coal fly ash from coal combustion (Bertine & Goldberg, 1971). Versar, Inc. (1975) estimated US boron air emissions as 10,500 tonnes annually from mining, processing, and coal burning. Few quantitative data on boron releases are available, because boron is not included in the US Environmental Protection Agency (EPA) Toxic Release Inventory (TRI) (ATSDR, 1992).
4. ENVIRONMENTAL TRANSPORT, DISTRIBUTION, AND TRANSFORMATION

4.1 Transport and distribution between media

4.1.1 Air

Boron is not present in the atmosphere at significant levels (Sprague, 1972), but the total amount in the air is very significant owing to the huge volume of the atmosphere. Borates exhibit low volatility; consequently, boron would not be expected to be present to a significant degree as a vapour in the atmosphere. Atmospheric emissions of borates and boric acid in particulate (<1–45 μm in size) or vapour form occur as a result of volatilization of boric acid from the sea, volcanic activity, mining operations, glass and ceramics manufacturing, the application of agricultural chemicals, and coal-fired power plants. As a particulate, boron would be removed from the atmosphere either by dry deposition or by wet deposition because of its relatively high water solubility (Versar, Inc., 1975; Gladney et al., 1978). Based on analogy with data on general particulate residence times (Nriagu, 1979), the half-life of airborne boron particles is expected to be on the order of days, depending on the size of the particles and atmospheric conditions.

Seawater evaporation is the biggest contribution to boron in air. The global removal of boron from marine sources has been estimated at between 800 000 and 4 000 000 tonnes/year and compares with an estimate of 2 000 000–7 200 000 tonnes/year for the total global release (Anderson et al., 1994a). Anderson et al. (1994a) estimate that the total anthropogenic release of boron to the atmosphere is between 180 000 and 650 000 tonnes/year (9–27% of the total global release). In spite of all these releases, the atmospheric concentration of boron is low (mean boron concentrations range from <0.5 to approximately 80 ng/m³).

4.1.2 Water and sediment

Waterborne boron may be adsorbed by soils and sediments. Adsorption–desorption reactions are expected to be the only
EHC 204: Boron

significant mechanism influencing the fate of boron in water (Rai et al., 1986). The extent of boron adsorption depends on the pH of the water and the concentration of boron in solution. The greatest adsorption is generally observed at pH 7.5–9.0 (Waggott, 1969; Keren & Mezuman, 1981; Keren et al., 1981).

Simsiman et al. (1987) conducted a field investigation to determine the leachability and groundwater transport of major and minor elements, including boron, from ash disposal ponds at the coal-fired Columbia Power Plant in Portage, Wisconsin, USA. The site is underlain by sands interspersed with lenses of silt and clay overlying sandstone (10–20 m below the surface). The soil pH ranged from 7.1 to 8.8, and the organic matter content was 0.2–0.8%. Boron plumes were identified in the groundwater at least 120 m down-gradient of the ponds. The boron plume from the secondary fly ash pond extended into the sandstone (26–30 m), which suggested rapid downward infiltration of the leachate. However, attenuation of the boron occurred at some point between the pond and the aquifer, based on observed decreases of approximately 40% in the boron concentration.

Barber et al. (1988) monitored the extent of groundwater contamination emanating from sewage disposal beds near Falmouth, Massachusetts, USA, by mapping the distribution of boron. Under the pH conditions of the aquifer (pH 5–7), dissolved boron occurred as the neutral undissociated orthoboric acid species, which should be transported with little sorption. The boron plume was 3500 m long, 1100 m wide, and 30 m deep during sampling in 1985.

Deverel & Millard (1988) demonstrated that boron is present in the oxidized, alkaline, shallow groundwater of the western San Joaquin Valley, California, USA. Boron was found to be geochemically mobile, with concentrations significantly correlated ($\alpha = 0.05$) with groundwater salinity in the alluvial-fan and basin-trough geological zones.

Corwin (1986) speculated that the adsorption of boron on sediments provides a means by which boron may persist for long periods of time in aquatic systems. The desorption (or leaching) of boron from the sediments would provide a long-term source until a
system equilibrium could be reached, based on differences in the concentrations of boron in the water column and in the sediment both at the sediment–water interface and with increasing depth below the interface. The primary desorption mechanism would be diffusion.

Boron levels (as admixed borate salt) as high as 1900 mg/kg have been reported in coal fly ash. Cox et al. (1978) reported that approximately 50% of the boron in 0.5-g samples of fly ash was leached from the ash into water within 2 h; the leaching rate increased with increased acidity. In a boron dissolution study, Hollis et al. (1988) observed that 60% of the boron was removed from 6 g of ash after three extractions at pH 9, whereas 100% was removed at pH 6 after two extractions. In a long-term (2-year) leachability study, Dudas (1981) observed that boron was readily leached, probably as a result of the moderate solubility of borate salts. Consequently, the disposal of coal fly ash in lagoons could provide a source of boron contamination in aquatic systems.

4.1.3 Soil

Boron is adsorbed onto the surfaces of soil particles, with the degree of adsorption depending on the type of soil, pH, salinity, organic matter content, iron and aluminium oxide content, iron- and aluminium-hydroxy content, and clay content (Sprague, 1972). Boron adsorption can vary from being fully reversible to irreversible (Rai et al., 1986; Shani et al., 1992). The lack of reversibility may be the result of solid-phase formation on mineral surfaces (Rai et al., 1986) and/or the slow release of boron by diffusion from the interior of clay minerals (Griffin & Burau, 1974).

At acidic pH, boron exists in solutions in the form of undissociated boric acid; at alkaline pH, it is present as a borate ion, which reaches maximum adsorption at pH 8.5–9 (Sprague, 1972). Sims & Bingham (1967) reported that hydroxy iron and aluminium compounds, present as interlayer-contained materials, coatings on individual particles, or impurities, resulted in increased boron retention in layer silicates. Rhoades et al. (1970) observed that in the silt and sand fractions of arid-zone soils, the sites of boron adsorption are the magnesium-hydroxy clusters and coatings found on the weathering
surfaces of ferromagnesian minerals and micaceous layer silicate minerals. Marzadoori et al. (1991) reported that the amount of boron adsorbed by soil was considerably greater after the organic matter had been removed from the soil. An increase in oxalate-extractable iron and aluminium in the soil was observed after destruction of the organic matter. It was suggested that a portion of the iron and aluminium oxides as well as other possible adsorption sites are generally coated or occluded by organic matter and become active only after its removal.

Couch & Grim (1968) studied the uptake of boron in illite clays and determined that uptake was enhanced at higher boron soil solution concentrations in direct relationship to the salinity and temperature of the solution. Following 30 days of treatment in soils containing 1 mol boric acid/litre at salinities of 0.1, 1.0, or 3.0 mol CaCl₂/litre, boron levels increased by 56, 70, and 98 mg/kg, respectively. Treatment of illites at 1 mol boric acid/litre for 30 days at 60 °C yielded 55 mg boron/kg, whereas the same concentration at 215 °C for 12 h yielded 180 mg boron/kg. The investigators also observed a direct relationship between the specific surface area of the clay types and boron uptake. Boron uptake in the illite clays was characterized as initially rapid adsorption, followed by diffusion of boron into the clay structure, requiring several months to reach equilibrium.

Several investigators have used either the Langmuir or the Freundlich adsorption equation to describe the relationship between adsorption and desorption of boron in soils. The Langmuir equation is based on the total adsorptive capacity of the soil, the concentrations of adsorbed boron and boron in solution, and an adsorption equilibrium constant (K), which represents the bonding energy of the soil. Using this equation, Hatcher & Bower (1958) determined that an equilibrium exists between boron in solid and liquid phases. At soil pH values of 6.6–7.7, the predominant boron species in the aqueous phase is undissociated boric acid, and the principal mechanism of retention is by reversible, molecular adsorption, which is non-uniform based on the energy characteristics of the bonding sites. These investigators also showed that boron desorption was reversible; in other words, boron that leached into the soil solution could again be adsorbed. However, based on the Freundlich adsorption isotherms, Elrashidi & O’Connor
(1982) observed incomplete adsorption reversibility in some soils from New Mexico, USA, at higher boron concentrations.

Biggar & Fireman (1960) determined that the fixation of boron in soils occurs by one of three mechanisms: physical (molecular) adsorption, in which the boron is held to the surface of the soil by van der Waals bonds; anion exchange; or chemical precipitation. Chemical adsorption involves ionic and covalent bonding. The investigators speculated that the initial adsorption is probably molecular in nature, followed by the formation of surface compounds that result in an increase in adsorption sites, particularly at higher boron concentrations in the soil solution. At higher concentrations, chemical bonding of borate ions with hydroxyl ions on the soil surface results in boron fixation to soluble aluminium, silicon, and iron. This same mechanism (chemisorption) was observed by Couch & Grim (1968) for the uptake of borate ions to clay mineral surfaces. The presence of calcium ions, drying, and high pH values will tend to increase the amount of fixed boron. Wetting and drying of the soil will increase the maximum adsorption capacity and bonding energy of the soil for boron.

Many of the surface boron compounds initially formed by adsorption mechanisms may be unstable and leached by water. However, as a result of the equilibrium that exists between adsorbed and dissolved boron in soils, the adsorbed boron may act as a buffer, impeding the leaching of excess boron from soils. Wierenga et al. (1975) conducted a study to determine the downward movement of boron through a sandstone formation in New Mexico, USA. The experimental dispersion coefficient was calculated as 1.06 cm$^2$/day, primarily resulting from diffusion. Assuming an average annual rainfall of 20 cm/year and an average annual recharge of 10% of the annual precipitation, the investigators determined that it would take 500 years for the boron front to reach a depth of 35 m into the sandstone. As the groundwater table at this site is at 86 m, Wierenga et al. (1975) calculated that it would take 1628 years for boron, at a concentration one-half that of the surface concentration, to reach the groundwater. A 10-fold increase in annual recharge from precipitation would reduce the transit time by one-tenth.
Bingham et al. (1971) concluded that the single most important property of soil that will influence the mobility of boron is the abundance of amorphous aluminium oxide. Gerritse et al. (1982) showed that the mobility of boron in sludge-amended sandy and sandy loam soils was increased as a result of complexation with dissolved organic compounds, high ionic strengths of the soil solutions, and other factors.

4.1.4 Vegetation and wildlife

Hingston (1986) investigated the components of the biogeochemical cycle for boron in two eucalypt forests. The importance of the biological component of the cycle was indicated by the amount of boron stored within trees (2.1 and 2.5 kg/ha for the two forests) compared with the amount of extractable boron in the soils to a depth of 1 m (2 and 7 kg/ha), and by the highly significant correlations between hot-water-soluble boron and organic carbon for these soils.

4.2 Transformation

4.2.1 Biotransformation

Borate ions present in aqueous solution are essentially in their fully oxidized state. No aerobic processes are likely to affect their speciation, and no biotransformation processes are reported in the literature (personal communication from Borax US to the IPCS, 1995). Therefore, there are unlikely to be any differences in boron species due to biotransformation.

4.2.2 Abiotic transformation

Inorganic borates such as boric acid, boric oxide, and sodium borates are stable, except for dehydration at high temperatures. Organoboron compounds are sufficiently uncommon in nature to be irrelevant to this document. In aqueous media, the chemical speciation of boron–oxygen compounds is pH and concentration dependent.
4.2.2.1 Air

No information was available in the current literature concerning the photolysis, oxidation, or hydrolysis of boron-oxygen compounds in the atmosphere. The small amount of boron in air is assumed to be in the form of boric acid.

4.2.2.2 Water

In natural waters, boron exists primarily as undissociated boric acid with some borate ions. As a group, the boron-oxygen compounds are sufficiently soluble in water to achieve the levels that have been observed (Sprague, 1972; see chapter 5).

In seawater, inorganic boron content generally bears a linear relationship to the amount of chloride ion present; a ratio of 0.000 24 g boron/g of total halogen expressed as chloride ion has been calculated (Mellor, 1980). Byrne & Kester (1974) demonstrated that weakly dissociated boric acid is the predominant species but also that there are weakly associated ion pair neutral and positively charged borate complexes of sodium, magnesium, and calcium. The metaborate ion will undergo rapid hydrolysis in seawater to form the borate ion and the weakly dissociated boric acid. Noakes & Hood (1961) concluded that organically bound boron contributes very little, if any, to the total boron content of seawater. Boron associated with organic matter was found to vary with oxygen content, with the lowest concentrations occurring in the minimum oxygen zone. Mance et al. (1988) described boron as a significant constituent of seawater, with an average concentration of 4.5 mg/litre.

Boric acid is a very weak acid, with a $pK_a$ of 9.15; in fresh water, therefore, boric acid and sodium borates exist predominantly as undissociated boric acid below pH 7, but the metaborate anion becomes the main species in solution above pH 10. Between these two pH bands, there is also a characteristic presence of complex polyborate anions in solution when the concentration is increased, leading to enhanced solubility.
4.2.2.3 Soil

Borates as such cannot degrade, but borate complexes with organic matter or sod mineral surfaces can be altered by water leaching or pH change.

4.2.3 Bioaccumulation

4.2.3.1 Aquatic organisms

Highly water soluble materials are unlikely to bioaccumulate to any significant degree, and borate species are all present essentially as undissociated boric acid at neutral pH. The octanol/water partition coefficient for boric acid has been measured as 0.175 (Barres, 1967), indicating low bioaccumulation potential.

Thompson et al. (1976) studied boron uptake in two saltwater species, juvenile Pacific oysters (Crassostrea gigas) and underyearling sockeye salmon (Oncorhynchus nerka), in continuous-flow systems with 95% solution replacement every 6 h. Oysters (30/tank) were exposed to two boron levels (1 mg/litre above background and 10 mg/litre above background) for 47 days, and salmon (3/tank) were exposed only to the higher concentration for 21 days. Control tanks received only seawater inflow. The background concentration of boron in seawater in this study was approximately 3.98 mg/litre. The oysters were sampled on days 0, 8, 16, 36, and 47 of exposure. After this time, the remaining oysters were maintained in seawater alone for another 24 days and then analysed for boron uptake. Following the 21-day exposure period, the sockeye salmon were killed and the boron concentration was determined in gill, liver, kidney, muscle, and bone tissue. For both species, the tissue levels approximated the boron concentrations in the test water, indicating that these species take up boron in relation to its availability.

In the oyster, tissue concentrations returned to background levels (3.67–4.13 μg/g) by the 71st day of the study, indicating a fairly rapid clearance of boron with no evidence of long-term retention. Boron concentrations in sockeye salmon tissues in normal seawater ranged from 0.5 to 1.5 μg/g wet weight, with concentrations increasing from muscle to gill and kidney, to liver, and to bone. Boron levels were
elevated in the bone and kidney tissue (5.9–17 μg/g wet weight and 4.5–11.9 μg/g wet weight, respectively) of the exposed salmon; however, they were not significantly different from test water levels. Consequently, there was no evidence for active bioaccumulation of boron in these species (Thompson et al., 1976).

Suloway et al. (1983) studied the bioaccumulation potential of the components of coal fly ash extract in fathead minnows (*Pimephales promelas*) and green sunfish (*Lepomis cyanellus*). Five fish of each species were exposed for 30 days to fly ash extracts containing boron at concentrations ranging from 1.23 to 91.7 mg/litre. Whole-body concentrations of boron ranged from 1.16 to 4.15 μg/g in the exposed fathead minnows and from 1.08 to 4.62 μg/g in the exposed green sunfish. The reported bioconcentration factor was 0.3 for both species. These results are consistent with those described above and indicate that boron does not bioaccumulate significantly in fish.

### 4.2.3.2 Terrestrial plants

Eaton (1944) investigated growth reaction and boron accumulation characteristics of plants grown in outdoor sand culture beds where cultures were supplied with nutrient solutions containing differing concentrations of boron. The concentrations of boron ranged from 58 to 1804 μg/g dry weight in the leaves of plants grown in 5 mg boron/litre and from 209 to 3875 μg/g dry weight in the leaves of plants grown in 25 mg boron/litre. The boron concentrations were generally lower in roots, stems, and fruits than in the leaves. This is consistent with the fact that boron is absorbed from the soil solution by the roots and passively carried in the transpiration stream to the leaves, where the water evaporates and the boron accumulates. The absorption into the roots usually occurs as active transport against a concentration gradient (the concentration in the soil solution is generally lower than in the root tissues); therefore, an expenditure of energy is required. However, at higher boron soil solution concentrations, which are toxic to some plant species, the mechanism of uptake is passive diffusion (Bingham et al., 1970). Boron is relatively immobile in the phloem; consequently, the accumulated boron does not move out of the leaf tissues and into the fruit and other tissues (Kohl & Oertli, 1961).
Several factors affect the uptake of boron, including the pH of the soil solution, temperature, light intensity, and the concentration of other elements (e.g. calcium and potassium). Uptake is reduced by a factor of four as soil pH increases from 4 to 9 (Bingham et al., 1970) and increased by an increase in light intensity (Tanaka, 1966); the rate of boron absorption rapidly increases at temperatures ranging from 10 to 30 °C and is sharply reduced above 35 °C (Reisenauer & Cox, 1971).

4.2.3.3 Birds

Pendleton et al. (1995) exposed adult male mallard ducks to a dietary concentration of 1600 mg boron/kg for up to 48 days. Equilibrium levels were reached between days 2 and 15. Boron concentrations were highest in the blood, followed by the brain and liver. Boron was rapidly eliminated, with few detectable residues after 1 day on a “clean diet.” The presence of arsenic (300 mg/kg) in the diet slowed the accumulation of boron.

4.3 Ultimate fate following use

No information was available in the current literature concerning the disposal of boron or boron compounds. Information was located, however, regarding the reclamation and revegetation of coal combustion products (i.e. ash) that contain high concentrations of metals, including boron. Although the chemical and physical properties of coal ash tend to be detrimental to plant growth and establishment, additions of fertilizer and manure provide a more suitable medium (Schwab et al., 1991). Plant establishment on the site is only the first phase of the reclamation process. It is also necessary to ensure that leachate from the ash does not contaminate the surface water and groundwater in the immediate region and that uptake of metals in the plant materials does not result in metal concentrations that are toxic to livestock or wildlife. In a study of the revegetation of several ash disposal sites in Kansas, USA, Schwab et al. (1991) noted variations in plant uptake of boron from coal ash owing to differences in ash type, plant species, and ash treatment. Boron contained in detergents after use releases to the municipal sewage system. It should be noted that boron is not removed by the usual water treatment processes. Landfill will tend to be the ultimate fate of many boron products.
5. ENVIRONMENTAL LEVELS AND HUMAN EXPOSURE

5.1 Environmental levels

5.1.1 Air

Boron, as boric acid, is released into the atmosphere during volcanic eruptions; however, most is captured by the oceans (Muettterties, 1967). Coal-fired power plants and agricultural burning are major sources of atmospheric boron contamination; at least 30% of boron in coal is lost in this manner (Eisler, 1990). Nevertheless, boron does not appear to be present in ambient air at significant levels (Sprague, 1972), presumably because of rapid transport to other media (see section 4.1.1). Although the concentration is low, the atmosphere carries a significant amount of boron as boric acid vapour.

Mean boron concentrations in emissions from active volcanic sites range from <2.5 to 31.4 μg/m$^3$ for gaseous boron and are below 4 μg/m$^3$ for particulate boron. Volcanic lake fumes (El Chichon, Mexico) contained mean boron concentrations of up to 8.5 μg/m$^3$ for particulate boron and up to 16.1 μg/m$^3$ for gaseous boron (Anderson et al., 1994a).

Anderson et al. (1994a) monitored atmospheric concentrations of boron at continental, coastal, and remote marine sites. Mean particulate boron concentrations ranged from 1.8 to 12.2 ng/m$^3$, from 2.4 to 3.7 ng/m$^3$, and from <0.5 to 2.8 ng/m$^3$ for the three types of site, respectively. Mean gaseous boron concentrations ranged from <0.5 to 20.7 ng/m$^3$, from 3.5 to 82.8 ng/m$^3$, and from 0.6 to 25 ng/m$^3$, respectively. Anderson et al. (1994a) assumed 90% of boron in the air is gaseous and 10% is in particulate form.

5.1.2 Water

5.1.2.1 Groundwater

Naturally occurring boron is present in groundwater primarily as a result of leaching from rocks and soils containing borates and
borosilicates (i.e. local geology). Concentrations of boron in groundwater throughout the world range widely, from <0.3 to >100 mg/litre. Boron levels in European groundwaters are presented in Table 5. In general, concentrations of boron were greatest in southern Europe (Italy, Spain, but not Greece) and least in northern Europe (Denmark, France, Germany, Netherlands, and the United Kingdom). For Italy and Spain, mean boron concentrations ranged from 0.5 to 1.5 mg/litre. Concentrations ranged up to approximately 0.6 mg boron/litre in the Netherlands and United Kingdom, and levels in approximately 90% of samples in Denmark, France, and Germany were found to be below 0.3, 0.3, and 0.1 mg boron/litre, respectively.

Table 5. Concentrations of boron in European groundwater

<table>
<thead>
<tr>
<th>Country</th>
<th>Area</th>
<th>No. of samples</th>
<th>Boron concentration (mg/litre)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td>92.2% ≤ 0.3</td>
</tr>
<tr>
<td>Denmark</td>
<td></td>
<td>525</td>
<td>7.4% ≥ 0.3</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>0.4% ≥ 1.0</td>
</tr>
<tr>
<td>France</td>
<td></td>
<td>716</td>
<td>99.5 ≤ 0.3</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>0.5 ≥ 0.3</td>
</tr>
<tr>
<td>Germany</td>
<td>Baden-Wurttemberg</td>
<td>2574</td>
<td>89% ≤ 0.1</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>10.7% ≥ 0.1</td>
</tr>
<tr>
<td></td>
<td>Lower Saxony</td>
<td>188</td>
<td>96% ≤ 1.0</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>4% ≥ 1.0</td>
</tr>
<tr>
<td>Greece</td>
<td>Patras</td>
<td>10</td>
<td>100% ≤ 0.1</td>
</tr>
<tr>
<td></td>
<td>Halkidiki</td>
<td>3</td>
<td>2.3-5.4</td>
</tr>
<tr>
<td>Italy</td>
<td>North of Rome</td>
<td>423</td>
<td>Mean = 1.0</td>
</tr>
<tr>
<td></td>
<td>Sicily</td>
<td>18</td>
<td>Mean = 1.5</td>
</tr>
<tr>
<td></td>
<td>Paglia</td>
<td>102</td>
<td>Mean = 0.75</td>
</tr>
<tr>
<td>Netherlands</td>
<td>Inland</td>
<td></td>
<td>0.08-0.6</td>
</tr>
<tr>
<td>Spain</td>
<td>Valencia</td>
<td>21</td>
<td>Mean = 0.64</td>
</tr>
<tr>
<td></td>
<td>Almeria</td>
<td>17</td>
<td>Mean = 0.98</td>
</tr>
<tr>
<td></td>
<td>Murcia</td>
<td>15</td>
<td>Mean = 0.51</td>
</tr>
<tr>
<td>United Kingdom</td>
<td>London</td>
<td>21</td>
<td>0.02-0.54</td>
</tr>
<tr>
<td></td>
<td>Northumbria</td>
<td>164</td>
<td>Mean = 0.31</td>
</tr>
<tr>
<td></td>
<td>Dumfries and Galloway</td>
<td></td>
<td>Mean = 0.04</td>
</tr>
<tr>
<td></td>
<td>Permo-Triassic (Scotland)</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

* ECETOC (1997).
Groundwater contaminated with excessive concentrations of boron from surface water recharge has been noted beneath the Kesterson Reservoir, California, USA. This reservoir serves as an evaporative sink for several metalloids, including boron, and receives agricultural drainage from farmlands within the San Joaquin River Valley. Benson et al. (1991) reported an average boron concentration of 15 mg/litre. Concentrations of boron elsewhere within the San Joaquin River Valley have been shown to range from 0.14 to 120 mg/litre, with a median of 4 mg/litre (Deverel & Millard, 1988; Butterwick et al., 1989).

5.1.2.2 Surface water

The majority of the Earth's boron occurs in the oceans, with an average concentration of 4.5 mg/litre (Weast et al., 1985). The amount of boron in fresh water depends on such factors as the geochemical nature of the drainage area, proximity to marine coastal regions, and inputs from industrial and municipal effluents (Butterwick et al., 1989). Concentrations of boron in fresh surface water are summarized in Table 6.

Concentrations ranged from 0.001 to 2 mg boron/litre in Europe, with mean values typically below 0.6 mg/litre. Similar concentrations have been reported for water bodies within Pakistan, Russia, and Turkey; concentrations range from <0.01 to 7 mg boron/litre, with most values below 0.5 mg/litre. Concentrations ranged up to 0.01 mg boron/litre in Japan and up to 0.3 mg boron/litre in South African surface waters. Samples taken in surface waters from two South American rivers (Rio Arenales, Argentina, and Loa River, Chile) contained boron at concentrations ranging between 4 and 26 mg/litre in areas rich in boron-containing soils. In other areas, the Rio Arenales contained less than 0.3 mg boron/litre. Concentrations of boron in surface waters of North America (Canada, USA) ranged from 0.02 mg/litre to as much as 360 mg/litre, indicative of boron-rich deposits. However, typical boron concentrations were less than 0.1 mg/litre, with a 90th-percentile boron concentration of approximately 0.4 mg/litre.
Table 6. Concentrations of boron in fresh surface water

<table>
<thead>
<tr>
<th>Area</th>
<th>Boron concentration (mg/litre)</th>
<th>Reference</th>
</tr>
</thead>
<tbody>
<tr>
<td>USA</td>
<td>Median = 0.076</td>
<td>ECETOC (1997)</td>
</tr>
<tr>
<td></td>
<td>90th percentile = 0.387</td>
<td></td>
</tr>
<tr>
<td>Drainage basins, USA</td>
<td>0.019–0.289</td>
<td>Kopp &amp; Kroner (1970)</td>
</tr>
<tr>
<td>Coastal drainage waters, California, USA</td>
<td>15 (boron-rich deposits)</td>
<td>Deverel &amp; Millard (1988)</td>
</tr>
<tr>
<td>Lakes, California, USA</td>
<td>157–360 (boron-rich deposits)</td>
<td>Deverel &amp; Millard (1988)</td>
</tr>
<tr>
<td>Ontario, Canada</td>
<td>0.029–0.086</td>
<td>Sekerka &amp; Lechner (1990)</td>
</tr>
<tr>
<td>Cold River drainage area, western Canada</td>
<td>0.0627</td>
<td>Tsui &amp; McCart (1981)</td>
</tr>
<tr>
<td>United Kingdom</td>
<td>0.046–0.822</td>
<td>Mance et al. (1988)</td>
</tr>
<tr>
<td>Italy</td>
<td>0.4–1.0 (range of means)</td>
<td>Manfredi et al. (1975)</td>
</tr>
<tr>
<td></td>
<td>&lt;0.1–0.5</td>
<td>Tartari &amp; Camusso (1988)</td>
</tr>
<tr>
<td>Sweden</td>
<td>0.013 (0.001–1.046)</td>
<td>Ahl &amp; Jönsson (1972)</td>
</tr>
<tr>
<td>Germany</td>
<td>0.02–2.0</td>
<td>Graffmann et al. (1974)</td>
</tr>
<tr>
<td>The Netherlands</td>
<td>Range of medians = 0.09–0.145</td>
<td>Unilever (1994)</td>
</tr>
<tr>
<td>Rivers, Austria</td>
<td>&lt;0.02–0.6 (background level)</td>
<td>Schöller &amp; Bolzer (1989)</td>
</tr>
<tr>
<td>River Neva, Russia</td>
<td>0.01–0.02</td>
<td>Huber (1994)</td>
</tr>
<tr>
<td>Degh Nala, Pakistan</td>
<td>&lt;0.01–0.46 (near effluent discharges)</td>
<td>Tehseen et al. (1994)</td>
</tr>
<tr>
<td>Simav River, Turkey</td>
<td>&lt;0.5 (uncontaminated) 4 (maximum 7) (contaminated with boron mine waste)</td>
<td>Okay et al. (1985)</td>
</tr>
<tr>
<td>Rio Arenales, Argentina</td>
<td>&lt;0.3</td>
<td>Bundschuh (1992)</td>
</tr>
<tr>
<td></td>
<td>6.9 (near borate plant)</td>
<td></td>
</tr>
<tr>
<td>Loa River Basin, Chile</td>
<td>3.99–26 (soil rich in minerals and natural salts; low rainfall)</td>
<td>Cáceres et al. (1992)</td>
</tr>
<tr>
<td>Japan (River Asahi)</td>
<td>0.009–0.0117</td>
<td>Korenaga et al. (1980)</td>
</tr>
<tr>
<td>South Africa</td>
<td>0.02–0.33</td>
<td>Reid &amp; Davies (1989)</td>
</tr>
</tbody>
</table>

* Lowest concentration in the western Great Lakes Basin to highest concentration in the western Gulf Basin.
5.1.2.3 Rainfall

The median and mean concentrations of borate in rain and snow at six sites in western Switzerland were found to be 0.0031 and 0.0056 mg boron/litre, respectively (Atteia et al., 1993).

5.1.3 Sewage

Concentrations of boron in sewage waters are summarized in Table 7.

Table 7. Concentrations of boron in sewage waters

<table>
<thead>
<tr>
<th>Area/source</th>
<th>Boron concentration (mg/litre)</th>
<th>Reference</th>
</tr>
</thead>
<tbody>
<tr>
<td>USA</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Industrial waste discharge</td>
<td>0.4–1.5 (maximum 4.05)</td>
<td>Banerji (1969)</td>
</tr>
<tr>
<td>Europe</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Domestic and industrial</td>
<td>2 (maximum 5)</td>
<td>Butterwick et al. (1989)</td>
</tr>
<tr>
<td>Egypt</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Sewage water</td>
<td>0.32–0.38</td>
<td>El-Hassanin et al. (1993)</td>
</tr>
<tr>
<td>Sweden</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Effluent</td>
<td>0.34–0.436</td>
<td>Ahl &amp; Jönsson (1972)</td>
</tr>
<tr>
<td>Spain, Alicante</td>
<td>1.45</td>
<td>Navarro et al. (1992)</td>
</tr>
<tr>
<td>Spain, Elche</td>
<td>3</td>
<td>Navarro et al. (1992)</td>
</tr>
<tr>
<td>United Kingdom</td>
<td>1.21–3.96 (range of means)</td>
<td>Waggott (1969)</td>
</tr>
</tbody>
</table>

The majority of the boron present in sewage occurs primarily as undissociated boric acid; reported levels of boron in sewage in the USA range from 0.4 to 1.5 mg/litre and up to 4.05 mg/litre because of industrial waste discharges (Banerji, 1969). In Europe, sewage from domestic and industrial sources typically has an average boron
concentration of 2 mg/litre, with levels up to 5 mg/litre (Butterwick et al., 1989). Calculations by the German Government Environment Agency attribute 50% of the boron in wastewater to the use of detergent products (Butterwick et al., 1989). In boron mine drainage waters in Turkey, the boron concentrations were reported to be 16–390 mg/litre (Okay et al., 1985). Boron levels in sewage sludge in 23 US cities ranged from 7.1 to 53.3 mg/kg dry weight (Mumma et al., 1984).

5.1.4 Soil

According to Whetstone et al. (1942), boron occurs in soils at concentrations ranging from 10 to 300 mg/kg (average 30 mg/kg), depending on the type of soil, amount of soil organic matter, and amount of rainfall. Background boron levels in US soils were reported at a geometric mean concentration of 26 mg/kg, with a maximum concentration of 300 mg/kg (Eckel & Langley, 1988).

5.1.5 Aquatic biota

Concentrations of boron in aquatic biota are summarized in Table 8.

Little specific information was found concerning the bioaccumulation of boron in aquatic plants. At Kesterson National Wildlife Refuge in the San Joaquin River Valley, California, USA (an evaporative sink that has high concentrations of boron, selenium, and arsenic and is supplied with subsurface drainage water from agricultural fields), studies of the aquatic food-chain contamination have suggested that aquatic plants bioaccumulate high levels of boron, but boron does not biomagnify in aquatic food-chains. The following studies report observed concentrations in marine algae and freshwater aquatic vascular species. Igelsrud et al. (1938) reported boron levels ranging from 4.2 to 14.9 mg/kg of dried material in marine algae. Yamamoto et al. (1973) compared the boron content in freshwater and marine phytoplankton and observed that minor differences occurred between forms, even though the boron content of seawater averages 460 times that of fresh water.
Table 8. Concentrations of boron in aquatic biota

<table>
<thead>
<tr>
<th>Species</th>
<th>Area</th>
<th>Tissue</th>
<th>Boron concentration (mg/kg)</th>
<th>Reference</th>
</tr>
</thead>
<tbody>
<tr>
<td>Marine algae</td>
<td></td>
<td></td>
<td>4.2–14.9 dw</td>
<td>Igelsrud et al. (1938)</td>
</tr>
<tr>
<td>Filamentous algae</td>
<td>Lower San Joaquin River and its tributaries, California, USA</td>
<td>3.5–280 dw</td>
<td>Saiki et al. (1993)</td>
<td></td>
</tr>
<tr>
<td>Plankton</td>
<td>Lower San Joaquin River and its tributaries, California, USA</td>
<td>1.1–46 dw</td>
<td>Saiki et al. (1993)</td>
<td></td>
</tr>
<tr>
<td>Aquatic plants</td>
<td>Lower San Joaquin River, California, USA</td>
<td>382 (270–510) dw</td>
<td>Ohlendorf et al. (1986)</td>
<td></td>
</tr>
<tr>
<td>Submerged and floating aquatic vascular plants</td>
<td>Pennsylvania, USA</td>
<td>26.3–170</td>
<td>Adams et al. (1973)</td>
<td></td>
</tr>
<tr>
<td>Emergent aquatic vascular plants</td>
<td>Pennsylvania, USA</td>
<td>11.3–57</td>
<td>Adams et al. (1973)</td>
<td></td>
</tr>
<tr>
<td>Various marine shellfish</td>
<td>British Columbia, Canada</td>
<td>0.9–5.5 ww</td>
<td>Thompson et al. (1976)</td>
<td></td>
</tr>
<tr>
<td>Benthic bivalve (Corbicula fluminea)</td>
<td>San Joaquin River and its tributaries, California, USA</td>
<td>Soft tissue &lt;2–2 dw</td>
<td>Leland &amp; Scudder (1990)</td>
<td></td>
</tr>
<tr>
<td>Clam (Elliptio dililata)</td>
<td>Precambrian Shield lake, Ontario, Canada</td>
<td>Soft tissue 2.6 ww</td>
<td>Wren et al. (1983)</td>
<td></td>
</tr>
<tr>
<td>Chironomid larvae</td>
<td>Lower San Joaquin River and its tributaries, California, USA</td>
<td>&lt;1.8–27 dw</td>
<td>Saiki et al. (1993)</td>
<td></td>
</tr>
<tr>
<td>Species</td>
<td>Area</td>
<td>Tissue</td>
<td>Boron concentration (mg/kg)&lt;sup&gt;a&lt;/sup&gt;</td>
<td>Reference</td>
</tr>
<tr>
<td>--------------------------</td>
<td>----------------------------------------------------------------------</td>
<td>--------</td>
<td>----------------------------------------</td>
<td>----------------------------</td>
</tr>
<tr>
<td>Amphipods</td>
<td>Lower San Joaquin River and its tributaries, California, USA</td>
<td></td>
<td>&lt;2.2–23 dw</td>
<td>Saiki et al. (1993)</td>
</tr>
<tr>
<td>Crayfish</td>
<td>Lower San Joaquin River and its tributaries, California, USA</td>
<td></td>
<td>1.2–23 dw</td>
<td>Saiki et al. (1993)</td>
</tr>
<tr>
<td>Freshwater fish</td>
<td>Cold River drainage area, western Canada</td>
<td>Muscle</td>
<td>3.23–12.44 (range of means)</td>
<td>Tsui &amp; McCart (1981)</td>
</tr>
<tr>
<td>Freshwater fish</td>
<td>Precambrian Shield lake, Ontario, Canada</td>
<td>Muscle</td>
<td>1.8–2.9 ww</td>
<td>Wren et al. (1983)</td>
</tr>
<tr>
<td>Bluegill (&lt;i&gt;Lepomis macrochirus&lt;/i&gt;)</td>
<td>San Joaquin River, California, USA</td>
<td>Whole body</td>
<td>14 dw (3.5 ww)</td>
<td>Saiki &amp; May (1988)</td>
</tr>
<tr>
<td></td>
<td>Lower San Joaquin River and its tributaries, California, USA</td>
<td></td>
<td>&lt;1.8–7.9 dw</td>
<td>Saiki et al. (1993)</td>
</tr>
<tr>
<td>Largemouth bass (Micropterus salmoides)</td>
<td>Lower San Joaquin River and its tributaries, California, USA</td>
<td></td>
<td>&lt;1.8–2.0 dw</td>
<td>Saiki et al. (1993)</td>
</tr>
<tr>
<td>Common carp (&lt;i&gt;Cyprinus carpio&lt;/i&gt;)</td>
<td>San Joaquin River, California, USA</td>
<td>Whole body</td>
<td>20 dw (5 ww)</td>
<td>Saiki &amp; May (1988)</td>
</tr>
<tr>
<td></td>
<td>San Joaquin River, California, USA</td>
<td>Whole body</td>
<td>0.5–6.2 dw&lt;sup&gt;b&lt;/sup&gt;</td>
<td>Klasing &amp; Pilch (1988)</td>
</tr>
<tr>
<td>Species</td>
<td>Location</td>
<td>Sample Type</td>
<td>Value 1</td>
<td>Value 2</td>
</tr>
<tr>
<td>-------------------------------</td>
<td>---------------------------------------------</td>
<td>-------------</td>
<td>------------</td>
<td>------------</td>
</tr>
<tr>
<td>Mosquitofish (Gambusia affinis)</td>
<td>Lower San Joaquin River and its tributaries, California, USA</td>
<td>Whole body</td>
<td>&lt;1.9–8.4 dw</td>
<td>Saiki et al. (1993)</td>
</tr>
<tr>
<td></td>
<td>Volta, California, USA</td>
<td>Whole body</td>
<td>mean = 2.8 dw</td>
<td>Ohlendorf et al. (1986)</td>
</tr>
<tr>
<td></td>
<td>Kesterson, California, USA</td>
<td>Whole body</td>
<td>mean = 11.1 dw</td>
<td>Ohlendorf et al. (1986)</td>
</tr>
<tr>
<td>Tilapia spp.</td>
<td>Mexicali Valley, Baja California, Mexico</td>
<td>Muscle</td>
<td>2.9 ww</td>
<td>Mora &amp; Anderson (1995)</td>
</tr>
<tr>
<td>Mugil spp.</td>
<td>Mexicali Valley, Baja California, Mexico</td>
<td>Muscle</td>
<td>1.9 ww</td>
<td>Mora &amp; Anderson (1995)</td>
</tr>
<tr>
<td>Sockeye salmon (Oncorhynchus nerka)</td>
<td>British Columbia, Canada</td>
<td>Gill</td>
<td>mean = 0.6 ww</td>
<td>Thompson et al. (1976)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Liver</td>
<td>mean = 0.7 ww</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>Bone</td>
<td>mean = 1.5 ww</td>
<td></td>
</tr>
<tr>
<td>Atlantic cod (Gadus morhua)</td>
<td>Northwest Atlantic Ocean</td>
<td>Muscle</td>
<td>28 (1–93) ww</td>
<td>Hellou et al. (1992)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Liver</td>
<td>9.7 (5.2–35.4) ww</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>Ovaries</td>
<td>&lt;0.8</td>
<td></td>
</tr>
<tr>
<td>Anchoveta (Cetengraulis mysticetus)</td>
<td>Precambrian Shield lake, Ontario, Canada</td>
<td>Whole body</td>
<td>3.3–3.8 aw</td>
<td>Jenkins (1980)</td>
</tr>
<tr>
<td>Aquatic birds</td>
<td>Grassland water district, California, USA</td>
<td>Muscle</td>
<td>2.5–3.7 ww</td>
<td>Wren et al. (1983)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Liver</td>
<td>1.7–40 dw</td>
<td>Paveglio et al. (1992)</td>
</tr>
<tr>
<td>Species</td>
<td>Area</td>
<td>Tissue</td>
<td>Boron concentration (mg/kg)&lt;sup&gt;a&lt;/sup&gt;</td>
<td>Reference</td>
</tr>
<tr>
<td>-------------------------------</td>
<td>------------------------------------</td>
<td>--------</td>
<td>----------------------------------------</td>
<td>-----------------------------</td>
</tr>
<tr>
<td>Double-crested cormorant</td>
<td>Mexicali Valley, Baja California,</td>
<td>Liver</td>
<td>4.2 (2.9–8.2) ww</td>
<td>Mora &amp; Anderson (1995)</td>
</tr>
<tr>
<td><em>Phalacrocorax auritus</em></td>
<td>Mexico</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Duck species</td>
<td>Grassland water district, California, USA</td>
<td>Egg</td>
<td>3.07–6.17 dw</td>
<td>Hothem &amp; Welsh (1994)</td>
</tr>
<tr>
<td>Wading bird species</td>
<td>Grassland water district, California, USA</td>
<td>Egg</td>
<td>2.2–3.45 dw</td>
<td>Hothem &amp; Welsh (1994)</td>
</tr>
<tr>
<td>Aquatic mammals</td>
<td>Precambrian Shield lake, Ontario, Canada</td>
<td>Muscle</td>
<td>7.9 ww</td>
<td>Wren et al. (1983)</td>
</tr>
</tbody>
</table>

<sup>a</sup> ww = wet weight; dw = dry weight; aw = ash weight; concentrations are given as means or ranges of means; ranges are given in parentheses.

<sup>b</sup> Exposed to tile drainage water.
Adams et al. (1973) conducted a survey to determine the concentration of 11 potentially polluting ions, including boron, in a wide variety of aquatic plants from three major watersheds in Pennsylvania, USA: the Delaware, Susquehanna, and Allegheny rivers. Sources of pollution in this area are quite diverse, including lumbering activities, coal strip-mining, recreation, agricultural use, and urban-industrial centres. Boron constituent levels in 21 species of submerged and floating aquatic vascular plants ranged from 26.3 to 170 μg/g, and levels in 8 species of emergent aquatic vascular plants ranged from 11.3 to 57 μg/g.

Tsui & McCart (1981) studied the bioaccumulation of several elements, including boron, in five freshwater fish species from the Cold River drainage area in western Canada. Test species were selected to represent different feeding habits and modes of life. Northern pike (Esox lucius) and lake trout (Salvelinus namaycush) are primarily predators; lake herring (Coregonus artedii) is a plankton feeder; and lake whitefish (Coregonus clupeaformis) and white sucker (Catostomus commersoni) are primarily bottom-feeders. The fish were collected during spring and summer of 1978 from seven lakes within this area, and the muscle tissue was analysed for the presence of boron. The maximum average concentration of boron in the lakes was 0.0627 mg/litre. The mean tissue concentrations of boron in the five fish species ranged from 3.23 μg/g for lake whitefish to 12.44 μg/g for white sucker.

Wren et al. (1983) reported boron concentrations in freshwater fish and clams from a Precambrian Shield lake in Ontario, Canada. The lake was free from direct human impact. Boron levels in the undeveloped and protected muscle tissue of the fish were generally lower than those observed in fish from the Cold River drainage area in western Canada. The mean concentrations (wet weights) in the fish ranged from 1.8 to 2.9 μg/g. The boron concentration in the soft tissue of the clam (Elliptio dilitata) was 2.6 μg/g.

In contrast, boron levels were only slightly elevated in whole-body samples of bluegill (Lepomis macrochirus) and common carp (Cyprinus carpio) from the San Joaquin River and two tributaries that receive agricultural subsurface drainage water. The highest boron
concentrations (dry weights) measured were 14 µg/g (3.5 µg/g wet weight) in bluegills and 20 µg/g (5 µg/g wet weight) in carp (Saiki & May, 1988). Ohlendorf et al. (1986) reported similar values for mosquitofish (Gambusia affinis) from the San Joaquin River Valley. However, Saiki & May (1988) reported that the elevated boron levels may also result from natural boron deposits in adjacent soils or from sand-and-gravel mining operations in the area.

Paveglio et al. (1992) analysed boron concentrations in livers of aquatic birds collected from the Grassland Water District of California, USA, during 1985–1988. The use of subsurface agricultural drainage water for marsh management resulted in trace element contamination of components of the food-chain in this region. During the breeding and wintering periods, livers of birds from northern and southern areas of the grasslands contained high concentrations of boron (1.7–40 mg/kg dry weight).

A number of studies have investigated the accumulation of boron in aquatic food organisms, such as plants, insects, and fish (Saiki & May, 1988; Hothem & Ohlendorf, 1989; Smith & Anders, 1989; Paveglio et al., 1992; Saiki et al., 1993). The results of these studies suggest that aquatic plants bioaccumulate boron, but that boron does not biomagnify in aquatic food-chains.

5.1.6 Terrestrial biota

Concentrations of boron in terrestrial biota are summarized in Table 9.

The studies discussed in section 4.2.3 suggest that plants grown in boron-rich soil often contain high levels of boron in their tissues. Another source of boron entry into the food-chain is through the reclamation and revegetation of areas containing coal combustion products (i.e. ash). Schwab et al. (1991) reported strong positive correlations between the concentration of boron in soybean and sorghum used to revegetate several ash disposal sites in Kansas, USA, and the level of extractable boron in the coal fly ash. Variations in plant uptake of boron from coal ash were attributed to differences in ash type, plant species, and ash treatment. In terrestrial food-chains, boron accumulates in plants; however, boron is not biomagnified to animals (Saiki et al., 1993).
### Table 9. Concentrations of boron in terrestrial biota

<table>
<thead>
<tr>
<th>Species</th>
<th>Area</th>
<th>Tissue</th>
<th>Boron concentration (mg/kg)*</th>
<th>Reference</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lichen (Parmelia caperata)</td>
<td>Travale-Radicondoli geothermal area, Italy</td>
<td>12.3 (nd-25.4) dw</td>
<td>Loppi &amp; Bargagli (1996)</td>
<td></td>
</tr>
<tr>
<td>Cereals&lt;sup&gt;b&lt;/sup&gt;</td>
<td></td>
<td>2.3–5.0 dw</td>
<td>Bergmann (1984)</td>
<td></td>
</tr>
<tr>
<td>Legumes&lt;sup&gt;c&lt;/sup&gt;</td>
<td></td>
<td>15.4–41.4 dw</td>
<td>Bergmann (1984)</td>
<td></td>
</tr>
<tr>
<td>Dandelion (Taraxacum officinale)</td>
<td></td>
<td>80 dw</td>
<td>Bergmann (1984)</td>
<td></td>
</tr>
<tr>
<td>Poppy (Papaver somniferum)</td>
<td></td>
<td>94.7 dw</td>
<td>Bergmann (1984)</td>
<td></td>
</tr>
<tr>
<td>Moss (Hylocomium splendens)</td>
<td>Norway</td>
<td>3.6 (0.38–21) dw</td>
<td>Bergmann et al. (1995)</td>
<td></td>
</tr>
<tr>
<td>Omnivorous terrestrial bird species</td>
<td>Mexicali Valley, Baja California, Liver Mexico</td>
<td>2.3–5.3 (1.2–8.7) ww</td>
<td>Mora &amp; Anderson (1995)</td>
<td></td>
</tr>
<tr>
<td>Mourning dove (Zenaida macroura)</td>
<td>Mexicali Valley, Baja California, Liver Mexico</td>
<td>10 (4.3–28.5) ww</td>
<td>Mora &amp; Anderson (1995)</td>
<td></td>
</tr>
</tbody>
</table>
Table 9 (contd).

<table>
<thead>
<tr>
<th>Species</th>
<th>Area</th>
<th>Tissue</th>
<th>Boron concentration (mg/kg)</th>
<th>Reference</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mule deer (Odocoileus hemionus)</td>
<td>Piceance Creek Basin, Colorado, USA</td>
<td>Metacarpal</td>
<td>2.3 (1.5–3.1) dw (fawn)</td>
<td>Stelter (1980)</td>
</tr>
<tr>
<td></td>
<td>Piceance Creek Basin, Colorado, USA</td>
<td>Metacarpal</td>
<td>1.4 (1.1–1.7) dw (adult)</td>
<td>Stelter (1980)</td>
</tr>
<tr>
<td>Deer mice (Peromyscus maniculatus)</td>
<td>Piceance Creek Basin, Colorado, USA</td>
<td>Whole skeleton</td>
<td>&lt;2 dw</td>
<td>Stelter (1980)</td>
</tr>
<tr>
<td>Four species of rodent</td>
<td></td>
<td></td>
<td>4.3–6.3</td>
<td>Wiener et al. (1977)</td>
</tr>
</tbody>
</table>

a dw = dry weight; ww = wet weight; nd = not detected.

b Barley (Hordeum vulgare), rye (Secale cereale), wheat (Triticum vulgare), maize (Zea mays).

c Fieldbean (Vicia faba), pea (Pisum sativum), soya bean (Glycine max), lentil (Lens esculenta).
5.2 General population exposure

Human exposure to boron could result from the following sources: the consumption of drinking-water from natural or municipal sources that contain boron; the consumption of crops grown in boron-enriched soils, irrigated with boron-enriched waters, or contaminated with airborne boron particles; the consumption of aquatic organisms inhabiting natural waters high in boron; the absorption of boron from cosmetic or medical preparations through mucous membranes or damaged skin; and the inhalation, dermal absorption, or accidental ingestion of boron-containing household cleaning products, pesticides, or fertilizers. The most frequent and appreciable general population exposures to boron are likely to be from ingestion of food and, to a lesser extent, from ingestion of drinking-water.

5.2.1 Ambient air

Boron does not appear to be present in ambient air at significant levels (Sprague, 1972). There are few studies available that estimate the concentration of boron-containing compounds in ambient air; this is partly due to the difficulties of analysis at the low levels involved (ATSDR, 1992). However, Anderson et al. (1994a) have estimated the continental levels. Using their assumption that particulate boron constitutes 10% and gaseous boron constitutes 90% of the total, the range is 0.36–19.9 ng/m³. Therefore, using the average adult air consumption of 22 m³/day and the maximum value in this range, a respiratory exposure of 438 ng/day (0.44 μg/day) is calculated.

5.2.2 Drinking-water

Drinking-water is derived from groundwater and/or surface water sources. Concentrations of boron found in drinking-waters of Chile, Germany, the United Kingdom, and the USA are presented in Table 10. Overall, boron concentrations ranged from 0.01 to 15.0 mg/litre, with most values below 0.5 mg/litre. These values are consistent with ranges and means observed for data presented for groundwater (Table 5) and surface water (Table 6). Further, the consistency is
Table 10. Concentrations of boron in drinking-water

<table>
<thead>
<tr>
<th>Area</th>
<th>Samples</th>
<th>Concentration (mg/litre)</th>
<th>Reference</th>
</tr>
</thead>
<tbody>
<tr>
<td>USA</td>
<td>2595</td>
<td>0.8% &gt; 1.0</td>
<td>McCabe et al. (1970); Choi &amp; Chen (1979)</td>
</tr>
<tr>
<td>Germany</td>
<td>240</td>
<td>&lt;0.25</td>
<td>Graffmann et al. (1974)</td>
</tr>
<tr>
<td></td>
<td>110</td>
<td>&lt;0.21</td>
<td>Wiecken &amp; Wübbold-Weber (1993)</td>
</tr>
<tr>
<td>United Kingdom</td>
<td>200</td>
<td>0.01-0.45</td>
<td>D.E. Wilkinson (personal communication)</td>
</tr>
<tr>
<td></td>
<td>0.05-0.505</td>
<td></td>
<td>J. Bennett (personal communication)¹</td>
</tr>
<tr>
<td>Chile</td>
<td>0.31-15.0</td>
<td></td>
<td>Barr et al. (1993)</td>
</tr>
</tbody>
</table>

¹ Boron levels at drinking-water abstraction points of the River Thames: letter of 22 February 1993 from National Rivers Authority, Thames Region, United Kingdom, to the IPCS.
² Boron values for Anglican Water Region (1.1.92-31.12.92): letter of 9 March 1993, ref. DEW/AH/1733CD, from Anglican Water Services Limited, United Kingdom, to the IPCS.

supported by two factors: 1) boron concentrations in water are largely dependent on the leaching of boron from the surrounding geology, and 2) boron is not removed by conventional drinking-water treatment methods. Hence, when considering the need for allocating a TI of boron via drinking-water, a mean boron concentration for the world is judged to be between 0.1 and 0.3 mg/litre.

5.2.3 Soil intake

An older report indicates that boron is found in soils at concentrations ranging from 10 to 300 mg/kg, with an average value of 30 mg/kg (Whetstone et al., 1942).

A more recent study (Eckel & Langley, 1988) gives a similar upper boron concentration range (300 mg/kg) and average value (26 mg/kg). The use of this latter average soil level with an incidental consumption of 20 mg soil/person per day (IPCS, 1994) yields an average boron intake of 0.5 μg/day (i.e. 26 mg boron/kg of soil ×
0.000 02 kg of soil consumed per person per day = 0.0005 mg boron/person per day).

5.2.4 Dietary intake

For the general population, the greatest exposure to boron comes from food. Most of the concentrations of boron in foods reported before 1985 are of questionable validity because of inadequate analytical methods. Two recent reports (Hunt et al., 1991; Anderson et al., 1994b) provide an adequate indication of the amounts of boron found in various foods (see Table 11).

**Table 11. Boron content of some common foods**

<table>
<thead>
<tr>
<th>Food</th>
<th>Boron concentration (µg/g, fresh weight basis)</th>
<th>Hunt et al. (1991)</th>
<th>Anderson et al. (1994b)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Fruits</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Apple, red with peel, raw</td>
<td>2.73</td>
<td>2.38</td>
<td></td>
</tr>
<tr>
<td>Apple juice</td>
<td>1.88</td>
<td>2.41</td>
<td></td>
</tr>
<tr>
<td>Apple sauce</td>
<td>2.83</td>
<td>1.04</td>
<td></td>
</tr>
<tr>
<td>Banana, raw</td>
<td></td>
<td>3.72</td>
<td></td>
</tr>
<tr>
<td>Cherries, dark</td>
<td>1.47</td>
<td>0.92</td>
<td></td>
</tr>
<tr>
<td>Grape juice</td>
<td>2.02</td>
<td>2.06</td>
<td></td>
</tr>
<tr>
<td>Orange juice</td>
<td>0.41</td>
<td>1.59</td>
<td></td>
</tr>
<tr>
<td>Peaches, canned</td>
<td>1.87</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Pears, canned</td>
<td>1.22</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Dried fruits</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Dates</td>
<td>9.2</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Prunes</td>
<td>27</td>
<td>21.5</td>
<td></td>
</tr>
<tr>
<td>Raisins</td>
<td>25</td>
<td>19.0</td>
<td></td>
</tr>
<tr>
<td><strong>Vegetables</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Beans, green</td>
<td>0.46</td>
<td>1.56</td>
<td></td>
</tr>
<tr>
<td>Broccoli, flowers</td>
<td>1.85</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Broccoli, stalks</td>
<td>0.89</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Lettuce, iceberg</td>
<td>≤0.015</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Carrots, canned</td>
<td>0.75</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Nuts</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Almonds</td>
<td>23</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hazelnuts</td>
<td>16</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Peanuts</td>
<td>18</td>
<td>13.8</td>
<td></td>
</tr>
</tbody>
</table>

47
### Food Boron concentration

<table>
<thead>
<tr>
<th>Food</th>
<th>Boron concentration (µg/g, fresh weight basis)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Hunt et al. (1991)</td>
</tr>
<tr>
<td>Meats</td>
<td></td>
</tr>
<tr>
<td>Beef, round, ground, raw</td>
<td>≤0.015</td>
</tr>
<tr>
<td>Chicken, breast, ground, raw</td>
<td>≤0.015</td>
</tr>
<tr>
<td>Turkey breast</td>
<td>≤0.015</td>
</tr>
<tr>
<td>Milk and milk products</td>
<td></td>
</tr>
<tr>
<td>Cheese, cream</td>
<td>≤0.015</td>
</tr>
<tr>
<td>Milk, 2%</td>
<td>≤0.015</td>
</tr>
<tr>
<td>Cereal grain products</td>
<td></td>
</tr>
<tr>
<td>Bread, white, enriched</td>
<td>0.20</td>
</tr>
<tr>
<td>Cornflakes, fortified</td>
<td>0.31</td>
</tr>
<tr>
<td>Flour, wheat, white</td>
<td>0.28</td>
</tr>
<tr>
<td>Noodles, egg, dry, enriched</td>
<td>0.37</td>
</tr>
<tr>
<td>Rice, white, instant</td>
<td>≤0.015</td>
</tr>
<tr>
<td>Spaghetti, dry, enriched</td>
<td>≤0.015</td>
</tr>
<tr>
<td>Miscellaneous</td>
<td></td>
</tr>
<tr>
<td>Catsup</td>
<td>0.85</td>
</tr>
<tr>
<td>Eggs, homogenized</td>
<td>≤0.015</td>
</tr>
<tr>
<td>Honey</td>
<td>7.2</td>
</tr>
<tr>
<td>Jelly, strawberry</td>
<td>0.41</td>
</tr>
<tr>
<td>Jelly, grape</td>
<td>1.47</td>
</tr>
<tr>
<td>Sugar, white</td>
<td>≤0.015</td>
</tr>
<tr>
<td>Beverages*</td>
<td></td>
</tr>
<tr>
<td>Wine</td>
<td>3.5</td>
</tr>
<tr>
<td>Beer</td>
<td>1.8</td>
</tr>
</tbody>
</table>

* Boron concentration in µg/ml.

The richest sources of boron are fruits, vegetables, pulses, legumes, and nuts. Dairy products, fish, meats, and most grains are poor sources of boron. Based on the recent analyses of foods and food products, estimations of daily intakes of various age/sex groups have been made. Rainey et al. (1996) estimated that the median, mean, and 95th-percentile daily intakes of boron are 0.76, 0.93, and 2.16 mg/day, respectively, for all 27 age/sex groups in the USA; 0.34, 0.50, and 1.49 mg/day, respectively, for infants aged 0–5 months; 1.00, 1.18, and 2.61 mg/day, respectively, for males aged 60–65 years; and 0.87, 1.0,
and 2.17, respectively, for females aged 60–65. Using food included in US Food and Drug Administration (FDA) Total Diet Studies, Iyengar et al. (1988) determined the mean adult male daily intake of boron to be 1.52 mg/day, whereas Anderson et al. (1994b) determined the intake to be 1.21 mg/day. Based on the United Kingdom National Food Survey (UK Ministry of Agriculture, Fisheries and Food, 1991), the dietary intake of boron in the United Kingdom ranges from 0.8 to 1.9 mg/day. It should be noted that increased consumption of specific foods with high boron content will increase boron intake significantly; for example, one serving of wine or avocado provides 0.42 or 1.11 mg, respectively (Anderson et al., 1994b). Moreover, for the population obtaining their drinking-water from the 10% of the public water systems that provide water containing >0.4 mg boron/litre, water used for drinking and cooking may be the major, or a significant, source of boron. Based on the preceding values, the mean daily intake of boron in the diet is judged to be near 1.2 mg/day.

5.2.5 Consumer products

Boric acid, borax, and other borates are used in a great array of consumer goods. The principal use of boric acid and borax in the USA is in the manufacture of glass products. The way boron is bound to glass products should not result in significant releases of boron in its production or use.

Other consumer products in which boron compounds are used include soaps and detergents (as a bleaching agent), preservatives, adhesives, porcelain, enamel, leathers, carpets, artificial gems, high-contrast photographic materials, wicks, electric condensers, fertilizers, insecticides, and herbicides (Moore et al., 1997).

Sodium borate and boric acid are also widely used in numerous cosmetic products, including makeup, skin and hair care preparations, deodorants, moisturizing creams, breath fresheners, and shaving creams, with concentrations up to 5% (US FDA, 1981; Beyer et al., 1983). In 1981, the US FDA limited boric acid concentrations in consumer goods to 5% (US FDA, 1981). Boric acid exposures from some personal care products, estimated by the European Union Subcommittee on “Cosmetic Ingredients,” include 0.09–0.46 mg boric
acid/kg body weight per day for oral hygiene products, 0.03 mg boric acid/kg body weight per day for eye products, and 0.25 mg boric acid/kg body weight per day for deodorants (SCC opinion XXIV/1820/95). Exposure is related to personal practices. Boric acid is used in vaginal products and contraceptives. Consequently, by topical application, these compounds may come in contact with body surfaces, including the ocular, buccal, and vaginal mucosae (Beyer et al., 1983).

Body-building supplements contain 1.5–10 mg boron/serving, with a median of 4 mg boron/serving. These supplements could result in daily exposures of 1.5–30 mg boron, as some are taken up to 3 times a day. Bottled water can contain <0.005–4.35 mg boron/litre, depending on its origin, with an average boron content of 0.75 mg/litre (Moore et al., 1997).

The European Union permits boric acid in certain consumer products (e.g. 3% boric acid in eye products, up to 0.5% in oral hygiene products) (SCC opinion XXIV/1820/95). Usage data provided by the industry (EU Technical Guidance Document, 1995) allow the estimation of total exposure to boric acid from consumer products as 22.8 mg/day per person, equivalent to 4 mg boron/day. If absorption across the dermis is assumed to range from 1 to 10%, the absorbed boron dose from the source is 0.04–0.4 mg boron/day. The Task Group felt that 0.1 mg/day would serve as a reasonable average estimate of boron exposure from consumer products.

5.3 Occupational exposure

Occupational exposures to boron compounds may be significant (ATSDR, 1992). Inhalation of dusts is the most significant route of exposure in occupational settings. Dermal absorption of boron may also occur if damaged skin is in contact with boron compounds, but this is considered a minor pathway (Culver et al., 1994a).

Borate dusts have been monitored in workplace air. Reported concentrations of borax dust in different areas of a large borax mining and refining plant ranged from 1.1 to 14.6 mg/m³ (Garabrant et al., 1985; see also section 8.2.1), and the mean boric acid/boric oxide dust concentration in a boric acid manufacturing plant was 4.1 mg/m³.
(Garabrant et al., 1984). Other industries where workers may be occupationally exposed to boron include manufacture of fibreglass and other glass products, cleaning and laundry products, fertilizers, pesticides, and cosmetics (Stokinger, 1981). The range of normal values of blood boron concentration for non-occupationally exposed working adults can be found in Culver et al. (1994a). NIOSH (1989) estimated that the number of workers potentially exposed to boric acid increased from 6500 in the early 1970s to 35 600 in the early 1980s. Information about frequency, concentration, and duration of exposures is not contained in the NOES or National Occupational Hazard Survey (NOHS) databases. Wegman et al. (1994) reported that NIOSH estimated that there were 420 000 US workers with potential occupational exposure to sodium borate.

As part of an epidemiological study of acute respiratory irritation, Woskie et al. (1994) assessed short-term (time-weighted average over 0.25 h) and daily (time-weighted average over 6 h) dust and boron exposures of workers in a sodium borate production facility. The investigators used personal monitors to measure the boron concentration in air and the mass concentration of total airborne dusts. The arithmetic mean for the total dust concentration ranged from 0.29 to 18.85 mg/m³, and the average concentration of boron relative to total dust ranged from 5.6 to 10.1%. Because the data demonstrated that a substantial portion of the total dust was non-borate material (e.g. cigarette smoke, vehicle exhaust, background or ambient dust), the authors cautioned against using total dust as an indicator or surrogate marker for actual exposure to boron compounds.

In a study in which chronic abnormality in pulmonary function and acute irritant symptoms associated with borate dust in mixing and processing operations were examined (Wegman et al., 1994; see also section 8.2.1), personal monitors were used to measure boron concentrations. The results showed that workers were exposed to dust concentrations ranging from 0.1 to 205 mg/m³. The arithmetic mean of daily exposures in the comparison group was 0.45 mg total dust/m³ (0.02 mg total boron/m³), whereas the average daily exposure for the exposed group was 5.72 mg total dust/m³ (0.44 mg total boron/m³).
Whorton et al. (1994) studied male employees exposed to borate dusts at a borax mine and production facility in California, USA, from the 1950s through the 1980s. Men were identified with two or more past consecutive years of "high" exposure to doses with a range of 17.6–44.8 mg dust/m³ (doses averaged 23.2 mg dust/m³, or 3.3 mg boron/m³). The average exposure to sodium borate dust was 203 mg/day, which assumes 7 h/day of actual exposure at an average concentration of 23.2 mg/m³. The estimated 8-h respiratory volume for light work is 10 m³. The average concentration of boron in sodium borates is 14%; the daily dose of boron, assuming 100% absorption, is therefore 28.4 mg.

In a study of workers occupationally exposed to borate dust, Culver et al. (1994a) compared the blood and urine levels from workers with the amount of boron exposure. Mean daily inspired boron was calculated for low-, medium-, and high-exposure groups of male workers; the numbers of workers in these groups were four, five, and five, respectively. Total daily boron intake was calculated for each individual, including the dietary contribution. Blood and urine samples were taken at the start of the work week and at the end of shifts on Monday, Thursday, and Friday and analysed for boron. An average blood level of boron of 0.26 µg/ml occurred in the high-exposure group of workers, where exposure was estimated to be 0.38 mg boron/kg body weight per day. Post-shift blood and urine boron concentrations did not increase with the days of the work week, indicating that boron did not accumulate when exposure was up to 0.38 mg/kg body weight per day during the work week.
6. KINETICS AND METABOLISM IN LABORATORY ANIMALS AND HUMANS

6.1 Absorption

Numerous studies have shown that boric acid and borax are absorbed from the gastrointestinal tract and from the respiratory tract, as indicated by increased levels of boron in the blood, tissues, or urine or by systemic toxic effects of exposed individuals or laboratory animals. Blood, tissue, and urine boron levels have rarely been reported in cases of fatal human exposures to inorganic borates.

6.1.1 Oral

Pharmacokinetic data indicate that boron, usually administered as boric acid, is absorbed rapidly and virtually completely from the gastrointestinal tract, as evidenced by recovery of >90% of the dose in urine (Jansen et al., 1984). In a study in which human volunteers were given a single known dose of boric acid (131 mg boron), 94% of the ingested boron was excreted in the urine over a 96-h period (Schou et al., 1984). Based on urinary excretion of boron, Job (1973) observed a similar degree of oral absorption in volunteers who drank curative spa waters with a daily dose of approximately 100 mg boron for 2 weeks. Similar results had previously been reported by Kent & McCance (1941). These investigators also showed that the urinary excretion of boron ingested solely from dietary sources also reflected absorption rates ranging from 83 to 98% (Kent & McCance, 1941). Ingested boron is also readily absorbed by other species, including rats (Ku et al., 1991), rabbits (Draize & Kelley, 1959), sheep (Brown et al., 1989), and cattle (Owen, 1944; Weeth et al., 1981), as indicated by high levels of boron in tissues or urine or systemic toxicity following oral exposure. A 20-μg dose of $^{10}$B fed to fasted rats resulted in peak liver concentrations at 3 h and a return to normal isotope ratios within 24 h. Absorption was essentially complete, as evidenced by 95% recovery of $^{10}$B from urine and 4% recovery from faeces within 72 h post-dosing (Vanderpool et al., 1994).

Barr et al. (1993) studied areas of northern Chile in which the concentrations of naturally occurring boron in the water supplies...
ranged from 0.31 to 15.2 mg/litre. Blood boron levels for residents from seven geographical regions showed a positive correlation with boron levels in the local drinking-water supplies. Rough extrapolation from the plotted data indicates that in three regions with boron levels in drinking-water below 2.5 mg/litre (i.e. estimated intake of 0.07 mg boron/kg body weight per day for a 70-kg human consuming 2 litres of water per day), blood boron levels were below 0.1 µg/g blood. In the region with the highest boron concentration in drinking-water (15.2 mg boron/litre) (i.e. estimated intake of 0.43 mg boron/kg body weight per day), average blood levels were approximately 0.7 µg boron/g blood. Accuracy of linear fitting for the original data was limited by the small sample size obtained in each region, as well as the absence of individual water intake data.

6.1.2 Inhalation

Absorption is indicated by increases in human blood and urine boron levels after inhalation exposure to borax in the range of 3.3–18 mg/m³ (Culver, 1994a). Mice exposed to amorphous boron at a concentration of 72.8 mg/m³ for 7 h/day, 5 days/week, for 30 days had significant concentrations of boron in the liver and kidney (Stokinger & Spiegl, 1953), indicating that amorphous boron is absorbed from the respiratory tract. High boron levels were also found in the lungs, indicating that absorption was not complete. Wilding et al. (1959) showed that rats exposed to aerosols of boron oxide by inhalation at 77 mg/m³ for 6 h/day, 5 days/week, for 6 weeks excreted boron in their urine, indicating that boron oxide is absorbed from the respiratory tract. Ingestion (i.e. swallowing particles cleared from the respiratory tract by the mucociliary escalator system and subsequent absorption from the gastrointestinal tract) may have contributed to systemic uptake.

6.1.3 Dermal

Dermal absorption across intact skin is negligible in all species evaluated, including human infants (Friis-Hansen et al., 1982), human adults (Stuttgen et al., 1982), rabbits (Draize & Kelley, 1959), and rats (Nielsen, 1970). Several investigators have demonstrated that dermal absorption of boron compounds may be affected by the vehicle used
to dissolve or suspend the compounds (Nielsen, 1970; Stuttgen et al., 1982). When boric acid is applied to broken or damaged skin, however, absorption of boric acid through the damaged skin has been demonstrated (Draize & Kelley, 1959; Nielsen, 1970). In a report by Vignec & Ellis (1954), infants 1.25–10 months old received applications of a talcum powder containing 5% boric acid 7–10 times/day for at least 1 month. The authors calculated that the infants were exposed to an estimated dose of 2.33 g boric acid/day (408 mg boron/day). The boron concentrations in a test group composed of 12 infants were $0.04 \pm 0.04 \text{ mg/100 ml}$ in blood and $0.16 \pm 0.14 \text{ mg/100 ml}$ in the urine. An additional group of 12 treated infants, who had developed a mild to moderate diaper rash, had an average blood boron concentration of $0.03 \pm 0.04 \text{ mg/100 ml}$. Although Vignec & Ellis (1954) did not analyse the data statistically, the range of the values obtained indicates that, at most, only traces of boric acid penetrated the skin, even in infants with moderate diaper rash.

### 6.2 Distribution

#### 6.2.1 Tissue levels

Boron is a normal constituent of blood and tissues in humans and animals as a result of ingestion in food and (in some locations) drinking-water. Blood and tissue levels under normal dietary conditions or with boron supplementation are summarized in Table 12.

Boric acid distributes evenly throughout the body fluids. The most complete study of boron distribution was conducted in male F-344 rats (30/dose group) fed a control diet (<20 mg boron/kg) or a diet containing 9000 mg boric acid/kg (approximately 68 mg boron/kg body weight per day) for up to 7 days (Ku et al., 1991). Six animals/group were killed at 1, 2, 3, 4, and 7 days after the start of exposure. Boron levels were determined in all major tissues and organs. The authors reported that boron concentrations were comparable in all tissues examined, including plasma, liver, kidney, muscle, colon, brain, testis, epididymis, seminal vesicles, prostate, and adrenals. Most of the tissues appeared to reach steady-state boron levels (12–30 mg boron/kg tissue) by 3–4 days; these levels were 3- to 20-fold above controls. Adipose tissue accumulated only 20% as much boron as
Table 12. Blood and tissue boron levels following ingestion of boron in diet or drinking-water

<table>
<thead>
<tr>
<th>Species</th>
<th>Ingested boron</th>
<th>Fluid/organ</th>
<th>Concentration(^a)</th>
<th>Reference</th>
</tr>
</thead>
<tbody>
<tr>
<td>Chick</td>
<td>0.465 µg/g diet</td>
<td>Plasma</td>
<td>0.077 µg/ml</td>
<td>Hunt (1989)</td>
</tr>
<tr>
<td></td>
<td>3.465 µg/g diet</td>
<td>Plasma</td>
<td>0.152 µg/ml</td>
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<tr>
<td></td>
<td>0.465 µg/g diet</td>
<td>Femur</td>
<td>0.251 µg/g dw</td>
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</tr>
<tr>
<td></td>
<td>3.465 µg/g diet</td>
<td>Femur</td>
<td>0.861 µg/g dw</td>
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</tr>
<tr>
<td>Chick</td>
<td>0.18 µg/g diet</td>
<td>Brain</td>
<td>1.05 µg/g dw</td>
<td>Bain &amp; Hunt (1996)</td>
</tr>
<tr>
<td></td>
<td>+ 3 µg/g diet</td>
<td>Brain</td>
<td>1.01 µg/g dw</td>
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<td>+ 20 µg/g diet</td>
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<td>1.61 µg/g dw</td>
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<tr>
<td></td>
<td>0.18 µg/g diet</td>
<td>Heart</td>
<td>0.25 µg/g dw</td>
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<tr>
<td></td>
<td>+ 3 µg/g diet</td>
<td>Heart</td>
<td>0.55 µg/g dw</td>
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</tr>
<tr>
<td></td>
<td>+ 20 µg/g diet</td>
<td>Heart</td>
<td>0.88 µg/g dw</td>
<td></td>
</tr>
<tr>
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<td>0.18 µg/g diet</td>
<td>Liver</td>
<td>1.35 µg/g dw</td>
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<tr>
<td></td>
<td>+ 3 µg/g diet</td>
<td>Liver</td>
<td>1.01 µg/g dw</td>
<td></td>
</tr>
<tr>
<td></td>
<td>+ 20 µg/g diet</td>
<td>Liver</td>
<td>1.22 µg/g dw</td>
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</tr>
<tr>
<td></td>
<td>0.18 µg/g diet</td>
<td>Kidney</td>
<td>0.55 µg/g dw</td>
<td></td>
</tr>
<tr>
<td></td>
<td>+ 3 µg/g diet</td>
<td>Kidney</td>
<td>0.66 µg/g dw</td>
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</tr>
<tr>
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<td>+ 20 µg/g diet</td>
<td>Kidney</td>
<td>1.11 µg/g dw</td>
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</tr>
<tr>
<td></td>
<td>0.18 µg/g diet</td>
<td>Spleen</td>
<td>2.22 µg/g dw</td>
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</tr>
<tr>
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<td>+ 3 µg/g diet</td>
<td>Spleen</td>
<td>2.02 µg/g dw</td>
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<td>Femur</td>
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<td>Muscle</td>
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<td>+ 3 µg/g diet</td>
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<td>+ 20 µg/g diet</td>
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<tr>
<td><strong>Chick</strong></td>
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<td>Femur</td>
<td>1.21 µg/g dw</td>
<td>Hunt et al. (1994a)</td>
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<tr>
<td>(Vitamin D-deficient diet)</td>
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<td>Femur</td>
<td>1.49 µg/g dw</td>
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<td>(Vitamin D-deficient diet)</td>
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<td>4.57 µg/g dw</td>
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<td>Liver, thalassaemic</td>
<td>1.72 µg/g dw</td>
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<td>Synovial fluid, arthritic</td>
<td>30.4 ng/ml</td>
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<td>Concentration</td>
<td>Reference</td>
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<tr>
<td>Human</td>
<td>27 mg/day (drinking-water computed)</td>
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<td>0.659 μg/g</td>
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<td>17 mg/day (drinking-water computed)</td>
<td>Blood</td>
<td>0.585 μg/g</td>
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<td>4.5 mg/day (drinking-water computed)</td>
<td>Blood</td>
<td>0.347 μg/g</td>
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<td>2.5 mg/day (drinking-water computed)</td>
<td>Blood</td>
<td>0.052 μg/g</td>
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<td>1.3 mg/day (drinking-water computed)</td>
<td>Blood</td>
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<td>0.56 mg/day (drinking-water computed)</td>
<td>Blood</td>
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<td>Human</td>
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<td>Blood</td>
<td>28 ng/ml</td>
<td>Ward (1993)</td>
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<td>1.05 μg/g fw</td>
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<td>Nails</td>
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<td>Kidney</td>
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<tr>
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<td>Brain</td>
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<td>0.08 μg/g fw</td>
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Table 12 (contd).

<table>
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<th>About 1.2 mg/day</th>
<th>About 3.3 mg/day</th>
<th>Human Unknown</th>
<th>Pre-term milk</th>
<th>Term milk</th>
<th>Human</th>
<th>Red blood cells</th>
<th>Plasma</th>
<th>0.21 µg/g dw</th>
<th>0.19 µg/g dw</th>
<th>Plasma</th>
<th>64 ng/ml</th>
<th>95 ng/ml</th>
<th>Aquilio et al. (1996)</th>
<th>Nielsen &amp; Shuler (1992)</th>
<th>Nielsen (1996)</th>
<th>Hunt et al. (1997)</th>
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<td>Plasma</td>
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<td>Term milk</td>
<td>Plasma</td>
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<tr>
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<td>Plasma</td>
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<td>Plasma</td>
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<td>Femur</td>
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<td>Nielsen &amp; Shuler (1992)</td>
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<td>3.17 µg/g diet</td>
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<td></td>
<td></td>
<td>Tibia</td>
<td>Tibia</td>
<td>0.91 µg/g</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Muscle</td>
<td>Muscle</td>
<td>1.3 µg/g</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
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<td></td>
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</tr>
</tbody>
</table>
Table 12 (contd).

<table>
<thead>
<tr>
<th>Species</th>
<th>Ingested boron</th>
<th>Fluid/organ</th>
<th>Concentration (^a)</th>
<th>Reference</th>
</tr>
</thead>
<tbody>
<tr>
<td>Rat (injected with mycobacterium tuberculosis)</td>
<td>0.15 µg/g diet</td>
<td>Muscle</td>
<td>0.12 µg/g dw</td>
<td>Bai &amp; Hunt (1996)</td>
</tr>
<tr>
<td></td>
<td>1.5 µg/g diet</td>
<td>Muscle</td>
<td>0.17 µg/g dw</td>
<td></td>
</tr>
<tr>
<td></td>
<td>3.0 µg/g diet</td>
<td>Muscle</td>
<td>0.18 µg/g dw</td>
<td></td>
</tr>
<tr>
<td></td>
<td>10.0 µg/g diet</td>
<td>Muscle</td>
<td>0.30 µg/g dw</td>
<td></td>
</tr>
<tr>
<td></td>
<td>0.15 µg/g diet</td>
<td>Heart</td>
<td>0.37 µg/g dw</td>
<td></td>
</tr>
<tr>
<td></td>
<td>1.5 µg/g diet</td>
<td>Heart</td>
<td>0.34 µg/g dw</td>
<td></td>
</tr>
<tr>
<td></td>
<td>3.0 µg/g diet</td>
<td>Heart</td>
<td>0.44 µg/g dw</td>
<td></td>
</tr>
<tr>
<td></td>
<td>10.0 µg/g diet</td>
<td>Heart</td>
<td>0.57 µg/g dw</td>
<td></td>
</tr>
<tr>
<td></td>
<td>0.15 µg/g diet</td>
<td>Liver</td>
<td>0.14 µg/g dw</td>
<td></td>
</tr>
<tr>
<td></td>
<td>1.5 µg/g diet</td>
<td>Liver</td>
<td>0.21 µg/g dw</td>
<td></td>
</tr>
<tr>
<td></td>
<td>3.0 µg/g diet</td>
<td>Liver</td>
<td>0.17 µg/g dw</td>
<td></td>
</tr>
<tr>
<td></td>
<td>10.0 µg/g diet</td>
<td>Liver</td>
<td>0.26 µg/g dw</td>
<td></td>
</tr>
<tr>
<td></td>
<td>0.15 µg/g diet</td>
<td>Kidney</td>
<td>0.81 µg/g dw</td>
<td></td>
</tr>
<tr>
<td></td>
<td>1.5 µg/g diet</td>
<td>Kidney</td>
<td>0.45 µg/g dw</td>
<td></td>
</tr>
<tr>
<td></td>
<td>3.0 µg/g diet</td>
<td>Kidney</td>
<td>0.61 µg/g dw</td>
<td></td>
</tr>
<tr>
<td></td>
<td>10.0 µg/g diet</td>
<td>Kidney</td>
<td>0.99 µg/g dw</td>
<td></td>
</tr>
</tbody>
</table>

\(^a\) dw = dry weight; fw = fresh weight.
other tissues (3.78 mg/kg tissue). Bone boron levels (47.4 mg/kg tissue) indicated greater accumulation in bone than in other tissues; in addition, bone boron levels continued to increase throughout the 7 days. The higher affinity of boron for bone is indicative of a second kinetic component in which a small percentage of the boron absorbed may be sequestered. Elimination kinetics from bone also differ from those from soft tissue and body fluids (see Chapin et al., 1997, in section 6.4). Accumulation of boron in bone has also been observed in humans (Alexander et al., 1951; Forbes et al., 1954) and other animal species (Forbes & Mitchell, 1957).

6.2.2 Blood levels

O'Sullivan & Taylor (1983) reported the blood boron levels in three of seven infants (6–16 weeks old) who had ingested borax from pacifiers dipped in a borax and honey mixture. These three infants ingested 8–30 g of borax (286–429 mg borax/day) over a 4- to 10-week time period. Signs of central nervous system (CNS) toxicity (seizures) were reported in all seven infants. The blood levels ranged from 0.26 to 0.85 mg boron/100 ml blood; these blood values did not correlate well with the estimated amount of borax ingested per individual, but were clearly elevated relative to 15 children (ages 2–21 months) without exposure (average 0.021 mg/100 ml, range 0–0.063 mg/100 ml).

In a review of 782 cases of accidental boric acid exposures (age range 2 weeks to 98 years), serum levels ranged from 0 to 5.94 mg boron/100 ml. However, these levels did not correlate with the estimated amount of boric acid ingested (Litovitz et al., 1988).

Magour et al. (1982) determined the tissue levels of boron in Wistar rats administered 20 mg boron/kg body weight per day as sodium borate in drinking-water; exposure was initiated at 3 weeks of age and continued for 21 days. Blood boron levels continually rose during the treatment period; the maximum level was approximately 3.2 μg/g or 0.32 mg/100 ml blood. Intraperitoneal administration of 42 mg boron/kg body weight to 3-week-old or 3-month-old female Wistar rats resulted in generally higher tissue levels in the older rats and slightly higher tissue/blood ratios across a 4-h post-administration
period (Magour et al., 1982). These data suggest that boron may be
distributed differently in mature versus immature rats, but the
differences were subtle and transient.

Table 13 shows that blood boron levels generally increase with
the increase in oral dose in both rats and humans. However, procedural
differences among studies currently preclude a definitive cross-species
comparison to determine comparability of blood boron levels at
similar doses. For example, studies may differ in their approach to
estimation of boron intake, duration of exposure, analytical
methodology, or temporal relationship between exposure and blood
collection. Recognizing these limitations, a preliminary comparison
across species has been made based on rats exposed to boron via diet
or drinking-water and humans exposed via diet, drinking-water, or
accidental ingestion (Fig. 1). In this context, good overlap occurs
between rat and human blood boron values in the dose ranges from
0.01 to 100 mg boron/kg body weight per day. These data reinforce
the perception that boron kinetics are similar in rats and humans, but
they also emphasize the need for additional data to strengthen the basis
for the comparison.

6.3 Metabolism

Metabolism of inorganic borates by biological systems is not
feasible owing to the excessive energy (523 kJ/mol) required to break
the boron–oxygen bond (Emsley, 1989). Inorganic borates, in low
concentrations, convert to boric acid at physiological pH in the
aqueous layer overlying mucosal surfaces prior to absorption. This is
supported by the evidence in both human and animal studies, where
more than 90% of the administered dose of borate is excreted as boric
acid. There is evidence in both in vitro and in vivo systems that boric
acid has an affinity for cis-hydroxyl groups, and this may be the
mechanism that explains the biological effects of boric acid. However,
this attachment is known to be reversible and concentration dependent,
responding to clearance mechanisms.
Table 13. Blood boron levels as a function of dose in humans and rats

<table>
<thead>
<tr>
<th>Boron dose (mg/kg body weight per day)</th>
<th>Blood boron level (ng/ml)</th>
<th>Comments</th>
<th>Reference</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Human</td>
<td>Rat</td>
<td></td>
</tr>
<tr>
<td>0.0054</td>
<td>64 (plasma)</td>
<td>Diet</td>
<td>Hunt et al. (1997)</td>
</tr>
<tr>
<td>0.01</td>
<td>22</td>
<td>Drinking-water</td>
<td>Barr et al. (1993)</td>
</tr>
<tr>
<td>0.017</td>
<td>55 (plasma)</td>
<td>Diet</td>
<td>Nielsen et al. (1992a)</td>
</tr>
<tr>
<td>0.02</td>
<td>34 (plasma)</td>
<td>Diet</td>
<td>Nielsen (1996)</td>
</tr>
<tr>
<td>0.02</td>
<td>68</td>
<td>Drinking-water</td>
<td>Barr et al. (1993)</td>
</tr>
<tr>
<td>0.04</td>
<td>52</td>
<td>Drinking-water</td>
<td>Barr et al. (1993)</td>
</tr>
<tr>
<td>0.049</td>
<td>95 (plasma)</td>
<td>Diet</td>
<td>Hunt et al. (1997)</td>
</tr>
<tr>
<td>0.05</td>
<td>53 (plasma)</td>
<td>Diet</td>
<td>Nielsen (1996)</td>
</tr>
<tr>
<td>0.08</td>
<td>347</td>
<td>Drinking-water</td>
<td>Barr et al. (1993)</td>
</tr>
<tr>
<td>0.2</td>
<td>200°</td>
<td>Diet</td>
<td>Chapin et al. (1997)</td>
</tr>
<tr>
<td>0.3</td>
<td>55 (plasma, uncertain)</td>
<td>Diet</td>
<td>Nielsen et al. (1992a)</td>
</tr>
<tr>
<td>0.35</td>
<td>585</td>
<td>Drinking-water</td>
<td>Barr et al. (1993)</td>
</tr>
<tr>
<td>0.4</td>
<td>450</td>
<td>229 ± 143°</td>
<td>Price et al. (1997)</td>
</tr>
<tr>
<td>0.5</td>
<td>659</td>
<td>Drinking-water</td>
<td>Barr et al. (1993)</td>
</tr>
<tr>
<td>1.4</td>
<td>3 000</td>
<td>Drinking-water</td>
<td>Job (1973)</td>
</tr>
<tr>
<td>1.7</td>
<td>800°</td>
<td>Diet</td>
<td>Chapin et al. (1997)</td>
</tr>
<tr>
<td>3.3</td>
<td>564 ± 211°</td>
<td>Diet</td>
<td>Price et al. (1997)</td>
</tr>
<tr>
<td>3.5</td>
<td>3 200 (uncertain)</td>
<td>Oral</td>
<td>Litovitz et al. (1988)</td>
</tr>
<tr>
<td>6.3</td>
<td>975 ± 261°</td>
<td>Diet</td>
<td>Price et al. (1997)</td>
</tr>
<tr>
<td>8.4</td>
<td>2 400°</td>
<td>Diet</td>
<td>Chapin et al. (1997)</td>
</tr>
<tr>
<td>Boron dose (mg/kg body weight per day)</td>
<td>Blood boron level (ng/ml)</td>
<td>Comments</td>
<td>Reference</td>
</tr>
<tr>
<td>--------------------------------------</td>
<td>---------------------------</td>
<td>----------------</td>
<td>---------------</td>
</tr>
<tr>
<td></td>
<td>Human</td>
<td>Rat</td>
<td></td>
</tr>
<tr>
<td>9.6</td>
<td>1 270 ± 298&lt;sup&gt;b&lt;/sup&gt;</td>
<td>Diet</td>
<td>Price et al. (1997)</td>
</tr>
<tr>
<td>13</td>
<td>1 530 ± 546&lt;sup&gt;b&lt;/sup&gt;</td>
<td>Diet</td>
<td>Price et al. (1997)</td>
</tr>
<tr>
<td>20</td>
<td>3 100</td>
<td>Drinking-water</td>
<td>Magour et al. (1982)</td>
</tr>
<tr>
<td>25</td>
<td>2 820 ± 987&lt;sup&gt;b&lt;/sup&gt;</td>
<td>Diet</td>
<td>Price et al. (1997)</td>
</tr>
<tr>
<td>26</td>
<td>6 700 (serum)</td>
<td>Diet</td>
<td>Ku et al. (1993a)</td>
</tr>
<tr>
<td>38</td>
<td>10 300 (serum)</td>
<td>Diet</td>
<td>Ku et al. (1993a)</td>
</tr>
<tr>
<td>40</td>
<td>6 500</td>
<td>Oral</td>
<td>O'Sullivan &amp; Taylor (1983)</td>
</tr>
<tr>
<td>52</td>
<td>13 300 (serum)</td>
<td>Diet</td>
<td>Ku et al. (1993a)</td>
</tr>
<tr>
<td>56</td>
<td>27 000 (uncertain)</td>
<td>Oral</td>
<td>Litovitz et al. (1988)</td>
</tr>
<tr>
<td>68</td>
<td>17 300 (serum)</td>
<td>Diet</td>
<td>Ku et al. (1993a)</td>
</tr>
<tr>
<td>95</td>
<td>16 000 (plasma)</td>
<td>Diet</td>
<td>Ku et al. (1991)</td>
</tr>
</tbody>
</table>

<sup>a</sup> Developed by R. Chapin. Estimated from measured bone boron concentrations and ratio of bone/blood boron levels, from Chapin et al. (1997) and Ku et al. (1993a).

<sup>b</sup> Mean ± SD (n = 27–30 per dose group; Price et al., 1997).

<sup>c</sup> Price et al. (1997) data are for pregnant rats.
Fig. 1. Blood boron concentration in humans, rats, and pregnant rats as a function of boron dose.
6.4 Elimination and excretion

Clearance of boron compounds is similar in humans and animals. Elimination of borates from the blood is largely by excretion of >90% of the administered dose via the urine, regardless of the route of administration. Excretion is relatively rapid, occurring over a period of a few to several days, with a half-life of elimination of 24 h or less. The kinetics of elimination of boron have been evaluated in human volunteers given boric acid via the intravenous and oral routes (Jansen et al., 1984; Schou et al., 1984). The half-life for elimination was the same by either route in these studies and was approximately 21 h. This value is corroborated by case reports of boric acid poisoning. Litovitz et al. (1988) examined the case reports of almost 800 patients accidentally or intentionally poisoned with boric acid and found a very comparable elimination half-life: 13.4 h (range 4–27.8 h). Incomplete or inconsistent patient histories (especially with regard to total dose or dose-to-sample interval) undoubtedly contributed to the variation in those half-life estimates.

In a study of workers occupationally exposed to borate dust, Culver et al. (1994a) compared the blood and urine boron levels from workers with the amount of boron exposure (see section 5.3). An average boron level of 0.26 μg/ml blood occurred in the highest exposure group, where exposure was estimated to be 0.38 mg boron/kg body weight per day. Post-shift blood and urine boron concentrations did not increase with the days of the work week. This lack of accumulation over the work week corroborates the relatively short elimination half-life for boron in humans.

Elimination times for animals have not been explicitly stated in the literature but can be either calculated or estimated from published data. Farr & Konikowski (1963) measured urinary boron concentrations in mice after intravenous injection of sodium pentaborate. Using their data and assuming first-order kinetics for elimination, the half-life for elimination in the mouse was on the order of 1 h. Ku et al. (1991) reported that an apparent steady-state level of boron is reached in the blood and tissues of rats after 3–4 days of oral dosing; again, assuming first-order kinetics, the half-life in rats would be on the order of 14–19 h.
Male Fischer-344 rats were exposed to boric acid at 3000–9000 mg/kg in the diet for up to 9 weeks (Ku et al., 1993a). Urinary boron was elevated (450–600 μg boron/mg creatinine) 24 h after the end of dosing. By 3–4 days post-treatment, urinary boron in all groups had returned to average control levels (8.97 ± 1.95 μg boron/mg creatinine for days 1, 7, and 14 post-treatment). Elimination of boron from bone followed a different time-course from elimination from serum or soft tissues. F-344 rats consuming boric acid in the diet for 9 weeks (~1.4–6.8 mg boron/kg body weight per day) showed dose-related elevation of bone boron, which declined very gradually during the post-treatment period. Bone boron levels remained elevated above controls in all exposed groups at 32 weeks post-treatment (Chapin et al., 1997). Longer post-treatment intervals, as well as factors influencing rates of accumulation or mobilization of boron in bone, remain to be evaluated.
7. EFFECTS ON LABORATORY MAMMALS AND IN VITRO TEST SYSTEMS

7.1 Short-term exposure

7.1.1 Oral route

The oral LD$_{50}$ values for boric acid and borax in laboratory animals are given in Table 14. Values for mice and rats are in the range of ~400–700 mg boron/kg body weight (Pfeiffer et al., 1945; Weir & Fisher, 1972). For guinea-pigs, Verbitskaya (1975) reported an oral LD$_{50}$ of 210 mg boron/kg body weight. Acute oral LD$_{50}$ values in the range of 250–350 mg/kg body weight for boric acid or borax exposure have also been reported for dogs, rabbits, and cats (Pfeiffer et al., 1945; Verbitskaya, 1975).

General clinical effects of boric acid or borax in rats, mice, and guinea-pigs given single large doses orally are depression, ataxia, occasional convulsions, decreased body temperature, and violet-red colour of skin and all mucous membranes (Pfeiffer et al., 1945; Weir & Fisher, 1972). Toxic signs in dogs given boric acid (0.2–2.0 g/kg body weight) orally in combination with subcutaneous morphine to prevent vomiting were cyanosis of mucous membranes, red-violet skin colour, rigidity of legs, convulsion, and shock-like syndrome (Pfeiffer et al., 1945). Rabbits given boric acid at 800 mg/kg body weight per day for 4 days showed anorexia, weight loss, and diarrhoea; 850 and 1000 mg/kg body weight per day for 4 days caused 100% mortality (Draize & Kelley, 1959). Cattle receiving 0.8, 150, or 300 mg boron/litre of drinking-water (as boric acid) for 30 days were lethargic at the highest dose and had swelling and irritation in the legs and around the dew claws, slight diarrhoea, and decreased food consumption at the middle and high doses (Green & Weeth, 1977).

Following exposure to boric acid, microscopic changes in tissues of mice, rats, and dogs involved primarily the kidneys and nervous system (Pfeiffer et al., 1945). Glomerular and tubular damage were noted in the kidneys. Glomerular damage consisted of changes in permeability of the capillaries, and tubular damage consisted of cellular vacuolization and shedding of cells into the tubular lumen.
Table 14. Acute toxicity of boron compounds in laboratory animals

<table>
<thead>
<tr>
<th>Route</th>
<th>Compound</th>
<th>Species</th>
<th>Compound LD$_{50}$ (mg/kg body weight)</th>
<th>Boron$<em>a$ LD$</em>{50}$ (mg/kg body weight)</th>
<th>Reference</th>
</tr>
</thead>
<tbody>
<tr>
<td>Oral</td>
<td>Boric acid</td>
<td>Mice</td>
<td>3450</td>
<td>603</td>
<td>Pfeiffer et al. (1945)</td>
</tr>
<tr>
<td></td>
<td>Borax</td>
<td>Rats</td>
<td>3493</td>
<td>396</td>
<td>Wang et al. (1984)</td>
</tr>
<tr>
<td></td>
<td>Borax</td>
<td>Rats</td>
<td>4500</td>
<td>510$_b$</td>
<td>Weir &amp; Fisher (1972)</td>
</tr>
<tr>
<td></td>
<td>Borax</td>
<td>Rats</td>
<td>4980</td>
<td>560$_b$</td>
<td>Weir &amp; Fisher (1972)</td>
</tr>
<tr>
<td></td>
<td>Borax</td>
<td>Rats</td>
<td>5660</td>
<td>642</td>
<td>Smyth et al. (1969)</td>
</tr>
<tr>
<td></td>
<td>Borax</td>
<td>Rats</td>
<td>6080</td>
<td>690$_b$</td>
<td>Weir &amp; Fisher (1972)</td>
</tr>
<tr>
<td></td>
<td>Boric acid</td>
<td>Rats</td>
<td>2660</td>
<td>465</td>
<td>Pfeiffer et al. (1945)</td>
</tr>
<tr>
<td></td>
<td>Boric acid</td>
<td>Rats</td>
<td>3160</td>
<td>550$_b$</td>
<td>Weir &amp; Fisher (1972)</td>
</tr>
<tr>
<td></td>
<td>Boric acid</td>
<td>Rats</td>
<td>3450</td>
<td>600$_b$</td>
<td>Weir &amp; Fisher (1972)</td>
</tr>
<tr>
<td></td>
<td>Boric acid</td>
<td>Rats</td>
<td>4080</td>
<td>710$_b$</td>
<td>Weir &amp; Fisher (1972)</td>
</tr>
<tr>
<td></td>
<td>Boric acid</td>
<td>Rats</td>
<td>5140</td>
<td>899</td>
<td>Smyth et al. (1969)</td>
</tr>
<tr>
<td>Subcutaneous</td>
<td>Boric acid</td>
<td>Mice</td>
<td>1740$_c$</td>
<td>304</td>
<td>Pfeiffer et al. (1945)</td>
</tr>
<tr>
<td></td>
<td>Boric acid</td>
<td>Mice</td>
<td>2070</td>
<td>362</td>
<td>Pfeiffer et al. (1945)</td>
</tr>
<tr>
<td></td>
<td>Boric acid</td>
<td>Guinea-pigs</td>
<td>1200</td>
<td>210</td>
<td>Pfeiffer et al. (1945)</td>
</tr>
<tr>
<td>Intravenous</td>
<td>Boric acid</td>
<td>Mice</td>
<td>1780</td>
<td>311</td>
<td>Pfeiffer et al. (1945)</td>
</tr>
<tr>
<td></td>
<td>Boric acid</td>
<td>Rats</td>
<td>1330</td>
<td>232</td>
<td>Pfeiffer et al. (1945)</td>
</tr>
</tbody>
</table>

$_a$ Calculated by multiplying the dose in mg boron compound/kg by the ratio of the molecular weights of boron/boron compound, except when noted otherwise.

$_b$ Reported by investigators.

$_c$ Solution adjusted to pH 7.4 with sodium hydroxide.
Nervous system damage consisted of an increase in small dark cells
(probably microglia) in the spinal cord and in the grey matter of the
brain cortex.

7.1.2 Inhalation route

The LC$_{50}$ for sodium perborate tetrahydrate by inhalation in rats
was >74 mg/m$^3$ (Silaev, 1984). The 1-h inhalation LC$_{50}$ values for
boron trichloride are reported as 12.2 g/m$^3$ for male rats and 21.1 g/m$^3$
for female rats; for boron trifluoride, the LC$_{50}$ values range from 0.89
to 1.2 g/m$^3$ for rats (Vemot et al., 1977). While these boron–halogen
compounds are not considered in this report because of apparent anion
toxicity, it is appropriate to note in passing the inhalation studies
performed with them (Stokinger & Spiegl, 1953; Rusch et al., 1986).
These studies evaluated rats, mice, and guinea-pigs and report various
dose-related toxic effects beginning at 24 mg/m$^3$.

7.2 Longer-term exposure

7.2.1 Oral route

The effects of longer-term oral exposure to boron compounds in
animals are summarized in Table 15.

In a 13-week study conducted by the US National Toxicology
Program (NTP, 1987; Dieter, 1994), B6C3F$_1$ mice (10/sex per dose)
were exposed to boric acid in the diet at concentrations sufficient to
produce estimated consumptions of approximately 0, 34, 70, 141, 281,
or 563 mg boron/kg body weight per day for males and 0, 47, 97, 194,
388, or 776 mg boron/kg body weight per day for females. The results
showed that female mice were less sensitive than male mice to the
lethal effects of boric acid; 8/10 high-dose males and 6/10 high-dose
females died, and 1/10 males receiving 281 mg boron/kg body weight
per day died. Clinical signs of toxicity were a thin, hunched
appearance, dehydration, foot lesions, and scaly tails. A dose-related
decrease in body weight gain was observed. Microscopic effects
included a dose-related incidence of minimal to mild extramedullary
haematopoiesis of the spleen in males and females, hyperkeratosis and
acanthosis of the stomach in eight males and three females receiving
the highest dose, and testicular lesions; the testicular lesions are
described in greater detail in section 7.4.
Table 15. Effects of longer-term oral exposure to boron compounds in experimental animals

<table>
<thead>
<tr>
<th>Compound</th>
<th>Species</th>
<th>Dose* (mg boron/kg body weight per day)</th>
<th>Vehicle</th>
<th>Duration</th>
<th>Effects</th>
<th>Reference</th>
</tr>
</thead>
<tbody>
<tr>
<td>Boric acid</td>
<td>Mice</td>
<td>0, 34, 70, 141, 281, 563 for males; 0, 47, 97, 194, 388, 776 for females(^b)</td>
<td>Diet</td>
<td>13 weeks</td>
<td>Over 60% mortality in both sexes at 563 and 776 mg/kg body weight per day; 10% in males at 281 mg/kg body weight per day. At 141 mg/kg body weight per day, degeneration in seminiferous tubules and decreased tubules in males and decreased weight gain in males and females. Extramedullary haematopoiesis of the spleen in all dosed groups, hyperkeratosis and acanthosis of stomach at 563 and 776 mg/kg body weight per day.</td>
<td>NTP (1987)</td>
</tr>
<tr>
<td>Boric acid</td>
<td>Mice</td>
<td>0, 48, 96</td>
<td>Diet</td>
<td>103 weeks</td>
<td>Decrease in body weight (10–17%) in high-dose males after week 32 and in high-dose females after week 52. No clinical toxic signs observed. Testicular atrophy and interstitial cell hyperplasia were seen in males at both levels. Dose-related increase in incidence of splenic lymphoid depletion in males. No other significant increase in non-neoplastic lesions.</td>
<td>NTP (1987)</td>
</tr>
<tr>
<td>Boric acid</td>
<td>Rats</td>
<td>0, 22.7, 57(^c) and higher</td>
<td>Drinking-water</td>
<td>30 days</td>
<td>Growth was not inhibited at the low dose, but it was delayed at ≥57 mg/kg body weight per day. No haematological effects or histological alterations.</td>
<td>Pfeiffer et al. (1945)</td>
</tr>
</tbody>
</table>
Table 15 (contd).

<table>
<thead>
<tr>
<th>Compound</th>
<th>Species</th>
<th>Dosea (mg boron/kg body weight per day)</th>
<th>Vehicle</th>
<th>Duration</th>
<th>Effects</th>
<th>Reference</th>
</tr>
</thead>
<tbody>
<tr>
<td>Borax</td>
<td>Rats</td>
<td>0, 0.056, 0.28, 2.8, 28</td>
<td>Drinking-</td>
<td>≤198 days</td>
<td>Decrease in pancreas-to-body weight ratio at all doses in females at day 98. Increase in pancreas-to-body weight ratio in males at day 198. No details given; normal histology.</td>
<td>Wang et al. (1984)</td>
</tr>
<tr>
<td>Boric acid</td>
<td>Rats</td>
<td>0.95, 3.65, 5.2, 9.9e</td>
<td>Diet</td>
<td>8 weeks</td>
<td>Decreased body weight at 5.2 and 9.9 mg/kg body weight per day. No other toxicity end-points evaluated.</td>
<td>Forbes &amp; Mitchell (1957)</td>
</tr>
<tr>
<td>Borax or boric acid</td>
<td>Rats</td>
<td>0, 2.6, 8.8, 26.3, 87.5, 262.5e</td>
<td>Diet</td>
<td>90 days</td>
<td>Mortality was 100% at the highest dose; testicular atrophy at 87.5 and 26.3 mg/kg body weight per day; decrease in body weight and in the weight of liver, kidney, spleen, and testes at 87.5 mg/kg body weight per day; weight changes were inconsistent at lower doses.</td>
<td>Weir &amp; Fisher (1972)</td>
</tr>
<tr>
<td>Borax or boric acid</td>
<td>Rats</td>
<td>0, 5.9, 17.5, 58.5e</td>
<td>Diet</td>
<td>2 years</td>
<td>Both compounds suppressed growth at 58.5 mg/kg body weight per day. Testes weight and testes-to-body weight ratios were decreased, and brain-to-body weight and thyroid-to-body weight ratios were increased at 58.5 mg/kg body weight per day; also, atrophy in seminiferous epithelium and decrease in tubular size; no effects observed at lower doses.</td>
<td>Weir &amp; Fisher (1972)</td>
</tr>
<tr>
<td>Compound</td>
<td>Species</td>
<td>Dose</td>
<td>Route</td>
<td>Duration</td>
<td>Effects</td>
<td></td>
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<td>-------------------------------------------------------------------------</td>
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</tr>
<tr>
<td>Boric acid or borax</td>
<td>Rabbits</td>
<td>31</td>
<td>Oral gavage</td>
<td>5 days/week for 4 months</td>
<td>Elevated serum glutamic-oxaloacetic transaminase (SGOT) and serum glutamic-pyruvic transaminase (SGPT) levels, serum lactate dehydrogenase and aldolase were transiently increased, catalase and amylase were decreased.</td>
<td></td>
</tr>
<tr>
<td>Sodium tetraborate (not specified whether anhydrous or decahydrate)</td>
<td>Rats</td>
<td>0, 3 g/litre sodium tetraborate (boron conversion not made due to uncertainty regarding compound)</td>
<td>Drinking-water</td>
<td>14 weeks</td>
<td>Increase in RNA concentration and in succinate dehydrogenase and acid proteinase activation in the brain. Decrease in NADPH-cytochrome reductase and in the content of cytochrome b$_5$ and P-450 in the liver. No effect on body or organ weight.</td>
<td></td>
</tr>
<tr>
<td>Sodium metaborate</td>
<td>Mice</td>
<td>0, 0.95$^e$</td>
<td>Drinking-water</td>
<td>Lifetime</td>
<td>No effects on body weight or longevity.</td>
<td></td>
</tr>
</tbody>
</table>

*a* Calculated by multiplying the dose in mg boron compound/kg body weight per day by the ratio of molecular weights of boron/boron compound.

*b* Estimated based on feed consumption values of 161 g/kg body weight per day for male and 222 g/kg body weight per day for female controls at week 4 of treatment.

*c* Calculated based on water consumption of 0.12–0.14 ml/g per day reported by authors.

*d* Calculated by using assumed body weight of 0.35 kg and reported daily water consumption of 19.5 ml.

*e* Calculated by assuming reference values of 0.35 kg body weight and daily water consumption of 0.049 litre for rats, or food factor of 0.05 for rats and 0.025 for dogs, or 0.03 kg body weight and daily water consumption of 0.0057 litre for mice.
Following this range-finding study, a 2-year study was conducted in which mice (50/sex per dose) received approximately 0, 275, or 550 mg boric acid/kg body weight per day (0, 48.1, or 96.3 mg boron/kg body weight per day) in the diet (NTP, 1987; Dieter, 1994). No clinical signs of toxicity were observed. Body weights were 10–17% lower in males after 32 weeks and in females after 52 weeks. Non-accidental mortality at the end of the study was 9/50, 20/50, and 23/50 in control, low-, and high-dose males and 17/50, 15/50, and 12/50 in control, low-, and high-dose females. The increased mortality rate was statistically significant in males. The only significant lesions in male mice appeared in the testes; no significant non-neoplastic lesions appeared in females.

Lee et al. (1978) fed borax in the diet to male Sprague-Dawley rats (18/dose) at concentrations of 0, 500, 1000, or 2000 mg boron/kg (equivalent to approximate doses of 0, 30, 60, or 125–131 mg boron/kg body weight per day) for 30 or 60 days. Body weights were not consistently affected by treatment; organ weights were not affected in the 30 mg/kg body weight per day group. At 60 and 125–131 mg/kg body weight per day, absolute liver weights were significantly lower after 60 days; epididymal weights were significantly lower (37.6% and 34.8%, respectively) after 60 days, but not after 30 days. Weights of prostate, spleen, kidney, heart, and lung were not changed at any dose; reproductive effects observed in the study are discussed in section 7.4.

In a 90-day study, Sprague-Dawley rats (10/sex per dose) received 0, 2.6, 8.8, 26.3, 87.5, or 262.5 mg boron/kg body weight per day in the diet as boric acid or borax (Weir & Fisher, 1972). Similar effects were observed with both boric acid and borax. All high-dose animals died within 3–6 weeks. In animals receiving 87.5 mg boron/kg body weight per day, body weights in males and females were reduced 43.8–54.9% and 10.1–12.6%, respectively. Absolute organ weights — including the liver, spleen, kidneys, brain, adrenals, and ovaries — in this dose group were also significantly decreased. Relative organ-to-body weights of the adrenals and kidneys were significantly increased, but relative weights of the liver and ovaries were decreased. A pronounced reduction in testicular weights in males in the 87.5 mg boron/kg body weight per day group was also observed; effects on the male reproductive system are discussed further in section 7.4.
Effects on Laboratory Mammals and In Vitro Test Systems

In a 2-year study, rats (35/sex per dose) were administered weight-normalized doses of 0, 5.9, 17.5, or 58.5 mg boron/kg body weight per day in the diet as borax or boric acid (Weir & Fisher, 1972). High-dose animals had coarse hair coats, scaly tails, hunched posture, swollen and desquamated pads of the paws, abnormally long toenails, shrunken scrotum, inflamed eyelids, and bloody eye discharge. These signs became frequent and more pronounced during the first year but did not change thereafter. Serum chemistry and urine values were normal; the haematocrit and haemoglobin levels were significantly lower than in controls. The absolute and relative weights of the testes were significantly lower, and relative weights of the brain and thyroid gland were higher, than in controls. In animals in the mid- and low-dose groups, no significant effects on general appearance, behaviour, growth, food consumption, haematology, serum chemistry, or histopathology were observed (Weir & Fisher, 1972).

Weir & Fisher (1972) also fed boric acid or borax to beagle dogs for 90 days or 2 years. In the 90-day study (weight-normalized doses of 0, 0.44, 4.38, or 43.75 mg boron/kg body weight per day; 5 animals/sex per dose), testicular effects were observed in males in the two highest dose groups. In the boric acid study, testis weight was significantly lower than controls in the middle- and upper-dose groups (reduced by 25% and 40%, respectively). Although testicular microscopic structure was not detectably abnormal in the controls and middle-dose group, 4 of 5 dogs in the high-dose group had complete atrophy, and the remaining high-dose dog had one-third of tubules showing some abnormality. In the borax study, testis weights in the low, middle-, and high-dose groups were 80%, 85%, and 50% of controls, respectively; only the last was significantly different from controls. No mention was made of the testicular microscopic structure of the controls or low-dose animals; middle-dose animals were not detectably altered (aside from the considerable fixation-induced artifact in the outer third of the tissue), whereas 4 of 5 high-dose dogs had complete testicular atrophy, and the remaining high-dose dog had "partial" atrophy. No other clinical or microscopic signs of toxicity were reported in any animals. In the 2-year study, the dogs (4/sex per dose) received the boric acid or borax in the diet at weight-normalized doses of 1.5, 2.9, or 8.8 mg boron/kg body weight per day. An additional group received 29 mg boron/kg body weight per day for 38
weeks. No effects were observed on general appearance, body weight, food consumption, organ weights, haematology, or serum chemistry. Changes in testicular morphology occurred in males in the highest (38-week) dose group; these reproductive changes are described in section 7.4.

Two reports are available on the toxic effects of boron on bones. Seffner et al. (1990) exposed growing pigs to boron (4 or 8 mg/kg body weight per day; source of boron was not specified). They reported a dose-related thinning of the cortex of the humerus and a reduction (significant at 8 mg/kg body weight per day) in presumably bone-derived serum alkaline phosphatase, suggesting reduced osteoblast activity. Confidence in this study is moderate because of the uncertainty of the form/source of boron and the authors’ inability to replicate several previous biochemical findings.

A second report investigated the effects of boric acid (calculated exposures: <0.2–68 mg boron/kg body weight per day) on several bone parameters in adult rats (Chapin et al., 1997). This study found no change in physical bone measures (size, cortical thickness, etc.) but reported a 5–10% increase in resistance of vertebrae to a crush force.

7.2.2 Inhalation route

Mice exposed to amorphous elemental boron at 72 mg/m³ for 7 h/day, 5 days/week, for 6 weeks did not exhibit any toxic effects (Stokinger & Spiegl, 1953). Wilding et al. (1959) conducted numerous longer-term experiments in rats and dogs exposed to boron oxide particles (median mass aerodynamic diameter [MMAD] 1.9–2.5 μm). The exposures took place for 6 h/day and 5 days/week and included rats exposed at 77 mg boric oxide/m³ for 24 weeks, 175 mg boric oxide/m³ for 12 weeks, or 470 mg boric oxide/m³ for 10 weeks; dogs were exposed to 57 mg boron oxide/m³ for 23 weeks. No toxic effects were observed, with normal values obtained for body weight gains, blood chemistry, haematology, and urinalysis; there were also no microscopic changes reported.

Subchronic inhalation studies have been performed with boron trifluoride (Torkelson et al., 1961; Rusch et al., 1986) at 2–18 mg/m³.
Effects on Laboratory Mammals and In Vitro Test Systems

Reported effects included pneumonitis and reduced body weight gains and organ weights.

7.3 Dermal and ocular effects

Animal studies show that boron oxide dust can affect the skin and eyes. When boron oxide dust (50 mg) was applied to the eyes of rabbits, conjunctivitis resulted (Wilding et al., 1959). Roudabush et al. (1965) determined that boric acid (5 ml, 10% in water, w/v) and borax (10 ml, 5% in water, w/v) were mild skin irritants after 24–72 h following application to abraded skin. Borax was also a mild skin irritant and boric acid a moderate irritant after 24 and 72 h when applied to the guinea-pig. Rats fed 88 or 263 mg boron/kg body weight per day as borax or boric acid had inflamed eyes and skin desquamation on their paws and tails (Weir & Fisher, 1972).

7.4 Reproductive toxicity

Reproductive and developmental effects of borates in laboratory animals are summarized in Table 16.

The data regarding subchronic and chronic oral exposure to boric acid or borax in laboratory animals have unequivocally demonstrated that the male reproductive tract is a consistent target of toxicity (Table 16). Testicular lesions have been observed in rats, mice, and dogs administered boric acid or borax in food or drinking-water (Truhaut et al., 1964; Weir & Fisher, 1972; Green et al., 1973; Lee et al., 1978; NTP, 1987; Ku et al., 1993a). The first clinical indication of testicular toxicity in dogs is shrunken scrota observed during treatment; significant decreases in absolute and relative testicular weight are also reported. After subchronic exposure, the histopathological effects range from inhibited spermiation (the process of release of mature spermatids from the seminiferous epithelium) to degeneration of the seminiferous tubules with variable loss of germ cells, to complete absence of germ cells, resulting in atrophy and transient or irreversible loss of fertility, but not of mating behaviour.

Time- and dose-response studies of the Sprague-Dawley male rat reproductive end-points after acute administration of boric acid
Table 16. Reproductive and developmental effects of boron compounds in laboratory animals

<table>
<thead>
<tr>
<th>Compound</th>
<th>Species</th>
<th>Dosea (mg boron/kg body weight per day)</th>
<th>Vehicle</th>
<th>Duration</th>
<th>Effects</th>
<th>Reference</th>
</tr>
</thead>
<tbody>
<tr>
<td>Boric acid</td>
<td>CD-1 mice</td>
<td>0, 19.2, 104.5, 220.2 for males; 0, 31.8, 147.9, 290.2 for females</td>
<td>Diet</td>
<td>27 weeks</td>
<td>None of the high-dose pairs was fertile. At the middle dose, there was a significant decrease in litters/pair, live pups/litter, percentage of pups born alive, and live pup weight. Fertility index was decreased at the middle dose. Body weight gain was reduced in males and females at the high dose, despite increases in food and water consumption. Cross-mating experiments showed that boric acid affected primarily the male reproductive system. A dose level of 220.2 mg/kg body weight per day significantly reduced reproductive organ weights in males and altered sperm motility, concentration, and morphology. At the high dose, fertility of the low-dose F1 mice was not affected, but marginally reduced sperm concentrations were seen in males; increases in uterus and kidney plus adrenal weights and shorter estrus cycles were seen in females; and F2 live pup weights were reduced.</td>
<td>Fail et al. (1990, 1991)</td>
</tr>
<tr>
<td>Boric acid</td>
<td>SD rats</td>
<td>0, 350</td>
<td>Gavage</td>
<td>2-57 days</td>
<td>Inhibited sperm release, adverse changes in sperm morphology; reversible by day 57.</td>
<td>Linder et al. (1990)</td>
</tr>
</tbody>
</table>
Table 16 (contd).

<table>
<thead>
<tr>
<th>Compound</th>
<th>Species</th>
<th>Route</th>
<th>Diet</th>
<th>Duration</th>
<th>Effects Description</th>
<th>Source</th>
</tr>
</thead>
<tbody>
<tr>
<td>Boric acid</td>
<td>Rats</td>
<td>0, 60.9&lt;sup&gt;o&lt;/sup&gt;</td>
<td>Diet</td>
<td>4–28 days</td>
<td>Decreased weight gain; inhibition of spermiation starting at day 7 and degeneration in seminiferous tubules at day 28; decreased serum testosterone starting at day 4; no effects on liver or kidney histology.</td>
<td>Treinen &amp; Chapin (1991)</td>
</tr>
<tr>
<td>Boric acid</td>
<td>F-344 rats</td>
<td>0, 26, 38, 52, 68</td>
<td>Feed</td>
<td>Weekly to 63 days</td>
<td>Mild inhibited sperm release at 26 mg/kg body weight per day; severe inhibited sperm release at 38 mg/kg body weight per day; progression to testicular atrophy at 52 and 68 mg/kg body weight per day, with many other changes resulting from these primary effects.</td>
<td>Ku et al. (1993a)</td>
</tr>
<tr>
<td>Boric acid</td>
<td>Rats</td>
<td>175</td>
<td>Water</td>
<td>15 days</td>
<td>Vacuolation and granulation of the cytoplasm and absence of nuclear chromatin in spermatids of seminiferous tubules. Reduction in tubule diameter and absence of germinative cells.</td>
<td>Silaev et al. (1977)</td>
</tr>
<tr>
<td>Borax or boric acid</td>
<td>Rats</td>
<td>0, 5.9, 17.5, 58.5&lt;sup&gt;c&lt;/sup&gt;</td>
<td>Diet</td>
<td>Multi-generation</td>
<td>Sterility, lack of spermatozoa, testicular atrophy, decreased ovulation at 58.5 mg/kg body weight per day. No effects at lower doses.</td>
<td>Weir &amp; Fisher (1972)</td>
</tr>
<tr>
<td>Borax or boric acid</td>
<td>Dogs</td>
<td>0, 0.44, 4.4, 44&lt;sup&gt;c&lt;/sup&gt;</td>
<td>Diet</td>
<td>90 days</td>
<td>One male dog died at 44 mg/kg body weight per day; decrease in thyroid- and testes-to-body weight ratios, and severe testicular atrophy in males at 44 mg/kg body weight per day. At 0.44 mg/kg body weight per day, decreased spleen-to-body weight ratio in males. At ≤4.4 mg/kg body weight per day, no changes in organ weight in females.</td>
<td>Weir &amp; Fisher (1972)</td>
</tr>
<tr>
<td>Compound</td>
<td>Species</td>
<td>Dose&lt;sup&gt;a&lt;/sup&gt; (mg boron/kg body weight per day)</td>
<td>Vehicle</td>
<td>Duration</td>
<td>Effects</td>
<td>Reference</td>
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<tr>
<td>Borax</td>
<td>Rats</td>
<td>0, 30, 60, 125-131</td>
<td>Diet</td>
<td>30 or 60 days</td>
<td>At the 60 and 125-131 mg/kg body weight per day doses, liver weights were significantly lower after 60 days; epididymal weights were significantly lower (37.6 and 34.8%) after 60 days. FSH levels were elevated in all treatment groups after 60 days, and at the highest dose FSH levels remained elevated after 12 months.</td>
<td>Lee et al. (1978)</td>
</tr>
<tr>
<td>Borax</td>
<td>Rats</td>
<td>0, 25, 50, 100&lt;sup&gt;c&lt;/sup&gt;</td>
<td>Diet</td>
<td>60 days</td>
<td>Decrease in weights of liver, testes, and epididymis at the two highest dietary levels. Seminiferous tubule diameter was decreased in a dose-related manner in all groups. Loss of germinal cell elements was seen only in 50 and 100 mg/kg body weight per day groups. Plasma levels of FSH were elevated. Reduced fertility only at two highest dosage levels.</td>
<td>Dixon et al. (1979)</td>
</tr>
<tr>
<td>Borax</td>
<td>Rats</td>
<td>0, 23.7, 44.7&lt;sup&gt;d&lt;/sup&gt;</td>
<td>Drinking-water</td>
<td>70 days</td>
<td>Significant decrease in body weight and decrease in weight of testes, seminal vesicles, spleen at both doses. Spermatogenesis impaired and haematocrit decreased slightly at highest dose.</td>
<td>Seal &amp; Weeth (1980)</td>
</tr>
<tr>
<td>Borax</td>
<td>Rats</td>
<td>0, 0.042, 0.14, 0.84&lt;sup&gt;b&lt;/sup&gt;</td>
<td>Drinking-water</td>
<td>90 days</td>
<td>No observable reproductive effects or changes in serum chemistry, body weight, or weight of testes, prostate, or seminal vesicles.</td>
<td>Dixon et al. (1976)</td>
</tr>
<tr>
<td>Borax or boric acid</td>
<td>Dogs</td>
<td>0, 1.5, 2.9, 8.8, 29c Diet</td>
<td>2 years</td>
<td>Severe testicular atrophy and spermatogenic arrest at week 26 with 29 mg/kg body weight per day; no effects on body or organ weights, gross morphology, or histological parameters at lower doses.</td>
<td>Weir &amp; Fisher (1972)</td>
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</tr>
<tr>
<td>Boric acid</td>
<td>Mice</td>
<td>0, 43.4, 79.0, 175.3 Diet</td>
<td>Gestation days 0–17</td>
<td>There was no effect on survival or pregnancy rate. Maternal effects included mild renal lesions at 43.4 mg/kg body weight per day and increased water intake, increased relative kidney weight, and decreased weight gain during treatment at 175.3 mg/kg body weight per day. At the high-dose level, there was a significant increase in the percentage of resorptions/litter. Average fetal body weight/litter was significantly reduced at 79.0 mg/kg body weight per day. Malformations included a missing or shortened XIII rib and variations on extra lumbar I rib. Malformations were significantly increased at 175.3 mg/kg body weight per day. The percentage of variations/litter decreased at 79.0 mg/kg body weight per day and was not affected at 175.3 mg/kg body weight per day.</td>
<td>NTP (1989); Heindel et al. (1992)</td>
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</tr>
</tbody>
</table>
Table 16 (contd).

<table>
<thead>
<tr>
<th>Compound</th>
<th>Species</th>
<th>Dose* (mg boron/kg body weight per day)</th>
<th>Vehicle</th>
<th>Duration</th>
<th>Effects</th>
<th>Reference</th>
</tr>
</thead>
<tbody>
<tr>
<td>Boric acid</td>
<td>Rats</td>
<td>0, 13.6, 28.5, 57.7, 94.2 Diet</td>
<td>Gestation days 0–20</td>
<td>The highest dose was administered to one group on gestation days 6–15. There was no effect on survival or pregnancy rate. Maternal rats showed increased relative liver and kidney weights at ≥28.5 mg/kg body weight per day, increased absolute kidney weight at 94.2 mg/kg body weight per day, and a decrease in body weight gain at ≥57.7 mg/kg body weight per day. At low doses, there was a decrease in extra lumbar rib I (a variation) and at high doses an increase in missing or shortened XIII rib (a malformation). The 94.2 mg/kg body weight per day level increased prenatal mortality. Fetal body weights were significantly reduced in all treated groups in a dose-related manner. Malformations increased at ≥28.5 mg/kg body weight per day; variations increased at 94.2 mg/kg body weight per day.</td>
<td>NTP (1990); Heindel et al. (1992)</td>
<td></td>
</tr>
</tbody>
</table>

* Dose values are given in mg boron/kg body weight per day.
Table 16 (contd).

<table>
<thead>
<tr>
<th>Boric acid</th>
<th>Rats</th>
<th>Phase 1</th>
<th>Diet</th>
<th>Phase 1</th>
<th>Price et al. (1996a)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>0, 3.3, 6.3, 9.6, 13.3, 25</td>
<td></td>
<td></td>
<td>Phase 1 — Fetal body weight was decreased on gestational day 20 in the 13.3 and 25 mg/kg body weight per day dose groups. On gd 20, incidences of short rib XIII or wavy rib were increased in these dose groups relative to controls. The high-dose group contained a biologically relevant but not statistically significant decrease in incidence of extra rib on lumbar I.</td>
<td>(1996a)</td>
</tr>
<tr>
<td></td>
<td>Phase 2</td>
<td></td>
<td></td>
<td>Phase 2 — On pn days 0–21, there were no decreased fetal body weight effects. On pn day 21, the percentage of pups per litter with short rib XIII was elevated in the 25.4 mg/kg body weight per day dose group. No wavy rib or extra rib on lumbar I was found at pn day 21.</td>
<td>(1996a)</td>
</tr>
</tbody>
</table>
Table 16 (contd).

<table>
<thead>
<tr>
<th>Compound</th>
<th>Species</th>
<th>Dose(^a) (mg boron/kg body weight per day)</th>
<th>Vehicle</th>
<th>Duration</th>
<th>Effects</th>
<th>Reference</th>
</tr>
</thead>
<tbody>
<tr>
<td>Boric acid</td>
<td>Rabbits</td>
<td>0, 10.9, 21.9, 43.7</td>
<td>Gavage in water</td>
<td>Exposure on gestation days 6–19; termination on gd 30</td>
<td>No treatment-related clinical signs of toxicity except for vaginal bleeding at 43.7 mg/kg body weight per day. This dose had no live fetuses on day 30. Food intake decreased during treatment (43.7 mg/kg body weight per day), but increased on days 25–30 (21.9 and 43.7 mg/kg body weight per day). Body weight and body weight gain were decreased during treatment at 43.7 mg/kg body weight per day, but corrected body weight increased at 21.9 and 43.7 mg/kg body weight per day. Gravid uterine weight and number of corpora lutea/dam were decreased at 43.7 mg/kg body weight per day. Significant developmental effects were limited to the high-dose group. Prenatal mortality was greatly increased. Malformations were also increased, primarily owing to the incidence of fetuses with cardiovascular defects. The skeletal variation observed was sternae. Fetal body weight was slightly reduced in the high-dose group.</td>
<td>Price et al. (1996b)</td>
</tr>
</tbody>
</table>

\(^a\) Calculated by multiplying the dose in mg boron compound/kg body weight per day by the ratio of molecular weights of boron/boron compound.

\(^b\) Estimated by the authors.

\(^c\) Calculated by assuming reference values of 0.35 kg body weight and daily water consumption of 0.049 litre for rats, or food factor of 0.05 for rats and 0.025 for dogs, or 0.03 kg body weight and daily water consumption of 0.0057 litre for mice.

\(^d\) Calculated by using assumed body weight of 0.35 kg and reported daily water consumption of 19.5 ml.
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(Linder et al., 1990) revealed adverse effects on spermiation, epididymal sperm morphology, and caput sperm reserves during histopathological examinations of the testes and epididymis. Rats were administered two doses in one day in both experiments, with a total dose of 0 or 350 mg boron/kg body weight in the time-response experiment where animals were sacrificed at 2, 14, 28, or 57 days after exposure and a total dose of 0, 44, 87, 175, or 350 mg boron/kg body weight in the dose-response experiment with animals sacrificed after 14 days. In animals receiving 175 or 350 mg boron/kg body weight, testicular effects apparent at 14 days were enlarged irregular cytoplasmic lobes of mature spermatids in stage VIII seminiferous tubules (Leblond & Clermont, 1952) and a substantial increase in the testicular spermatid head count per testis. The first visible lesion was inhibited spermiation. Epididymal effects after 14 days included an increase in abnormal sperm forms, reduced caput epididymal sperm morphology with head and tail defects, and reduced caput epididymal sperm reserves. Epididymal sperm parameters had returned to normal and only minimal testicular changes remained by post-treatment day 57, indicating that these effects were reversible at these dose levels. The NOAEL for male reproductive effects in this study was 87 mg boron/kg body weight.

In a 2-year study by Weir & Fisher (1972), groups of 4 male and 4 female beagle dogs were fed diets containing boric acid or borax to provide doses of 0, 1.45, 2.93, or 8.75 mg boron/kg body weight per day. No evidence of toxicity was observed. An additional group of dogs (4 male and 4 female) was fed diets containing boric acid or borax leading to doses of 0 or 29.3 mg boron/kg body weight per day for 38 weeks. Testicular atrophy was observed in 2 test dogs receiving borax at 26 weeks. The authors stated that boric acid caused testicular degeneration in dogs, including spermatogenic arrest and atrophy of the seminiferous epithelium. This study was terminated at 38 weeks. In the study, the number of dogs was small and variable (1–2 dogs at each of three time points) and inadequate to allow statistical analysis. A common control group was used for both borax and boric acid exposure groups. Testicular lesions occurred in the controls (1 of 4 controls had slight to severe seminiferous tubular atrophy, another had moderate to severe atrophy, whereas a third had a detectable but insignificant reduction in spermatogenesis and 5% atrophic semini-
ferous tubules). This study was conducted before the advent of Good Laboratory Practices (GLP). Confidence in this study is low, and it was considered not suitable for inclusion into the risk assessment because of 1) small and variable numbers of dogs, 2) variable background lesions in controls leading to uncertainty regarding the strength of the response to treatment, 3) lack of GLP, and 4) other, more recent studies of greater scientific quality with findings at a similar or lower intake level of boron (Ku et al., 1993a; Price et al., 1996a).

Weir & Fisher (1972) fed Sprague-Dawley rats (35/sex per group) a diet containing borax or boric acid for 2 years at 0, 5.9, 17.5, or 58.5 mg boron/kg body weight per day. At the high dose, rats receiving either compound had decreased food consumption during the first 13 weeks of study and decreased growth throughout the study. Testes weights were significantly decreased at 58.5 mg/kg body weight per day. The seminiferous epithelium was atrophied, and the tubular size in the testes was decreased. No treatment-related effects were observed in rats receiving 5.9 or 17.5 mg boron/kg body weight per day. The LOAEL in this study was 58.5 mg boron/kg body weight per day for decreased testes weights, atrophied testes, histopathological alterations of the testes, and increased brain and thyroid weights. The NOAEL for this study was 17.5 mg boron/kg body weight per day.

In a companion three-generation reproduction study in rats, Weir & Fisher (1972) found that 58.5 mg boron/kg body weight per day produced testicular atrophy and complete suppression of fertility in rats. Lower doses (17.5 or 5.9 mg boron/kg body weight per day) did not reduce fertility. The small group size ($n = 8$), low control fertility rates ($\sim 60\%$), limited data reported, and inappropriate statistics all limit the applicability of these data for risk assessment.

In a multigeneration continuous-breeding experiment (Fail et al., 1990, 1991), Swiss CD-1 mice ($F_0$ generation) were fed boric acid in the diet at 0, 1000, 4500, or 9000 mg/kg feed for 27 weeks, which gave calculated doses of 0, 19.2, 104.7, and 222.1 mg boron/kg body weight per day for males and 0, 31.9, 148.1, and 290.5 mg boron/kg body weight per day for females. Treatment with boric acid
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significantly impaired fertility: no males or females in the high-dose groups were fertile. At the middle dose, the number of litters per pair, number of live pups per litter, proportion of pups born alive, and pup weight adjusted for litter size were all decreased. The trend towards a lower fertility index at this dose level started with the first litter and progressed in severity with subsequent matings. Animals from different treatment groups were cross-mated to determine the affected sex at this dose. When mid-dose males were mated with control females, mating and fertility indices were significantly depressed, with only one pair in that group producing a live litter; these indices were not affected when control males were mated with mid-dose females, confirming that the male was the affected sex. At \(F_0\) necropsy, sperm motility was significantly reduced in all exposed groups (by 12%, 32%, and 47%, from low- to high-dose groups, respectively). Low-dose and mid-dose animals from the \(F_1\) generation were exposed during gestation and lactation. The fertility of the low-dose \(F_1\) mice was not affected, but the litter-adjusted body weights of the \(F_2\) pups were significantly decreased (by 3.3%) relative to controls. The low dose was considered the LOAEL for decreased sperm motility in the \(F_0\) males, 26% increased uterine weight and 8% increased kidney/adrenal weight in \(F_1\) females, and a 3.3% reduction in litter-adjusted birth weight in the \(F_2\) pups. This study had no NOAEL, but the magnitude of the changes at the low dose (a 12% decrease in \(F_0\) sperm motility, an 8% increase in \(F_1\) kidney/adrenal weights, and a 3% reduction in \(F_2\) pup weights) is small and indicates that this dose level is close to the NOAEL.

Fail et al. (1989) utilized both CD-1 mice and wild deer mice (\textit{Peromyscus maniculatus}) to characterize the effects of boric acid on fertility and to test the reversibility of these effects. Adult CD-1 mice were exposed to boric acid in the feed for 27 weeks at 0, 1000, 4500, or 9000 mg/kg (consumed doses were not given). The males at the high and middle doses had testicular atrophy and decreased spermatogenesis. Fertility was diminished in animals receiving the middle dose and completely absent in the high-dose group. The same doses were used to test toxicity and reversibility in the wild mouse. The ability to produce offspring was significantly reduced by boric acid: none of the males in the high-dose group sired litters. Weight gain was similar for the treated and control wild mice. Although body and organ weights
were similar between the mid-dose and control groups at necropsy, the testis and total accessory sex organ weights were significantly lower in the high-dose group. These two species appear to differ in their sensitivity to boric acid. The CD-1 mice had body weight loss as early as 5 weeks at the mid-dose level, whereas deer mice did not lose weight even at the high dose. Tissue pathology findings at the middle dose were significant in CD-1 mice but not in deer mice. Deer mice were found to recover from boric acid exposure.

The development of the testicular lesion was investigated by Treinen & Chapin (1991), who fed boric acid at a level of 0 or 60.9 mg boron/kg body weight per day to male F-344 rats and sacrificed six treated and four control male rats at intervals from 4 to 28 days after the start of exposure. In half of the treated rats, there was inhibition of spermiation in 10–30% of stage IX tubules at 7 days and inhibition in all stage IX and stage X tubules of exposed rats at 10 days. At 28 days, there was significant loss of spermatocytes and spermatids from all tubules in exposed rats, and basal serum testosterone levels were significantly decreased from 4 days on.

Secondary to the loss of germ cells, the activities of enzymes found primarily in spermatogenic cells were significantly decreased, and enzyme activities associated with premeiotic spermatogenic cells were significantly increased in Sprague-Dawley rats exposed to 60 or 125–131 mg boron/kg body weight per day for 30 or 60 days (Lee et al., 1978). Mean plasma follicle stimulating hormone (FSH) levels were significantly elevated in a dose-dependent manner in all treatment groups in this study (30 to 125–131 mg boron/kg body weight per day) after 60-day exposures. FSH levels in animals exposed to the highest dose tested (125–131 mg boron/kg body weight per day) were still elevated 12 months after treatment termination, owing to atrophied testes and no recovery of spermatogenesis. Plasma luteinizing hormone (LH) levels were not significantly elevated, and mean plasma testosterone levels were within the normal range throughout the study (Lee et al., 1978).

Reversibility of testicular lesions was evaluated by Ku et al. (1993a) in an experiment in which F-344 rats were dosed at 3000, 4500, 6000, or 9000 mg boric acid/kg (26, 38, 52, and 68 mg boron/kg
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body weight per day) in the feed for 9 weeks and assessed for recovery up to 32 weeks post-treatment. Inhibited spermiation was exhibited at 3000/4500 mg boric acid/kg (5.6 μg boron/mg tissue), whereas inhibited spermiation progressed to atrophy at 6000/9000 mg boric acid/kg (11.9 μg boron/mg testes), with no boron accumulation in the testes to levels greater than found in blood during the 9-week period. After treatment, serum and testis boron levels in all dose groups fell to background levels. Inhibited spermiation at 4500 mg/kg was reversed by 16 weeks post-treatment, but focal atrophy was detected that did not recover up to 32 weeks post-treatment.

An unpublished study by W.W. Ku and colleagues (reported in Ku et al., 1993a) found no detectable treatment-related changes in testicular structure in rats induced by consumption of 17.5 mg boron/kg body weight per day for up to 9 weeks.

In a follow-up study to explore/identify the mechanism for this testicular toxicity of boric acid, Ku et al. (1993b) evaluated several end-points in cell culture systems following in vitro boric acid exposure. The data suggest an effect of boric acid on the DNA synthesis activity of mitotic and meiotic germ cells and, to a lesser extent, on energy metabolism in Sertoli cells. The effect on DNA synthesis occurred at boron concentrations that were associated with atrophy in vivo and shows that boric acid interferes with the production and/or maturation of early germ cells; this offers an explanation for atrophy, but not for inhibited spermiation.

Additional mechanistic studies by Ku & Chapin (1994) showed that testicular toxicity and CNS hormonal effects were not due to selective boron accumulation in testis or brain/hypothalamus, with testis boron concentrations at 1–2 mmol/litre. Changes in testis phosphorus, calcium, and zinc levels did not precede atrophy. In vitro studies showed no effect on the steroidogenic functions of isolated Leydig cells, supporting the suggestion of a CNS-mediated hormonal effect. The authors showed that inhibited spermiation was not due to increased testicular cyclic adenosine monophosphate or reduced serine protease plasminogen activators. Also evaluated were effects of boric acid in Sertoli–germ cell co-cultures on Sertoli cell energy metabolism (lactate secreted by Sertoli cells is a preferred energy source for germ
cells) and DNA/RNA synthesis (germ cells synthesize DNA/RNA, and boric acid impairs the synthesis of these nucleic acids in the liver). The most sensitive \textit{in vitro} end-point was DNA synthesis in mitotic/meiotic germ cells; energy metabolism in germ cells was affected to a lesser extent, which was manifested \textit{in vivo} as a decrease in early germ cell/Sertoli cell ratio prior to atrophy in the testes. The mechanisms of inhibited spermiation are still not defined.

In summary, male reproductive effects from boron have been noted in mice, rats, and dogs. Reproductive effects observed include inhibition of spermiation in stage IX and X tubules, followed by germ cell loss, changes in epididymal sperm morphology and caput sperm reserves, decreased serum testosterone levels, and testicular atrophy. Male reproductive effects have been reported in oral exposure studies at doses as low as 29 mg boron/kg body weight per day in dogs exposed for 2 years to dietary boric acid or borax (Weir & Fisher, 1972); for rats in this same study, the LOAEL for reproductive toxicity was 58.5 mg boron/kg body weight per day.

7.5 \textbf{Developmental toxicity}

Developmental toxicity has been demonstrated experimentally in rats, mice, and rabbits (see Table 16) (Heindel et al., 1992; Price et al., 1996b).

Sprague-Dawley rats were fed a diet containing 0, 13.6, 28.5, or 57.7 mg boron/kg body weight per day as boric acid from gestation days 0 to 20 (Heindel et al., 1992). An additional group of rats received boric acid at 94.2 mg boron/kg body weight per day on gestation days 6–15 only. Maternal effects included a significant and dose-related increase in relative liver and kidney weights at $\geq$28.5 mg boron/kg body weight per day. Treatment with 94.2 mg boron/kg body weight per day significantly increased prenatal mortality. Average fetal body weight per litter was significantly reduced in a dose-related manner in all treated groups compared with controls. The percentage of malformed fetuses per litter and the percentage of litters with at least one malformed fetus were significantly increased at $\geq$28.5 mg boron/kg body weight per day. Malformations consisted primarily of anomalies of the eyes, the CNS, the cardiovascular system, and the
axial skeleton. The most common malformations were enlargement of lateral ventricles in the brain and agenesis or shortening of rib XIII. The percentage of fetuses with variations per litter was reduced relative to controls at 13.6 and 28.5 mg boron/kg body weight per day (due to a reduction in the incidence of rudimentary or full ribs at lumbar 1) but was significantly increased in rats exposed to 94.2 mg boron/kg body weight per day. The variation with the highest incidence among fetuses was wavy ribs. The LOAEL of 13.6 mg boron/kg body weight per day (lowest dose tested) for rats occurred in the absence of maternal toxicity; a NOAEL was not found in this study.

Price et al. (1996a) did a follow-up to the Heindel et al. (1992) study in Sprague-Dawley (CD) rats to determine a NOAEL for fetal body weight reduction and to determine whether the offspring would recover from prenatally reduced body weight during postnatal development. Skeletal malformations and variations were also studied to further characterize the low end of the dose–response curve (phase 1) and to determine whether the incidence of skeletal defects in offspring changed during postnatal life (phase 2). Boric acid was administered in the diet to CD rats from gestational day 0 to 20. In phase 1, dams were terminated and uterine contents examined on gestational day 20. During phase 1, the intake of boric acid was 0, 3.3, 6.3, 9.6, 13.3, or 25 mg boron/kg body weight per day. For the low- to high-dose groups, fetal body weights were 99, 98, 97, 94, and 88% of controls; the reduction was significant only in the 13.3 and 25 mg boron/kg body weight per day dose groups on gestational day 20. During phase 1, incidences of short rib XIII (a malformation) and wavy rib (a variation) were increased in the ≥13.3 mg boron/kg body weight per day dose groups relative to control litters. There was a decreased incidence of rudimentary extra rib on lumbar 1 (a variation) in the high-dose group that was deemed biologically but not statistically significant. During phase 2, the intake of boric acid during gestation was 0, 3.3, 6.5, 9.8, 12.9, or 25.3 mg boron/kg body weight per day. At birth, boric acid exposure stopped and dams were allowed to deliver and rear their litters until postnatal day 21. On postnatal day 0 of phase 2, there were no effects of boric acid on offspring body weight, nor were any differences seen through postnatal day 21. On postnatal day 21 of phase 2, the percentage of pups per litter with short
rib XIII was elevated only in the 25.3 mg boron/kg body weight per day dose group, but there was no treatment-related increase in wavy rib or extra rib (full or rudimentary) on lumbar 1 observed in these pups on day 21. The NOAEL for phase 1 of this study is 9.6 mg boron/kg body weight per day based on a decrease in fetal body weight. The LOAEL was 13.3 mg boron/kg body weight per day for phase 1. The NOAEL for phase 2 was 12.9 mg boron/kg body weight per day, and the LOAEL was 25.3 mg boron/kg body weight per day. The results of this study provide a NOAEL and LOAEL that complement the rat LOAEL of 13.6 mg/kg body weight per day in the Heindel et al. (1992) study.

Heindel et al. (1992) also investigated the developmental toxicity and teratogenicity of boric acid in mice at 0, 43, 79, or 175 mg boron/kg body weight per day in the diet. There was a significant dose-related decrease in average fetal body weight per litter at 79 and 175 mg boron/kg body weight per day. In offspring of mice exposed to 79 or 175 mg boron/kg body weight per day during gestation days 0–17, there was an increased incidence of skeletal (rib) malformations. These changes occurred at doses for which there were also signs of maternal toxicity (increased kidney weight and pathology); the LOAEL for developmental effects (decreased fetal body weight per litter) was 79 mg boron/kg body weight per day, and the NOAEL for developmental effects was 43 mg boron/kg body weight per day.

Price et al. (1996b) investigated the developmental toxicity and teratogenicity of boric acid in rabbits at doses of 0, 10.9, 21.9, or 43.7 mg boron/kg body weight per day given by gavage. Frank developmental effects in rabbits exposed to 43.7 mg boron/kg body weight per day included a high rate of prenatal mortality, increased number of pregnant females with no live fetuses, and fewer live fetuses per live litter on day 30. Also at 43.7 mg boron/kg body weight per day, malformed live fetuses per litter increased significantly, primarily because of the incidence of fetuses with cardiovascular defects, the most prevalent of which was interventricular septal defect. Skeletal variations observed were extra rib on lumbar 1 and misaligned sternebrae. The NOAEL for maternal and developmental effects was 21.9 mg boron/kg body weight per day, and the LOAEL for maternal and developmental effects was 43.7 mg boron/kg body weight per day.
7.6 Mutagenicity and related end-points

Boric acid was not mutagenic in *Salmonella typhimurium* with or without rat or hamster S9 fraction (Haworth et al., 1983; Benson et al., 1984; NTP, 1987) or in mouse lymphoma L5178Y/TK+/− cells with or without rat liver S9 (NTP, 1987; McGregor et al., 1988). Borax was not mutagenic in *Salmonella* with or without rat liver S9 (Benson et al., 1984). Refined borax, crude borax ore, and kermite ore were not mutagenic in V79 Chinese hamster cells, C3H/1OT1/2 mouse embryo fibroblasts, or diploid human foreskin fibroblasts (Landolph, 1985). Sodium perborate (NaB0₃) was shown to interact with DNA in the *Escherichia coli* Pol A assay, presumably by being converted to hydrogen peroxide (Rosenkranz, 1973). Other tests showed that boric acid did not induce chromosomal aberrations or sister chromatid exchanges in Chinese hamster ovary cells (NTP, 1987). Existing data suggest that genotoxicity is not an area of concern following exposure to boron compounds in humans.

7.7 Carcinogenicity

The 2-year feeding study (NTP, 1987; Dieter, 1994) showed no evidence of carcinogenicity in B6C3F₁ mice. The Weir & Fisher (1972) study showed no evidence of boric acid-related carcinogenicity in rats, although not all tissues were examined. Based on the lack of human data and on the data from these two animal tests, boron is classified by the US EPA as a Group D chemical (not classifiable as to human carcinogenicity) (US EPA, 1994).

7.8 Toxicity effects summary

The laboratory animal toxicity data show that boric acid (and other borates) is not a carcinogen and lacks significant mutagenicity. The crossover mating trial in the Fail et al. (1991) study showed that female mouse reproduction was unaffected by about 120 mg boron/kg body weight per day. The NOAELs and LOAELs of reproductive/developmental effects from various studies are ranked in Table 17. The Weir & Fisher (1972) dog study is omitted from this summary because of low numbers of animals and the presence of lesions in the controls. It can be seen that rat fetal development is more sensitive
<table>
<thead>
<tr>
<th>Species/duration$^{a}$</th>
<th>Dose (mg boron/kg body weight per day)</th>
<th>Effect</th>
<th>Reference</th>
</tr>
</thead>
<tbody>
<tr>
<td>SD rat/gd 0–20</td>
<td>9.6</td>
<td>NOAEL for developmental effects immediately pre-term</td>
<td>Price et al. (1996a)</td>
</tr>
<tr>
<td>SD rat/gd 0–20</td>
<td>12.9</td>
<td>NOAEL for developmental effects measured at weaning</td>
<td>Price et al. (1996a)</td>
</tr>
<tr>
<td>SD rat/gd 0–20</td>
<td>13.3</td>
<td>LOAEL for reduced fetal weight, increased rib malformations/variations</td>
<td>Price et al. (1996a)</td>
</tr>
<tr>
<td>SD rat/gd 0–20</td>
<td>13.6</td>
<td>LOAEL for reduced fetal weight, increased rib malformations/variations</td>
<td>Heindel et al. (1992)</td>
</tr>
<tr>
<td>Male SD rat/multigeneration</td>
<td>17.5</td>
<td>NOAEL for reduced fetal weight, increased rib malformations/variations</td>
<td>Weir &amp; Fisher (1972)</td>
</tr>
<tr>
<td>SD rat/gd 0–20</td>
<td>25.4</td>
<td>LOAEL for reduced fetal weight, increased rib malformations/variations</td>
<td>Ku et al. (1993a)</td>
</tr>
<tr>
<td>Male SD rat/63 days</td>
<td>26</td>
<td>LOAEL for reduced fetal weight, increased rib malformations/variations</td>
<td>Ku et al. (1993a)</td>
</tr>
<tr>
<td>Male SD rat/≤63 days</td>
<td>52</td>
<td>LOAEL for testicular atrophy</td>
<td>Ku et al. (1993a)</td>
</tr>
<tr>
<td>Male beagle dogs/2 years</td>
<td>29</td>
<td>Altered testis weight and histopathology</td>
<td>Weir &amp; Fisher (1972)</td>
</tr>
<tr>
<td>Male beagle dogs/90 days</td>
<td>44</td>
<td>Altered testis weight and histopathology</td>
<td>Weir &amp; Fisher (1972)</td>
</tr>
<tr>
<td>CD-1 mouse/multigeneration</td>
<td>19.2</td>
<td>LOAEL for reduced sperm motility, reduced F2 pup weight</td>
<td>Fail et al. (1991)</td>
</tr>
<tr>
<td>CD-1 mouse/gd 0–17</td>
<td>43</td>
<td>NOAEL for mouse developmental toxicity</td>
<td>Heindel et al. (1992)</td>
</tr>
<tr>
<td>CD-1 mouse/gd 0–17</td>
<td>79</td>
<td>LOAEL for decreased fetal body weight</td>
<td>Price et al. (1996b)</td>
</tr>
<tr>
<td>New Zealand white rabbits/gd 6–19</td>
<td>21.9/43.7</td>
<td>NOAEL/LOAEL for decreased fetal body weight, increased fetal cardiovascular malformations and maternal toxicity</td>
<td>Price et al. (1996b)</td>
</tr>
</tbody>
</table>

$^{a}$ gd = gestational days.
than other processes to the adverse effects of elevated boron exposure, with a LOAEL in rats of 13.3 mg boron/kg body weight per day reducing fetal weight gain and increasing rib anomalies (reversibly). The current NOAEL for these effects in rats is approximately 10 mg boron/kg body weight per day. Increased doses produced sequentially additional effects on sperm release, increased rabbit cardiovascular defects, reduced epididymal sperm counts, testicular atrophy, and mouse fetal defects.

The Task Group recognized the lack of a NOAEL in the Fail et al. (1991) study. The effects of concern in part duplicated the developmental toxicity findings (reduced pup body weight). However, the unique effects in the adult F1 female mice (increased uterine weight, reduced cycle length) are consistent with an effect on female reproduction that was not seen in the F0 females. The possibility of unique transgenerational or functional developmental toxicity in the absence of an available dose–response concerned the Task Group.

Although the current NOAEL is based on rat fetal body weight effects, the Task Group noted that this could be lowered and a new "critical effect" could emerge if the significant data gap (second-generation fertility and necropsy data for multiple doses including a NOAEL in rats) were filled.

7.9 Physiological effects

Since 1981, circumstantial evidence has been accumulating that suggests that boron may be an essential nutrient for higher animals; that is, a dietary deprivation of boron consistently results in changed biological functions that can be construed as detrimental and are preventable or reversible by an intake of physiological amounts of boron. Convincing findings have been reported that show that dietary boron deprivation affects mineral and energy metabolism in chicks and rats (Hunt, 1994); these effects are more marked when a physiological stressor is present, especially marginal cholecalciferol (vitamin D3) nutriture. For example, a boron supplement of 3 μg/g to a basal diet containing 0.465 μg boron/g alleviated the marginal cholecalciferol deficiency-induced changes in bone, plasma glucose, energy substrate utilization, and growth (Hunt, 1994). Hunt et al. (1994) have found
that boron deprivation depresses macromineral content in bone and some indices of the maturation of the cartilage growth plate independently of vitamin D nutriture. Brain composition and function in rats are also affected by dietary boron. Boron deprivation was found to systematically influence brain electrical activity assessed by an electrocorticogram in mature rats (Penland & Eberhardt, 1993). In this study, brain copper concentrations were higher in boron-deprived than in boron-supplemented rats. Furthermore, calcium concentrations in total brain and in brain cortex, as well as phosphorus concentration in the cerebellum, were found to be higher in boron-deprived (0.158 µg/g diet) than in boron-supplemented (2.72 µg/g diet) rats fed a cholecalciferol-deficient diet (Hegsted et al., 1991). This study also found that the apparent absorption and balance of calcium, magnesium, and phosphorus were decreased by boron deprivation. Hunt (1988) has reported that chicks apparently require about 1.0 µg boron/g diet for normal development. These studies collectively indicate that boron in physiological amounts is beneficial to, if not essential for, higher animals (see also section 8.4).
8. EFFECTS ON HUMANS

8.1 General population exposure

8.1.1 Short-term toxicity and poisoning incidents

Available human exposure data on boron compounds for routes other than inhalation focus on boric acid and borax. According to Stokinger (1981), the lowest lethal dose for humans exposed to boric acid is 640 mg/kg body weight by oral exposure, 8600 mg/kg body weight by dermal exposure, and 29 mg/kg body weight by intravenous injection. Stokinger (1981) stated that deaths can occur at doses between 5 and 20 g of boric acid total for adults and below 5 g total for infants. Litovitz et al. (1988) stated that potential lethal doses are usually cited as 3–6 g total for infants and 15–20 g total for adults. A case-series report of seven infants (aged 6–16 weeks) who used pacifiers coated with a borax and honey mixture for 4–10 weeks reported that exposures ranged from 4 to 30 g, with an estimated average daily ingestion of 0.143–0.429 g (O’Sullivan & Taylor, 1983). The actual relative doses are unknown. Toxicity was manifested by generalized or alternating focal seizure disorders, irritability, and gastrointestinal disturbances. Other findings included inflammation, congestion, oedema, exfoliation of the mucosa, cloudy swelling and granular degeneration of tubular cells, and exfoliative dermatitis. Although infants appear to be more sensitive than adults to boron compounds, lethal doses are not well documented in the literature.

A few case reports have been published for poisoning incidents. Teshima et al. (1992) reported that a 26-year-old woman ingested 21 g of boric acid. The elimination of boric acid was about 4 times faster with haemodialysis than with conventional medical treatment. The patient was discharged from the hospital 12 days following admission. In another case report, Grella et al. (1976) described transplacental poisoning. A pregnant woman who had a personal history of diabetes was accidentally given 70 g of boric acid instead of 70 g of glucose for the glucose tolerance test at 33 weeks’ gestation. She was immediately treated with gastric lavage and intravenous sodium bicarbonate fructose. The woman developed contractions, and an emergency caesarean delivery was scheduled. The infant was born alive weighing
2.5 kg and had spontaneous respirations. Soon afterwards, the infant developed cardiac arrest, was resuscitated, and died. Cause of death was attributed to cardiocirculatory collapse.

Boric acid and borax were widely used in medicine at the beginning of the century for therapeutic purposes, both locally as well as orally. Boric acid was used to treat various diseases, such as epilepsy and infectious diseases. Several case studies reviewed by Kliegel (1980) describe mild to severe responses to boron compounds. Among all 19 patients with reported body hair loss as a response to boron compound treatment, 16 persons had epilepsy and 3 had urinary or genital infections. Stein et al. (1973) described an extremely unusual case of a 32-year-old woman who ingested and swallowed several bottles of mouthwash containing boric acid daily for a minimum of 1 year. The woman was reported to have pancreatitis resulting from heavy alcohol ingestion and medications for epilepsy. The woman lost almost all of her body and scalp hair; other clinical signs included erythema on the palms of her hands, severe fatigue, anorexia, and mental confusion. Her blood boric acid level was 3.2 mg/100 ml, corresponding to 0.56 mg boron/100 ml (the normal value was reported as 0.3 mg boric acid/100 ml). Upon cessation of mouthwash consumption, hair growth returned, suggesting that the effect was reversible.

Goldbloom & Goldbloom (1953) reported four cases of boric acid poisoning and reviewed an additional 109 cases in the literature. The four cases were infants exposed to boric acid by repeated topical applications of baby powder. Toxicity was manifested by cutaneous lesions (erythema over the entire body, excoriation of the buttocks, and desquamation), gastrointestinal disturbances, and seizures. One patient died, but cause of death was not specifically attributed to boric acid. Approximately 35% of the 109 other case reports involved children under 1 year of age. The mortality rate was 70.2% for children compared with 55.0% for all cases combined. Death occurred in 27/51 (53%) patients exposed by ingestion, in 3/4 (75%) patients subjected to gastric lavage with boric acid, in 19/28 (68%) patients exposed by dermal application for treating burns, wounds, and skin eruptions, and in 14/26 (54%) patients exposed by other routes. Information on signs and symptoms for 80 patients showed that
Effects on Humans

gastrointestinal disturbances were prevalent (73%), followed by CNS effects (67%). Cutaneous lesions were prevalent in 76% of the cases and in 88% of cases involving children under 2 years of age. Gross and microscopic findings were reported for 27/60 (45%) fatal cases. In general, boric acid caused chemical irritation primarily at sites of application and excretion and in organs with maximum boron concentrations. The most common CNS findings were oedema and congestion of the brain and meninges. Other common findings included liver enlargement, vascular congestion, fatty changes, swelling, and granular degeneration ($n = 13$).

In addition to case reports, poison centres have published case-series reports. Unlike the case reports reviewed by Goldbloom & Goldbloom (1953), more recent reports suggest that the oral toxicity of boron in humans is milder than previously thought. Litovitz et al. (1988) conducted a retrospective review of 784 cases of boric acid ingestion reported to the National Capital Poison Center in Washington, DC, USA, during 1981–1985 and the Maryland Poison Center in Baltimore, MD, USA, during 1984–1985. The amount of boric acid ingested and clinical manifestations of toxicity were reported; 88.3% of the cases were asymptomatic. All but two of the cases had acute (single) ingestion, and 80.2% involved children under 6 years of age. No severe toxicity or life-threatening effects were noted, although boric acid levels in blood serum ranged from 0 to 340 µg/ml. The most frequently occurring symptoms, which involved the gastrointestinal tract, included vomiting ($n = 32$), abdominal pain ($n = 15$), diarrhoea ($n = 13$), and nausea ($n = 7$). Other symptoms (primarily CNS and cutaneous) occurred in six or fewer cases: lethargy, rash, headache, light-headedness, fever, irritability, and muscle cramps. The average dose ingested estimated from 659 cases was 1.4 g (range 0.010–88.8 g). For children under 6 years, the average dose was 0.5 g (range 0.010–22.2 g), compared with 4.1 g (range 0.030–88.8 g) for individuals age 6 years or above. The average dose for asymptomatic cases was 0.9 g (range 0.010–88.8 g), compared with 3.2 g (range 0.10–55.3 g) for symptomatic cases. According to Litovitz et al. (1988), 21 of the children under 6 years of age, 15 of whom were under 2 years of age, ingested the reported potential lethal dose of 3 g; 8 adults ingested the reported potential lethal dose of 15 g without evidence of lethal effects.
Linden et al. (1986) published a retrospective review of 364 cases of boric acid exposure reported to the Rocky Mountain Poison and Drug Center in Denver, CO, USA, between 1983 and 1984. Vomiting, diarrhoea, and abdominal pain (incidence not reported) were the most common symptoms given by the 276 cases exposed in 1983. Of the 72 cases reported in 1984 for whom medical records were complete, 79% were asymptomatic, whereas 20% had mild gastrointestinal symptoms noted. One 2-year-old child died, presumably from repeated ingestion of an insecticide containing 99% boric acid.

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).

8.1.2 Reproductive effects

An ecological study assessed boron exposure from drinking-water and fertility among residents in two geographical regions in Turkey. Region I comprised 2368 residents, whereas Region II comprised 2319 residents. Boron levels in drinking-water were noticeably higher in Region I (range 2.05–29 mg/litre) than in Region II (range 0.03–0.40 mg/litre). Ever-married residents from each region who could provide reproductive histories for three generations of family members represented the study sample — i.e. 159 probands (6.7% of population) in Region I and 154 (6.7%) in Region II. The percentages of married couples with one or more live births (≥90%) were comparable for the two regions, regardless of generation assessed. The overall percentage of couples with unresolved infertility or those without children across three generations was comparable for the two regions (i.e. 6.0% and 4.6%, respectively). Secondary sex ratios (ratio of male to female live births) appeared to be different for the two regions. Region I had a ratio below 1 (0.89), suggesting an excess of female births; Region II had a ratio slightly above 1 (1.04), suggesting a slight

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excess of male births. Statistical significance was not formally evaluated in any of the above analyses. The results of this descriptive study suggest that fertility, as measured by the ability to produce a live birth, is not adversely affected for residents of this geographical area with high levels of boron in their drinking-water and soil. The observed reversal of the secondary sex ratio for Region I requires careful interpretation, as no attention was given to factors reported to alter sex ratios (e.g. advancing parental age, elective abortion rates, and multiple births). Further consideration of potential sources of bias stemming from the selection of respondents who were largely male and their ability to accurately recollect and report fertility outcomes is needed. The extent to which these findings are generalizable, if at all, to other populations is unknown.

8.2 Occupational exposure

8.2.1 Short-term irritative effects

The majority of toxic effects reported in occupational studies are acute or short-term in nature and result from the irritant effects of boron compounds. Several studies have shown that workers exposed to borax complain of symptoms that are due to respiratory irritation, which include nosebleeds, eye and nasal irritation, sore throats, cough, and shortness of breath; dermatitis has also been reported (Birmingham & Key, 1963; NIOSH, 1978). Generally, people with hyperreactive respiratory tracts (e.g. asthmatics) may experience more severe irritant effects following inhalation exposure. However, there is a lack of data to support the existence of an especially sensitive high-risk human population for exposure to boron or boron compounds.

A medical survey of 113 workers employed in a borax mining and refining plant was conducted by Garabrant et al. (1984). The reference group comprised 214 workers employed in areas with low or minimal exposure to boric acid and boron oxide; exposed workers had been employed for a minimum of 5 years or were currently employed in areas of heavy borax exposure. The average air concentration of particles $\leq 5 \mu m$ in diameter measured from samples taken between 1979 and 1981 was 4.1 mg/m$^3$ (range 1.2–8.5 mg/m$^3$).
The workers in both groups were predominantly white males; the mean age of the exposed group was 38.2 years, compared with 42.1 years in the referent group. The mean duration of employment for exposed and unexposed workers was 11.0 and 12.9 years, respectively. Smoking patterns were similar for the two groups. Symptoms reported more frequently by exposed workers than by unexposed workers \((p < 0.001)\) were eye irritation (12.4% and 2.8%, respectively), dry mouth, nose, or throat (10.6% and 1.9%, respectively), sore throat (5.3% and 0.5%, respectively), and productive cough (4.4 and 0%, respectively). No significant differences were noted between the two groups of workers with respect to dry cough, shortness of breath, chest tightness, chest pain, and nosebleeds.

A more detailed analysis of 629 (93% participation) workers in this plant was presented by Garabrant et al. (1985). This analysis was based on frequency of acute symptoms in four mean boron dust exposure categories (1.1, 4.0, 8.4, and 14.6 \(\text{mg/m}^3\)) and persistent symptoms (presumably chronic effects) in three exposure categories (0.9, 4.5, and 14.6 \(\text{mg/m}^3\) of total particulates). The particles were composed almost entirely of borax. Acute symptoms showing a significant linear trend \((p < 0.0001)\) in order of decreasing frequency were dryness of mouth, nose, throat, and eye irritation, dry cough, nosebleeds, sore throat, productive cough, shortness of breath, and chest tightness. The frequency of these symptoms in the highest exposure category ranged from 5% to 33%. The only symptom reported by 5% or more of workers exposed to 4.0 \(\text{mg/m}^3\) was eye irritation; no symptoms were reported by 5% or more of workers exposed to 1.1 \(\text{mg/m}^3\). The pulmonary function findings were not significantly affected by exposure to boron. Chest X-rays did not show abnormal regions indicative of boron exposure. The authors concluded that borax caused simple respiratory irritation that produces chronic bronchitis with no impairment of pulmonary function. Also, borax dust appeared to cause acute and persistent respiratory irritation at concentrations \(\geq 4.5 \text{ mg/m}^3\). Therefore, the value for the intermediate exposure category for persistent symptoms (4.5 \(\text{mg/m}^3\) as borax) was considered to be the LOAEL.

Wegman et al. (1994) conducted a prospective cohort study to examine acute irritative effects as well as chronic pulmonary function
abnormalities in mine and processing plant workers exposed to sodium borate dust. Exposure–response associations were also examined as related to acute irritant symptoms associated with sodium borate dust exposure in mining and processing plants. In comparison with unexposed workers, exposed workers reported significantly more nasal irritation (rate ratio [RR] = 8.8), eye irritation (RR = 5.2), throat irritation (RR = 2.9), cough (RR = 1.7), and breathlessness (RR = 7.1). Continuous measures of particulate exposure were made throughout the day and were related to hourly measurements of health outcomes. Exposure–response relationships were present for each of the specific symptoms at several symptom intensity levels. Acute irritant effects did not lead to any undue chronic sequelae. With regard to the acceptable level of risk, Wegman et al. (1994) concluded that a threshold limit value (TLV) exposure of 10 mg borate/m^3 was protective of workers' health. This value is consistent with the nuisance dust standard (ACGIH, 1991).

8.2.2 Male reproductive and other long-term health effects

Effects on the male reproductive system have also been reported, although data regarding subchronic or chronic exposure on the population in general are limited.

In the study by Wegman et al. (1994), sodium borate particulate exposure estimates were used to estimate cumulative exposure in relation to long-term pulmonary function. Of the 631 workers who originally underwent pulmonary evaluation 7 years earlier, 336 (53%) underwent a subsequent evaluation. Ninety (303/336) per cent of workers were found to have acceptable pulmonary test results. After the expected smoking-related pulmonary abnormalities were taken into account, no relation was observed between forced expiratory volume in 1 second (FEV_1) and accumulated exposure to sodium borate. People with hyperreactive respiratory tracts such as those with asthma may experience more severe irritant effects following inhalation exposure. However, a sensitive population was not found.

Fertility following occupational exposure to boron was assessed in a descriptive study. Whorton et al. (1994) estimated the standardized birth ratio (SBR) to assess fertility in 542/750 (72% participation).
occupational workers in a US borax mine located in the Mojave Desert, California, USA. These workers are unique, in that their occupational exposure to sodium borate dust and desert soil is uncontaminated by other exposures and given their long average length of employment (mean 18 years). Self-administered questionnaires were used to ascertain the observed number of live births fathered by male workers following employment. The US general population adjusted for age, race, parity, and calendar time period was used to estimate the expected number of live births. The SBR is simply a ratio of the observed number of live births to the expected number. An SBR above 100 reflects an excess of live births in relation to the US general population, whereas an SBR below 100 reflects a deficit. Occupational boron exposure was based on job titles and categorized into quintiles of mean exposure levels ranging from <0.82 mg/m$^3$ to $\geq 5.05$ mg/m$^3$.

SBRs were significantly elevated for workers in the lowest (<0.82 mg/m$^3$) and highest ($\geq 5.05$ mg/m$^3$) exposure categories (i.e. 151 and 125, respectively). No significant trend between exposure and SBRs was observed. An excess percentage of female live births in comparison with male births was observed across most categories of exposure and length of employment. The authors noted that this female excess did not reflect a deficiency of male births, as an excess of births for both genders was found. None of the findings, however, was statistically significant. These findings need to be carefully interpreted, largely given the selection of the US general population as the standard. (The authors state that fertility rates were not available for their target population.) The extent to which this sample of workers is comparable to the US general population with respect to factors that affect fecundity and fertility remains to be established. Further considerations are needed with respect to the calculation of SBRs, such as the exclusions of multiple births, and in terms of potential response bias. The authors did attempt to enhance the validity of self-reported fertility data and select co-variates by using additional data sources and by efforts to minimize selection bias. In sum, the findings do not support an adverse effect of boron on demonstrated fertility for this occupational sample of male workers in comparison with the US general population.
8.3 Carcinogenicity

Evidence for carcinogenicity of boron and boron compounds in humans is not available, largely because it has not been studied. Based on the evidence from two lifetime studies in mice (NTP, 1987) and rats (Weir & Fisher, 1972), boron compounds have been classified by the US EPA in Group D (i.e. not classifiable as to human carcinogenicity) (US EPA, 1994).

8.4 Physiological effects

Since 1987, circumstantial evidence has been accumulating that suggests that boron may be an essential nutrient for humans; that is, a dietary deprivation of boron consistently results in changed biological functions that could be construed as detrimental and that are preventable or reversible by an intake of physiological amounts of boron. Many of these changed functions caused by boron deprivation have been duplicated in animal models. The major reason boron is not generally recognized as essential or nutritionally important for humans is probably that a specific biochemical function for boron has not been elucidated, or, as demonstrated for plants (also for which no biochemical function has been elucidated), boron has not been shown necessary to complete the life cycle. Nonetheless, findings from human experiments show that boron is a dynamic trace element that can affect the metabolism or utilization of numerous substances involved in life processes, including calcium, copper, magnesium, nitrogen, glucose, triglycerides, reactive oxygen, and estrogen. Through these effects, boron can affect the function or composition of several body systems, including blood, brain, and skeleton, in a positive manner, which demonstrates that boron is a beneficial element, if not an essential mineral element, at physiological amounts.

Although the first findings involving boron deprivation of humans appeared in 1987 (Nielsen et al., 1987), the most convincing findings have come mainly from two studies in which men over the age of 45, postmenopausal women, and postmenopausal women on estrogen therapy were fed a low-boron diet (0.25 mg/2000 kcal) for 63 days and then fed the same diet supplemented with 3 mg boron/day for 49 days (Nielsen, 1989, 1994; Nielsen et al., 1990, 1991, 1992b;
Penland, 1994). These dietary intakes were near the low and high values in the range of usual dietary boron intakes (see section 5.2.4). The major differences between the two studies were the intakes of copper and magnesium; in one experiment they were marginal or inadequate, whereas in the other they were adequate. Boron deprivation had several effects, regardless of dietary copper and magnesium. In addition, the marginal or inadequate copper and magnesium caused apparent detrimental changes that were more marked during boron deprivation than during boron repletion. Among the effects of boron supplementation after 63 days of boron depletion in these experiments were the following: an effect on macromineral metabolism, evidenced by increased serum 25-hydroxycholecalciferol and a decrease in the elevated calcitonin that was apparently caused by inadequate copper and magnesium; an effect on energy metabolism, suggested by decreased serum glucose and increased serum triglycerides; an effect on nitrogen metabolism, indicated by decreased blood urea nitrogen and serum creatinine and increased urinary hydroxyproline excretion; an effect on reactive oxygen metabolism, indicated by increased serum erythrocyte superoxide dismutase and serum ceruloplasmin; and an effect on erythropoiesis and haematopoiesis, suggested by increased blood haemoglobin and mean corpuscular haemoglobin content but decreased haematocrit, platelet number, and erythrocyte number. Boron supplementation after depletion also enhanced the elevation in serum 17β-estradiol and plasma copper caused by estrogen therapy, altered electroencephalograms such that they suggested improved behavioural activation (e.g. less drowsiness) and mental alertness, and improved processes of attention and memory.

Two hypotheses have appeared to account for the multiple effects described above. One hypothesis is that boron has a role in cell membrane function, stability, or structure, such that it influences the response to hormone action, transmembrane signalling, or transmembrane movement of regulatory cations or anions (Nielsen, 1991); a similar hypothesis has also appeared for the functional role of boron in plants (Parr & Loughman, 1983; Blaser-Grill et al., 1990; Blevins & Lukaszewski, 1994). The other hypothesis is that boron is a negative regulator that influences a number of metabolic pathways by competitively inhibiting some key enzyme reactions (Hunt, 1994).
Regardless of the fact that the function of boron remains undefined, boron is becoming recognized as an element of potential nutritional importance because of the findings from human and animal studies. The latest report on trace elements in human nutrition and health published by the World Health Organization (WHO, 1996) suggested that an individual mean basal requirement for adults may be about 0.375 mg/day, and the minimum mean population intake that meets basal needs could be about 0.75 mg/day for adults. The report also indicated that an acceptable safe range of population mean intakes for boron for adults could well be 1–13 mg/day.
9. EFFECTS ON OTHER ORGANISMS IN THE LABORATORY AND FIELD

9.1 Laboratory experiments

9.1.1 Microorganisms

9.1.1.1 Water

Several investigators have studied the effects of borates on bacteria, protozoa, and algae (see Table 18). Effect concentrations for the bacterium *Pseudomonas putida* range widely. No observed effects were noted after 72 h at 291 mg boron/litre by Schöberl & Huber (1988), whereas Guhl (1996) found a 16-h EC$_{10}$ of 7.6 mg boron/litre. Guhl (1996) and Bringmann & Kuhn (1980) reported 30-min EC$_{10}$ and 72-h EC$_3$ values of 340 and 290 mg boron/litre, respectively. Twenty per cent light loss, compared with controls, from *Photobacterium phosphoreum* was determined to occur after 30 min at 18 mg boron/litre (Guhl, 1996). Nitrogen-fixing cyanobacteria require boron for proper functioning of the heterocyst cell wall (Bonilla et al., 1990). Mateo et al. (1986) concluded that boron is essential for nitrogen fixation in *Anabaena*.

A wide range of effect concentrations was reported for two protozoan species. Bringmann & Kuhn (1980) reported a 72-h EC$_3$ of 0.3 mg boron/litre for *Entosiphon sulcatum*, whereas Guhl (1996) showed a 72-h NOEC of >10 mg boron/litre. Reproduction of *Paramecium caudatum* was completely inhibited at 70 mg boron/litre (Bringmann & Kuhn, 1980), and no effects were observed at 18 mg boron/litre by Sprague (1972).

De Jong (1965) determined the sensitivity of another green alga, *Chlorella vulgaris*, to borax concentrations ranging from 0.0001 to 30% of the medium. Inoculated cultures were cultivated at room temperature in daylight for 3–4 months. The highest concentration of borax tolerated by *C. vulgaris* was 0.6 mg boron/litre, and the lowest concentration inhibiting growth was 1.2 mg boron/litre.
Table 18. Borate toxicity to bacteria, protozoa, and algae

<table>
<thead>
<tr>
<th>Species</th>
<th>Duration</th>
<th>End-point</th>
<th>Parameter</th>
<th>Borate concentration in solution (mg boron/litre)</th>
<th>Reference</th>
</tr>
</thead>
<tbody>
<tr>
<td><em>Pseudomonas putida</em></td>
<td>30 min</td>
<td>Growth inhibition</td>
<td>EC&lt;sub&gt;10&lt;/sub&gt;</td>
<td>340</td>
<td>Guhl (1996)</td>
</tr>
<tr>
<td></td>
<td>16 h</td>
<td>Growth inhibition</td>
<td>EC&lt;sub&gt;10&lt;/sub&gt;</td>
<td>7.6</td>
<td>Guhl (1996)</td>
</tr>
<tr>
<td></td>
<td>72 h</td>
<td>Growth inhibition</td>
<td>NOEC</td>
<td>291</td>
<td>Schöberl &amp; Huber (1988)</td>
</tr>
<tr>
<td></td>
<td>72 h</td>
<td>Growth inhibition</td>
<td>EC&lt;sub&gt;3&lt;/sub&gt;</td>
<td>290</td>
<td>Bringmann &amp; Kuhn (1980)</td>
</tr>
<tr>
<td><em>Photobacterium phosphoreum</em></td>
<td>30 min</td>
<td>Light loss</td>
<td>EC&lt;sub&gt;20&lt;/sub&gt;</td>
<td>18</td>
<td>Guhl (1996)</td>
</tr>
<tr>
<td><em>Entosiphon sulcatum</em></td>
<td>72 h</td>
<td>Growth inhibition</td>
<td>EC&lt;sub&gt;3&lt;/sub&gt;</td>
<td>0.3</td>
<td>Bringmann &amp; Kuhn (1980)</td>
</tr>
<tr>
<td></td>
<td>72 h</td>
<td>Growth inhibition</td>
<td>NOEC</td>
<td>&gt;10</td>
<td>Guhl (1996)</td>
</tr>
<tr>
<td><em>Paramecium caudatum</em></td>
<td>72 h</td>
<td>Growth inhibition</td>
<td>EC&lt;sub&gt;100&lt;/sub&gt;</td>
<td>&lt;70</td>
<td>Bringmann &amp; Kuhn (1980)</td>
</tr>
<tr>
<td></td>
<td>72 h</td>
<td>Growth inhibition</td>
<td>NOEC</td>
<td>18</td>
<td>Sprague (1972)</td>
</tr>
<tr>
<td>Algae, <em>Scenedesmus quadricauda</em></td>
<td>8 days</td>
<td>Growth inhibition</td>
<td>EC&lt;sub&gt;3&lt;/sub&gt;</td>
<td>0.16</td>
<td>Bringmann &amp; Kuhn (1978)</td>
</tr>
<tr>
<td>Algae, <em>Scenedesmus subspicatus</em></td>
<td>72 h</td>
<td>Growth inhibition</td>
<td>EC&lt;sub&gt;0&lt;/sub&gt;</td>
<td>10</td>
<td>Guhl (1996)</td>
</tr>
<tr>
<td></td>
<td>72 h</td>
<td>Growth inhibition</td>
<td>EC&lt;sub&gt;10&lt;/sub&gt;</td>
<td>24</td>
<td>Guhl (1996)</td>
</tr>
<tr>
<td></td>
<td>72 h</td>
<td>Growth inhibition</td>
<td>EC&lt;sub&gt;50&lt;/sub&gt;</td>
<td>34</td>
<td>Guhl (1996)</td>
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<td></td>
<td>72 h</td>
<td>Growth inhibition</td>
<td>EC&lt;sub&gt;100&lt;/sub&gt;</td>
<td>100</td>
<td>Guhl (1996)</td>
</tr>
<tr>
<td></td>
<td>Chronic</td>
<td>Growth inhibition</td>
<td>EC&lt;sub&gt;50&lt;/sub&gt;</td>
<td>52</td>
<td>Kopf &amp; Wilk (1995)</td>
</tr>
<tr>
<td></td>
<td>Chronic</td>
<td>Growth inhibition</td>
<td>EC&lt;sub&gt;90&lt;/sub&gt;</td>
<td>109</td>
<td>Kopf &amp; Wilk (1995)</td>
</tr>
<tr>
<td>Algae, <em>Microcystis aeruginosa</em></td>
<td>8 days</td>
<td>Growth inhibition</td>
<td>EC&lt;sub&gt;3&lt;/sub&gt;</td>
<td>20.3</td>
<td>Bringmann &amp; Kuhn (1978)</td>
</tr>
</tbody>
</table>
Concentrations above 50 mg boron/litre induce the formation of giant cells in *Chlorella pyrenoidosa* as a result of a stronger inhibition of the formation of daughter cells compared with the synthesis of biomass. For cells grown in 100 mg boron/litre, cell division was severely inhibited for the first 72 h of exposure. During this time, photosynthesis was inhibited by only 47%. The protein and nucleic acid content of the giant cells increased and nitrate uptake was also enhanced, whereas the lipid content decreased. The authors therefore concluded that the delay in cell division is probably a direct effect of boron on cytokinesis, as nuclear division is unaffected (Maeso et al., 1985).

Martinez et al. (1986) observed that boric acid caused a decrease in growth rates, protein content, and chlorophyll content in the blue-green alga *Anacystis nidulans*, following exposure to 75 and 100 mg boron/litre as boric acid. The photosynthetic pigments completely disappeared after 72 h of exposure. Nitrate uptake was also lowered. An accumulation of carbohydrates was observed, probably because the loss of the photosynthetic pigments inhibited their degradation.

Lewin (1966) concluded that borate is an essential micronutrient for growth in marine diatoms, whereas Smyth & Dugger (1981) concluded that boron is essential for *Cylindrotheca fusiformis*. Antia & Cheng (1975) studied the effects of boric acid on the growth of 19 species (10 classes) of marine phytoplankton. Axenic cultures in a nutrient-enriched, pH-controlled seawater (33‰ salinity) medium were exposed to the following concentrations of boric acid: 0, 5, 10, 50, or 100 mg boron/litre. Growth measurements were taken every 2–4 days by determining the optical density at 600 nm after vortex mixing. Concentrations of 5 and 10 mg boron/litre did not inhibit the growth of any species tested, with 10 mg boron/litre actually stimulating growth in the blue-green alga *Anacystis marina*, the diatom *Skeletonema costatum*, and the cryptomonad *Rhodomonas lens*. Growth was strongly inhibited in 26% of the species at 50 mg boron/litre (e.g. green alga *Tetraselmis maculata*; haptophyte *Emiliania huxleyi*; diatom *Phaeodactylum tricornutum*) and in 63% of the species at 100 mg boron/litre (e.g. chrysophyte *Monochrysis lutheri*). The highest concentration was also lethal to 37% of the species (e.g. diatom *Cyclotella cryptica*; dinoflagellate *Amphidinium*).
Effects on Other Organisms in the Laboratory and Field

carteri). Some species (e.g. green alga Monallantus salina) required an adaptation period, with growth imperceptible until 34–36 days after inoculation. Sequential transfer tests showed that many of the initially inhibited species recovered after exposure to 50 mg boron/litre, but not after exposure to 100 mg boron/litre. The authors concluded that higher concentrations would be expected to cause species redistribution, favouring growth of some forms and suppressing growth of others.

A few studies have investigated the effects of boron on microorganisms in sewage treatment plants. A boron concentration of 20 mg/litre had no effect on activated sewage treatment (Gerike et al., 1976), and boron levels below 200 mg/litre resulted in no significant inhibition of anaerobic sludge digestion (Butterwick et al., 1989).

9.1.1.2 Soil

Information concerning the effects of boron on soil microorganisms is scarce. Butterwick et al. (1989) reported results of a study in which actinomycetes were found to undergo genetic transformations at boron concentrations of 1000–6000 mg/litre. Bowen & Gauch (1966) exposed the fungi Saccharomyces cerevisiae, Neurospora crassa, Aspergillus niger, and Penicillium chrysogenum to boron. They found that growth was significantly reduced at boron concentrations of 50, 250, 1300, and 4000 mg/litre for the four species, respectively. The authors concluded that boron was not essential for any of the species tested.

9.1.2 Aquatic organisms

9.1.2.1 Plants

Nobel (1981) studied the effect of several boron compounds on photosynthesis in submerged macrophytes, watermilfoil (Myriophyllum alterniflorum), buttercup (Ranunculus penicillatus), and waterweed (Elodea canadensis). The watermilfoil and buttercup (four plants/concentration) were exposed to the following concentrations of boric acid for 28 days: 0, 1, 2, 5, or 10 mg boron/litre. The waterweed (eight plants/concentration) was exposed to the following concentrations of boric acid for 21 days — 0, 1, 2, 5, 10, or 250 mg
boron/litre — and also to the following boron compounds at a concentration of 2 mg boron/litre: boron trioxide, sodium perborate, sodium metaborate, and borax. The test water was characterized as an oligotrophic calcium-deficient nutritive medium. Net photosynthesis was measured weekly as a function of the dissolved oxygen content. Significant reductions \((p = 0.01)\) in photosynthesis compared with controls were observed at 2 mg boron/litre in the buttercup and waterweed and at 5 mg boron/litre in the watermilfoil. The LC\(_{50}\) values for each species were as follows: 5 mg boron/litre for the waterweed and the watermilfoil and 10 mg boron/litre for the buttercup. Boron trioxide did not adversely affect photosynthesis in the waterweed. The toxicity of the other boron compounds in the waterweed at 2 mg boron/litre exhibited the following trend: borax > metaborate > perborate > boric acid. Because calcium is known to inhibit the uptake of boron in plants and, therefore, to mitigate the damaging effects (Reeve & Shive, 1944), the authors concluded that the toxic effects of boron in macrophytes are more pronounced in soft (low-calcium) water.

In phytoassays conducted by Wang (1986), boron at concentrations up to 60 mg/litre did not significantly affect the growth of duckweed \((Lemna minor)\), expressed by the increase in frond number. In addition, a concentration of 40.3 mg boron/litre added as a tetraborate salt led to 50% inhibition of root growth in the freshwater Eurasian watermilfoil \((Myriophyllum spicatum)\) after 32 days of treatment (Stanley, 1974).

A pot study was carried out on the reed \(Phragmites australis\) during the growth seasons of 1992 and 1993. Both soil culture in the presence of free water and a gravel hydroculture with graduated repeated additions of boron (as boric acid) were used during the growth seasons to maintain the water phase at 0, 0.5, 1.0, 2.0, 4.0, 8.0, 16.0, and, in the case of the hydroculture, even 32.0 mg boron/litre. The number of stalks per pot, height growth of the plants, and the yield of dry substance of leaves, stalks, and roots at post-harvest time were determined. The boron content in leaves, stalks, and roots, the appearance of boron toxicity symptoms in leaves, and differences in growth at each of the exposure concentrations were monitored. It was concluded from the study that \(Phragmites australis\) can tolerate a relatively high boron content (up to 4 mg boron/litre) in the liquid
nutrient substrate; for a period of 2–3 months, even 8 mg/litre was tolerated without noticeable damage. Boron toxicity symptoms in the leaves of *Phragmites australis* arose first at leaf boron concentrations of around 150–180 mg/kg dry weight; however, no adverse effects on growth, development, or dry substance yields of the plants could be established at these leaf boron concentrations. Long-term exposure to 8 mg boron/litre in waters would lead to symptoms of damage, growth reductions, and yield reductions of plants (Marks et al., 1994; Bergmann et al., 1995).

9.1.2.2 Invertebrates

1) Freshwater

*Acute toxicity*

Summaries of the median response toxicity data for aquatic invertebrates are given in Table 19. These studies are also described in detail in the following text.

Gersich (1984) studied the acute toxicity of boric acid to *Daphnia magna*. Static (48-h) tests were conducted following the methodology approved by the American Society for Testing and Materials. Three replicates of 10 neonates each were exposed to seven nominal concentrations: 0 (control), 54, 91, 151, 252, 420, or 700 mg boron/litre. The 48-h *LC*$_{50}$ for *D. magna* was 133 mg/litre as boron, with a 95% confidence interval of 115–153 mg/litre, calculated by probit analysis. All test organisms died at 420 mg/litre, 0% mortality was observed at 54 mg/litre, and control mortality averaged 7%.

Lewis & Valentine (1981) also investigated the toxicity of boric acid to *D. magna*. The investigators followed US EPA-approved procedures and exposed <24-h-old neonates to five nominal test concentrations (not given in paper). The 48-h *LC*$_{50}$, calculated using probit analysis, was determined to be 226 mg/litre as boron (95% confidence interval of 200–246 mg/litre). The no-kill (0% mortality) concentration was <200 mg/litre. Comparison of these results with those of Gersich (1984) indicates a factor of 1.7 difference in the 48-h *LC*$_{50}$ values; however, Canton & Adema (1978) report that a difference of 2.0 may be normal in *LC*$_{50}$ values not determined at the same time or under similar conditions.
Table 19. Median response concentrations for aquatic invertebrates exposed to boron compounds

<table>
<thead>
<tr>
<th>Organism</th>
<th>Chemical</th>
<th>Test method*</th>
<th>Median response concentration (as mg boron/litre)</th>
<th>Comments</th>
<th>Reference</th>
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<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td>24 h</td>
<td>48 h</td>
<td>96 h</td>
</tr>
<tr>
<td>ARTHROPODA</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Crustacea – Daphnidae</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>Daphnia magna</td>
<td>Boric acid</td>
<td>S, N</td>
<td>133.0</td>
<td></td>
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<tr>
<td>Daphnia magna</td>
<td>Boric acid</td>
<td>S, N</td>
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<td>Daphnia magna</td>
<td>Borax</td>
<td>S, N</td>
<td>73.0</td>
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<tr>
<td>Daphnia magna</td>
<td>Anhydrous borax</td>
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<td>&lt;52.0</td>
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</tr>
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<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Daphnia magna</td>
<td>Sodium tetraborate pentahydrate</td>
<td>S, N</td>
<td>&gt;182.0</td>
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<td></td>
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<td>Daphnia magna</td>
<td>Sodium tetraborate</td>
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<td>Crustacea – Limnoriidae</td>
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</tr>
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<td>Limnoria lignorum</td>
<td>Borax</td>
<td>S, N</td>
<td>28.35</td>
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<tr>
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<tr>
<td>Insecta – Chironomidae</td>
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<tr>
<td>Chironomus decorus</td>
<td>Sodium tetraborate</td>
<td>S, N</td>
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<td>MOLLUSCA</td>
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<tr>
<td>Gastropoda – Onchidiidae</td>
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<td></td>
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<td></td>
</tr>
<tr>
<td>Onchidoris fusca</td>
<td>Borax</td>
<td>S, N</td>
<td>&lt;28.35</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

* S = static test; N = nominal concentration.
Effects on Other Organisms in the Laboratory and Field

A few studies have been conducted to assess the toxicity of the sodium borates to *D. magna*. As part of the study conducted by NAPM (1974), the effects of sodium tetraborate pentahydrate on *D. magna* were investigated. Static (96-h) tests were performed in which 10–20 organisms per test were exposed to the following nominal concentrations of sodium tetraborate pentahydrate: 0, 18, 33, 58, 102, or 182 mg/litre. The highest test concentration resulted in only 26.7% mortality at 96 h; consequently, the 96-h LC₅₀ for *D. magna* was >182 mg sodium tetraborate pentahydrate/litre (>27 mg boron/litre).

Bringmann & Kuhn (1977) reported a 24-h LC₅₀ of 340 mg disodium tetraborate (anhydrous borax)/litre (73 mg boron/litre) for *D. magna* in static tests using tap-water free of chlorine. The LC₀ was 61 mg disodium tetraborate/litre (13 mg boron/litre), and the LC₁₀₀ was 1930 mg disodium tetraborate/litre (415 mg boron/litre). Anderson (1946) obtained similar results with *D. magna*, reporting a threshold concentration based on immobilization of <240 mg anhydrous borax/litre (<52 mg boron/litre) at 48 h. Maier & Knight (1991) reported a 48-h LC₅₀ value of 141 mg boron/litre (95% confidence limits 123–159 mg boron/litre) for *D. magna* exposed to sodium tetraborate. Increasing water hardness and sulfate concentrations did not affect the toxicity of boron to *D. magna*. In this study, boron was much more toxic to daphnids than to *Chironomus decorus* 4th-instar larvae, for which the 48-h LC₅₀ was 1376 mg boron/litre (95% confidence limits 1298–1453 mg boron/litre) (Maier & Knight, 1991).

Tubificid worms (*Tubifex* sp.) appear to be less sensitive than *D. magna* to sodium borate, with concentrations of sodium borate decahydrate (borax) as high as 750 mg/litre (85 mg boron/litre) causing no effect after a 24-h exposure. The 24-h LC₁₀₀ was reported as 2000 mg/litre (227 mg boron/litre). The tubificid also exhibited less sensitivity to boric acid, with a no-effect level at 24 h of exposure of 7500 mg/litre (1311 mg boron/litre) and an LC₁₀₀ of 10 000 mg/litre (1748 mg boron/litre) (Mann, 1973).

In an early study, Fay (1959) determined the effects of metaboric acid (B₂O₃·H₂O) on various life stages of three species of mosquitos: *Aedes aegypti, Anopheles quadrimaculatus,* and *Culex quinquefasciatus*. A concentration of 8000 mg/litre (1973 mg boron/litre) did not
affect hatching of *A. aegypti* eggs following 72 h of exposure. However, newly hatched larvae of *C. quinquefasciatus* and *A. quadrimaculatus* were quite sensitive to metaboric acid. Complete mortality of *C. quinquefasciatus* larvae was observed after 24 h of exposure to 2000 mg metaboric acid/litre (493 mg boron/litre). Complete mortality of *A. aegypti* was observed after 24 h of exposure to 4000 mg/litre (986 mg boron/litre), with complete mortality occurring in *A. quadrimaculatus* only at the 8000 mg/litre (1973 mg boron/litre) level. In contrast, at the 2nd- and 3rd-instar stage, *A. quadrimaculatus* was more sensitive than the other species. In 2nd-instar larvae, 100% mortality occurred at 500 mg/litre (123 mg boron/litre) in *A. quadrimaculatus*, 96% mortality occurred at 1500 mg/litre (370 mg boron/litre) in *A. aegypti*, and 100% mortality occurred at 2000 mg/litre (493 mg boron/litre) in *C. quinquefasciatus*. The 3rd-instar larvae were less sensitive than the 2nd-instar larvae, with 100% mortality of *A. quadrimaculatus* at 2500 mg/litre (617 mg boron/litre), 88% mortality of *A. aegypti* at 3000 mg/litre (740 mg boron/litre), and 48% mortality of *C. quinquefasciatus* at 4000 mg/litre (986 mg boron/litre). Pupae of the three species were even less sensitive to metaboric acid, requiring concentrations ranging from 6000 mg/litre (1480 mg boron/litre) to 16000 mg/litre (3946 mg boron/litre) to prevent emergence to the adult stage. From the information provided in this study, it appears that the 2nd-instar larva was the life stage that was most sensitive to exposure to metaboric acid.

Fay (1959) also studied the effects of prolonged exposure to boron trioxide (*B₂O₃·H₂O*) on the immature stages of the same three species of mosquitoes. Newly hatched larvae were reared in the following concentrations of metaboric acid to determine the percentage of successful adult emergence: 10, 25, 50, 100, or 250 mg/litre. No significant reduction in maturation was observed in *A. aegypti* or *C. quinquefasciatus* at any test concentration ≤100 mg/litre. However, at 50 mg/litre, only 2% of the larvae of *A. quadrimaculatus* reached the adult stage. At 250 mg metaboric acid/litre, only 1% of *A. aegypti* and only 3% of *C. quinquefasciatus* reached the adult stage.

Maier & Knight (1991) evaluated the chronic sublethal effects of boron to *Chironomus decorus* larvae. A significantly decreased growth rate over a 96-h period was observed at 20 mg boron/litre.
Effects on Other Organisms in the Laboratory and Field

Chronic toxicity

Gersich (1984) conducted a 21-day static renewal chronic toxicity test with *D. magna*. Daphnids (20 organisms/concentration, or four replicates with 5 organisms/replicate) were exposed to the following nominal concentrations of boric acid: 0, 7, 14, 28, 56, or 105 mg/litre as boron. The test concentrations remained stable during testing; the mean measured concentrations ranged from 91.4 to 106% of the nominal test concentrations. The 21-day LC$_{50}$, calculated using the moving average method, was 52.2 mg boron/litre, and the 95% confidence interval was 42.6–66.7 mg boron/litre. No mortality was observed in the control group. The mean number of broods per daphnid, mean total young per daphnid, mean brood size per daphnid, and mean size differed significantly ($\alpha = 0.05$) from the control at the 13.6 mg boron/litre concentration. Therefore, the maximum acceptable toxicant concentration (MATC) was determined based on the most biologically and statistically significant end-points, reproduction and growth. The MATC for boric acid was estimated to be between 6.4 and 13.6 mg boron/litre, or 9.3 mg boron/litre (the geometric mean of these two values).

Lewis & Valentine (1981) also conducted a 21-day static renewal chronic toxicity test with *D. magna*. The test was conducted similarly to that of Gersich (1984), except for the exposure regimen. Ten test chambers were set up for each test concentration: three beakers contained five daphnids each for obtaining data on survival, and seven beakers each contained one daphnid for obtaining data on survival, growth, and reproduction. Twenty control chambers were used: 6 chambers contained five daphnids each, and 14 chambers each contained one daphnid. Daphnids were exposed to the following nominal concentrations of boric acid: 0, 6, 13, 27, 53, or 106 mg/litre as boron. The concentration of the test solution remained stable during testing, with mean measured concentrations exceeding 95% of the nominal concentration. The 21-day LC$_{50}$, calculated by probit analysis, was 53.2 mg boron/litre, with a 95% confidence interval of 44.1–64.5 mg boron/litre. Mortality was 9% in the control group. The mean brood size and total number of young produced were significantly reduced ($p < 0.05$) compared with controls at concentrations of $>13$ mg boron/litre. Mean length of daphnids was significantly reduced ($p < 0.05$) compared with controls at 53 mg boron/litre. The
NOEC was 6 mg boron/litre. Therefore, based on the most sensitive parameters, the MATC was >6 and <13 mg boron/litre, or 8.83 mg boron/litre (geometric mean of these values).

2) Marine

In static tests, Mann (1973) determined 24-h LC$_{100}$ values for the amphipod *Gammarus tigrinus* exposed to boric acid, borax, and sodium perborate at two salinities (32.23% and 17.66%). The LC$_{100}$, 10 000 mg/litre, was the same for all three compounds at both salinities. The no-effect concentration for all of the compounds was 7500 mg/litre. In contrast, Robinson & Perkins (1977) reported toxicity values for borax in the isopod *Limnoria lignorum* and the sea slug *Onchidoris fusca* that are roughly two orders of magnitude lower than those reported by Mann (1973) for the amphipod *Gammarus tigrinus*. The salinity of the test water was 30%. The 24-h static LC$_{50}$ values, after a 5-day recovery period, were 250 mg/litre (28.35 mg boron/litre) for the isopod and >250 mg/litre (>28.35 mg boron/litre) for the sea slug. In studies with sea urchin (*Anthocidaris crassispina*) embryos, exposure to boric acid at a concentration of 37 mg boron/litre had no effect on development, whereas exposure to 75 mg boron/litre was fatal (Eisler, 1990).

3) Biocenosis studies

Three biocenosis studies (also known as microcosms, mesocosms, and experimental ecosystems) have been conducted (summarized in ECETOC, 1997). A 28-day laboratory microcosm test with microorganisms consisting of six trophic stages yielded a NOEC and LOEC of 2.5 and 5.0 mg boron/litre, respectively. Studies with outdoor ponds containing up to 29 species and treated with 0.7 mg boron/litre over a 2-year period resulted in no significant differences compared with untreated control ponds. Further, field studies carried out in seven different water bodies subjected to different levels of anthropogenic boron inputs yielded no toxic effects of boron at concentrations between 0.16 and 1.52 mg/litre.
Effects on Other Organisms in the Laboratory and Field

9.1.2.3 Vertebrates

1) Freshwater

Acute toxicity

Summaries of the acute toxicity data for aquatic vertebrates are given in Table 20. These studies are also described in detail in the following text.

For boron compounds, three studies are available that provide information concerning the 96-h LC$_{50}$ values, the toxicity value established by the US EPA (Stephan et al., 1985) for use in the derivation of water quality criteria for the protection of aquatic life and its uses. Wallen et al. (1957) conducted 96-h static toxicity tests with mosquitofish. The test water, turbid pond water, was selected to simulate the commonly turbid wastewater from oil refinery operations; however, it was determined that the highest turbidities used in the study should not produce direct effects on the fish during the exposure time. Adult female fish (10/concentration) were exposed to the following nominal concentrations of boric acid or borax: 10, 18, 32, 56, or 100 mg/litre. If no deaths occurred at 96 h, the tests were rerun at concentrations of 100, 180, 320, 560, or 1000 mg/litre and, subsequently, at concentrations 10 times these values (1000–10 000 mg/litre). The 96-h LC$_{50}$ for mosquitofish exposed to boric acid was 5600 mg/litre (979 mg boron/litre), and the 96-h LC$_{50}$ for borax was 3600 mg/litre (408 mg boron/litre).

As part of the study conducted by NAPM (1974), static bioassays were conducted to determine the toxicity of sodium tetraborate pentahydrate to fathead minnows. The tests were conducted using standard methods and filtered tap-water. Fish (15/treatment) were exposed to the following nominal concentrations: 0, 200, 360, 640, 1120, or 2000 mg/litre. The 96-h LC$_{50}$ was 1900 mg/litre (332 mg boron/litre).

Hamilton & Buhl (1990) reported the results of 96-h static toxicity tests with two life stages of chinook salmon (Oncorhynchus tshawyts-chu) and coho salmon (O. kisutch). Swim-up fry (8–12 weeks old) were tested in fresh water, and advanced fry (15–21 weeks old)
Table 20. Acute toxicity for aquatic vertebrates exposed to boron compounds

<table>
<thead>
<tr>
<th>Organism</th>
<th>Chemical</th>
<th>Test method</th>
<th>Median response concentration (as mg boron/litre)</th>
<th>Comments</th>
<th>Reference</th>
</tr>
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<tbody>
<tr>
<td></td>
<td></td>
<td>24 h</td>
<td>48 h</td>
<td>96 h</td>
<td></td>
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<tr>
<td>Coho salmon (Oncorhynchus kisutch)</td>
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<td>S, N</td>
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<td>Swim-up fry</td>
<td>Hamilton &amp; Buhl (1990)</td>
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<tr>
<td></td>
<td>Boric acid</td>
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<td>105</td>
<td>Advanced fry</td>
<td>Hamilton &amp; Buhl (1990)</td>
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<td>Chinook salmon (Oncorhynchus tshawytscha)</td>
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<td></td>
<td>Boric acid</td>
<td>S, N</td>
<td>105</td>
<td>Advanced fry</td>
<td>Hamilton &amp; Buhl (1990)</td>
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<tr>
<td>Rainbow trout (Oncorhynchus mykiss)</td>
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<td>S, N</td>
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<td>65</td>
<td>Embryo, hardness of 50 mg CaCO₃/litre</td>
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<tr>
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<td>Embryo, hardness of 200 mg CaCO₃/litre</td>
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<td>Fathead minnow (Pimephales promelas)</td>
<td>Sodium tetraborate pentahydrate</td>
<td>S, N</td>
<td>332</td>
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<td>NAPM (1974)</td>
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Table 20 (contd).

<table>
<thead>
<tr>
<th>Organism</th>
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<tr>
<td>Mosquitofish (Gambusia affinis)</td>
<td>Borax</td>
<td>S, N</td>
<td>1361 930 408</td>
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<td>Wallen et al. (1957)</td>
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<tr>
<td>Golden orfe (Leuciscus idus)</td>
<td>Boric acid</td>
<td>S, N</td>
<td>3146 1835 979</td>
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<td>Wallen et al. (1957)</td>
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<td>Zebra fish (Brachydanio rerio)</td>
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<td>173</td>
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<td>Schöberl &amp; Huber (1988)</td>
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<td>Bluegill (Lepomis macrochirus)</td>
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<td>S, N</td>
<td>4.6</td>
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<td>Turnbull et al. (1954)</td>
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<td>Dab (Limanda limanda)</td>
<td>Anhydrous</td>
<td>Semi-static, borax N</td>
<td>88.3 74 Salinity 34.62 ± 0.2‰</td>
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<td>Taylor et al. (1985)</td>
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<td>Colorado squaw-fish (Ptychocheilus lucius)</td>
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<td>279b &gt;100c 527d</td>
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<td>Razorback sucker (Xyrauchen texanus)</td>
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<td>233b 279c &gt;100d</td>
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<td>Hamilton (1995)</td>
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<td>Bonytail (Gila elegans)</td>
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<td>280b &gt;100c 552d</td>
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<td>Hamilton (1995)</td>
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</table>

*S = static test; FT = flow-through test; N = nominal concentration.

b Swim-up fry.
c 1-g juvenile.
d 2-g juvenile.
were tested in brackish water. The 96-h LC$_{50}$ values for chinook salmon swim-up fry and advanced fry were 725 mg/litre (127 mg boron/litre) and 600 mg/litre (105 mg boron/litre), respectively. The 96-h LC$_{50}$ values for coho salmon swim-up fry and advanced fry were 447 mg/litre (78.1 mg boron/litre) and 600 mg/litre (105 mg boron/litre), respectively.

Results of 24- and 48-h static acute tests with rainbow trout, guppy (Poecilia reticulata), and mosquitofish clearly show the difference in the degree of toxicity resulting from exposure to boric acid versus sodium borate. Mann (1973) reported the following 24-h LC$_{100}$ values for rain-bow trout and guppy, respectively: boric acid, 10 000 mg/litre (1748 mg boron/litre) and 7500 mg/litre (1311 mg boron/litre); borax, 5000 mg/litre (567 mg boron/litre) for both species. Static 24-h LC$_{50}$ values determined by Wallen et al. (1957) for the mosquitofish are 18 000 mg/litre (3146 mg boron/litre) for boric acid and 12 000 mg/litre (1361 mg boron/litre) for borax. The 48-h LC$_{50}$ values determined in this study were 10 500 mg/litre (1835 mg boron/litre) for boric acid and 8200 mg/litre (930 mg boron/litre) for borax. Rainbow trout are more sensitive to borax than mosquitofish, with 24- and 48-h static LC$_{50}$ values of 2800 mg/litre (602 mg boron/litre) and 1800 mg/litre (387 mg boron/litre), respectively (Alabaster, 1969). Juhnke & Ludemann (1978) reported an LC$_{50}$ of 807 mg/litre as boron for golden orfe (Leuciscus idus) exposed to anhydrous borax in static acute tests (exposure time not given).

Mann (1973) reported 24-h LC$_{100}$ values for rainbow trout and guppies exposed to sodium perborate (500 mg/litre or 66.1 mg boron/litre) that were considerably lower than those reported for boric acid and borax. The authors attributed this increased toxicity to a pH shift into the alkaline range (up to 9.1), which resulted in increased mucilage formation, with the fish exhibiting a crippling behaviour.

The treatment of embryos of the toad *Bufo vulgaris* with 0.5% boric acid for 24 h from the two-cell stage to the tail-bud stage resulted in several developmental malformations, including a reduction or lack of external gills, short tail, bifurcation of the epiphysis, suppression of forebrain development, and inhibition of sensory organ development.
Several of these effects were attributed to the direct action of boric acid on the ectoderm (Takeuchi, 1958).

Chronic toxicity

Toxicity of borate to early life stages of fish has been documented for several species (Birge & Black, 1977; Black et al., 1993). Embryonic and early larval stages of rainbow trout, largemouth bass, channel catfish, and goldfish were exposed to boron, as boric acid or borax, from fertilization up to 8 days post-hatch. All exposures were in soft (50 mg CaCO₃/litre) or hard (~200 mg CaCO₃/litre) reconstituted water. Test responses included embryonic mortality, teratogenesis, and larval mortality. Gross debilitating anomalies of survivors were classified as mortalities. Effect concentrations (LC₅₀, NOEC, and LOEC) for each species are presented in Table 21. Neither water hardness nor the form of boron (boric acid, borax) added to the test aquaria consistently affected embryo–larval survival of rainbow trout, channel catfish, and goldfish (Birge & Black, 1977).

On the basis of median lethal concentrations (LC₅₀), no species was found to be especially sensitive. The range of LC₅₀s for all species was 12.2–235 mg boron/litre. In addition, Birge & Black (1977) reported LC₁s ranging from 0.001 to 0.1 mg boron/litre for rainbow trout, from 0.2 to 5.5 mg boron/litre for channel catfish, and from 0.2 to 1.4 mg boron/litre for goldfish. The LC₁ showed rainbow trout to be the most sensitive species. The NOEC ranged from 0.009 to 0.103 mg boron/litre for rainbow trout and was 1.39 mg boron/litre for largemouth bass. These were consistent with the acute toxicity results that indicated rainbow trout and zebra fish as the most sensitive species (see Table 20).

The effect of natural dilution water on boron toxicity was reported by Black et al. (1993). Natural surface waters were collected from three US locations: the Erwin National Fish Hatchery in Tennessee, Brookville Lake in Indiana, and Firehole River in Yellowstone National Park, Wyoming. Surface water control boron concentrations were 0.023, 0.091, and 0.75 mg/litre for Erwin, Brookville, and Yellowstone waters, respectively. Total organic carbon for the three surface waters ranged from 0.8 to 1.9 mg/litre.
<table>
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<th>Organism</th>
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$^a$ S = static test; FT = flow-through test; N = nominal concentration.
Effects on Other Organisms in the Laboratory and Field

Hardness levels for these natural waters ranged from 24 to 209 mg CaCO\textsubscript{3}/litre. In the surface water tests, three nominal treatments were used: surface water control, control plus 1.0 mg boron/litre added (as boric acid), and control plus 10 mg boron/litre added. Total and dissolved boron levels were measured for each of the surface water treatments. No statistically significant differences were noted between total and dissolved boron concentrations, except for Yellowstone (1.0 mg boron/litre) and Erwin (10 mg boron/litre) treatments. The true significance of this, however, is minimal, as total versus dissolved concentrations for Yellowstone and Erwin waters were 1.61 vs. 1.52 mg boron/litre and 9.91 vs. 9.48 mg boron/litre, respectively. Hence, it is reasonable to assume that all boron was in solution. Boron did not elicit toxicity to embryo-larval stages of rainbow trout exposed to surface water control boron levels up to 0.75 mg/litre. LOECs for Erwin, Brookville, and Yellowstone treatments were 1.10, 1.24, and 1.73 mg boron/litre, respectively, indicating that the threshold for no effects is approximately 1 mg boron/litre. In addition, deep (600 m) well-water, typically used for aquatic toxicity tests, from a contract laboratory located in Wareham, Massachusetts, USA, was also used. Boron was spiked into well-water to obtain an exponential series of nominal concentrations: 0.0017, 0.017, 0.17, 1.7, and 17 mg boron/litre, respectively. Analytical confirmation of exposure was obtained for the two highest concentrations, 2.1 and 18.0 mg boron/litre. No effects were observed, even at the highest boron concentration.

The effect concentrations generated in natural waters were greater than those from the reconstituted water experiments. The cause of these differences is not readily apparent, particularly as bioavailability was not reduced by natural water. However, some investigators (Belanger et al., 1989; Farris et al., 1994) have shown that organisms cultured in natural water often grow and reproduce better than their counterparts in reconstituted or laboratory dechlorinated water. Therefore, a reasonable hypothesis that may explain, in part, the differences in reconstituted versus natural water responses is the better health experienced by organisms exposed to boron in natural water. The causative agents for this lack of health in laboratory water are not certain but may include nutrient deficiencies (Keating & Dagbusan, 1984; Belanger et al., 1989).
Early life stage tests have been conducted with fathead minnows to determine effects of chronic exposure (30–60 days) to boric acid. The 30-day NOEC and LOEC were 14 and 24 mg boron/litre, respectively, based on growth reduction; the 60-day NOEC and LOEC were 24 and 88 mg boron/litre, respectively, based on reduction in fry survival (Butterwick et al., 1989).

Birge & Black (1977) also studied the effect of boric acid and borax on embryos and larvae of the leopard frog (Rana pipiens) and the effect of boric acid on embryos and larvae of the Fowler’s toad (Bufo fowleri). The embryos were exposed for 3.5 days and the larvae for 7.5 days to concentrations of boric acid and borax ranging from 0.05 to 300.00 mg boron/litre in hard (200 mg CaCO₃/litre) and soft (50 mg CaCO₃/litre) water (as described above for fish exposures). The leopard frog and Fowler’s toad were equisensitive to borax and boric acid. For the leopard frog, LC₁ and LC₅₀ values were 13 and 130 mg boron/litre (dosed as boric acid) in soft water and 22 and 135 mg boron/litre in hard water. Lower toxicity values were observed via borax exposures, with LC₁ and LC₅₀ values of 5 and 47 mg boron/litre in soft water and 3 and 54 mg boron/litre in hard water, respectively. The LC₁ and LC₅₀ values for Fowler’s toad exposed to boric acid were 25 and 145 mg boron/litre in soft water and 5 and 123 mg boron/litre in hard water, respectively.

2) Marine

Taylor et al. (1985) studied the toxicity of several metals, including boron (as anhydrous borax), to a saltwater fish (dab, Limanda limanda). The tests were conducted following standard procedures under semi-static conditions, in which the test solution was replaced at 24-h intervals. The salinity of the test water was 34.62 ± 0.2‰. Adult fish obtained from wild populations (20/concentration) were exposed to a series of five concentrations (not given in the paper) for 96 h. The LC₅₀, calculated by probit analysis, was 74.0 mg boron/litre, with a 95% confidence interval of 66.4–83.0 mg boron/litre. Pre-death symptoms included minor respiratory problems.

Similar results were observed in bioassays conducted by Thompson et al. (1976) with two life stages of coho salmon. Coho alevins (0.19–0.7 g) were tested in aerated well-water (fresh water),
and coho underyearlings (1.8–3.8 g) were tested in aerated seawater with a salinity of $28 \pm 1\%$. Test solutions were prepared using sodium metaborate tetrahydrate ($\text{Na}_2\text{B}_4\text{O}_7\cdot 4\text{H}_2\text{O}$), and exposure lasted in excess of 12 days. The 283-h LC$_{50}$ for freshwater coho alevins was 113 mg boron/litre, with 95% confidence limits of 104–123 mg boron/litre. The 283-h LC$_{50}$ for saltwater coho underyearlings was 12.2 mg boron/litre, with 95% confidence limits of 10.89–14.56 mg boron/litre. The authors attributed the difference in toxicity in freshwater and saltwater to differences in fish age, test temperature (11 °C in fresh water; 8 °C in salt water), and available boron levels. Seawater also has higher background levels of boron than fresh water. The results reported by Hamilton & Buhl (1990), discussed above, do not indicate significant differences in acute toxicity between different life stages of chinook and coho salmon.

In static tests, Mann (1973) observed differing sensitivities in the common eel (Anguilla anguilla) to both boric acid and borax at two salinities: 12.39 and 25.05%. At the lower salinity, a 24-h LC$_{100}$ of $\geq 10000$ mg/litre was reported for both borax and boric acid; at the higher salinity, the 24-h LC$_{100}$ was 7500 mg/litre for both compounds. The authors speculated that differences in pH could contribute to the toxicity of the boron compounds at the higher salinity. At a boric acid concentration of 7500 mg/litre, the pH in the lower-salinity test water was 7.2; the pH in the higher-salinity test water was 6.6. As was observed with rainbow trout and mosquitofish, Mann (1973) also observed greater toxicity in the common eel following exposure to sodium perborate. The LC$_{100}$ at both salinities was 750 mg/litre (99.2 mg boron/litre), resulting from the damaging effects of an alkaline pH shift.

9.1.3 Terrestrial organisms

9.1.3.1 Plants

1) Essentiality

Boron is an essential micronutrient for higher plants, with interspecies differences in the levels required for optimum growth. Boron plays a role in carbohydrate metabolism, sugar translocation, pollen germination, hormone action, normal growth and functioning
of the apical meristem, nucleic acid synthesis, and membrane structure and function (Lovatt & Dugger, 1984). Recent work shows important involvement of boron in cell wall cross-linking, involving complexation with specific pectin components (Loomis & Durst, 1992; Hu et al., 1996).

Early investigation of the effects of boric acid and borax on the fieldbean (*Vicia faba*) and other plants indicated the role of boron in plant nutrition (Warrington, 1923). The first comprehensive study of the effects of boron on plant growth was conducted by Eaton (1944). Fifty species of plants were grown in sand cultures with standard nutrient solutions containing the following boron concentrations: trace (0.03–0.04), 1, 5, 10, 15, or 75 mg/litre. For each species, Eaton (1944) recorded the boron concentration resulting in the best growth, the lowest concentration resulting in injury, and the symptoms of deficiency with trace boron levels. Approximately 82% of the plants exhibited the best growth at concentrations from trace to 5 mg/litre, and 35% of the plants grown in trace boron levels developed morphological symptoms of deficiency. Eaton (1944) concluded that there was overlap of the beneficial and injurious effects of boron between species; therefore, three broad categories of tolerance (sensitive, semi-tolerant, and tolerant) were established. The tolerant plants endure a wide range of boron concentrations with little effect, and the sensitive plants exhibit a strong reaction to either too much or too little boron.

Boron generally occurs in soils at concentrations ranging from 10 to 30 mg/kg, depending on such factors as soil type, amount of rainfall, and irrigation type (Sprague, 1972). Boron deficiencies usually occur in soil solutions from sandy soils or acid peat soils, soils derived from igneous rocks, soils low in organic matter, and irrigated soils (Sprague, 1972).

The symptoms of boron deficiency in plants include cessation of root and leaf growth, necrosis of leaf primordia and primary root tips, necrosis of stem and leaf phloem, bark splitting, retardation of enzyme reactions, reduced pollen germination, and even death (Versar, Inc., 1975; Wells & Whitton, 1977). Normal growth will usually resume if boron is added to the growth medium.
Hudak (1973) found that a boron-deficient nutrient solution inhibited mitosis in the root tip of the fieldbean within 72 h. A 10 mg boron/litre solution produced optimum cell division and elongation of the root tip; however, 50 mg boron/litre caused a reduction in mitosis within 24 h.

Ludbrook (1942) studied the effects of boron deficiency and toxicity in Monterey pine (Pinus radiata) seedlings grown in water culture. The suboptimal concentrations of boron added to the nutrient solution were 0, 0.005, 0.01, or 0.05 mg/litre, and the potentially toxic concentrations of boron were 0.5, 2.5, 5.0, 10.0, 20.0, or 40.0 mg/litre. Seedlings exposed to the toxic levels were initially grown for 2 months in a nutrient solution containing added boron at 0.5 mg/litre. Marked reduction in root growth was observed at the two lowest suboptimal concentrations; however, improved root growth was observed at 0.05 mg/litre, with the development of small lateral roots. At 10.0 mg boron/litre, a slight yellowing of the tips of the needles developed, followed by browning and drying at 20.0 mg/litre, until all plants died at 40.0 mg/litre. Ludbrook (1942) concluded that the optimum growth range for Monterey pine was 0.05–5.0 mg boron/litre.

Recent work has shown that boron in a number of plant species is tightly bound in the polysaccharide cell wall. Boron deficiency leads to profound changes in cell wall morphology, suggesting that boron is critical to cell wall expansion. It has been proposed that this structural, cross-linking function of boron is involved with the pectin fraction, which contains apiose and other hydroxylated fragments amenable to complexation by borate (Loomis & Durst, 1992). Fourteen species of crop plants were studied, and it was concluded that high pectin content requires more boron for forming cell walls or that pectin forms a tightly held boron complex that depletes boron availability for other critical functions, thereby increasing the overall demand for boron (Hu et al., 1996). Kobayashi et al. (1996) have isolated and characterized a rhamnogalacturonan II/borate complex from enzyme-digested cell wall pectin.
2) Toxicity

Boron excesses usually occur in soil solutions from geologically young deposits, arid soils, soils derived from marine sediments, and soils contaminated by pollutant sources, such as releases from coal-fired power plants and mining operations (Sprague, 1972).

The initial symptom of boron toxicity in plants is chlorosis (yellowing) of the leaf tip, progressing along the leaf margin and into the blade. Necrosis of the chlorotic tissue occurs, followed by leaf abscission. Necrosis of the leaf tissue results in a loss of photosynthetic capacity, which reduces plant productivity (Lovatt & Dugger, 1984). Pollen germination and pollen tube growth may also be inhibited (Versar, Inc., 1975).

Several investigators have shown a direct relationship between the boron content in leaves (foliar) and the severity of the symptoms of toxicity. Gilliam & Watson (1981) conducted an experiment in which Anderson yews (Taxus media) were grown in soil at four boron concentrations (0.5, 5.0, 25.0, or 50 mg/kg). Symptoms of toxicity were observed when foliar boron accumulation reached concentrations ranging from 85 to 100 µg/g of dry tissue. The observed symptoms included leaf tip yellowing, followed by necrosis and premature defoliation. Suppression of shoot and root growth was observed at 50 mg boron/kg soil.

Shopova et al. (1981) found that concentrations of 16, 24, and 32 mg boron/kg soil resulted in a decline in plant development, yellowing of leaves, late flowering, reduction of mitotic frequency in root tip cells, and abnormalities during meiosis in the poppy (Papaver somniferum).

Kluge & Podlesak (1985) found that symptoms due to boron excess begin to develop on the leaves (leaf tip necroses) of pot-grown spring barley (Hordeum vulgare) as soon as the boron content of the leaf tissue reaches 60–80 mg/kg dry weight.

Gestring & Soltanpour (1987) grew alfalfa (Medicago sativa) in three soil types amended with sodium borate at rates of 0, 10, 20, and
40 mg boron/kg. Alfalfa yield was significantly reduced by boron application in both the sandy loam and loam soils; however, no yield reduction was observed in the silt loam soil. Soil extractable boron did not adequately assess boron toxicity, whereas plant boron levels were a more reliable index of toxicity. The critical range of plant boron resulting in a yield reduction was 850–975 mg boron/kg plant tissue (dry weight). The significant difference between the soils shows the importance of soil pH, organic matter content, and per cent clay to the toxicity of boron to plants.

Sage et al. (1989) exposed the rare serpentine plant (*Streptanthus morrisonii*) to boron (0, 20, 60, 240, 650, 1200, or 2400 μmol/litre) via watering. Plants showed mild to moderate toxicity symptoms (older leaves exhibiting chlorosis and necrosis) at boron concentrations of 240 and 650 μmol/litre. Severe toxicity symptoms (significant leaf loss) were apparent at 1200 and 2400 μmol/boron/litre. Boron levels in the leaves of plants showing severe toxicity were an order of magnitude higher than those in the leaves of plants in the field.

Glaubig & Bingham (1985) reported significant linear relationships between both soil and leaf tissue boron concentrations and foliar damage in four tree species endemic to California (digger pine, *Pinus sabiniana*; California laurel, *Umbellularia californica*; madrone, *Arbutus menziesii*; bigleaf maple, *Acer macrophyllum*). Foliar damage over 25% of the leaf/needle area occurred at saturated soil concentrations ranging from 0.08 to 1.2 mmol boron/litre for the four species and at leaf/needle concentrations ranging from 30 to 115 mmol boron/kg. The bigleaf maple was the most sensitive of the four species, and the digger pine was the most tolerant species.

Under experimental conditions, Shann & Adriano (1988) demonstrated that chronic foliar aerosol exposures of boron produced phytotoxicity in relation to boron accumulation in the leaves. Five crop species (swiss chard, beet, radish, tomato, and cucumber) were exposed to aerosol concentrations of 0, 1.55, or 3.09 μg boron/cm² leaf area. The authors concluded that the visual damage (leaf tip necrosis) resulting from aerosol exposure was identical to that observed from root boron toxicity for all crops tested.
9.1.3.2 Invertebrates

Boric acid is an effective stomach poison for several species of insects, including the German cockroach (*Blattella germanica*). Pretreatment of wood and other substrates with boric acid or borax can prevent insect infestation. Baits and aerosols containing boron compounds (e.g. borax and boric acid) have been shown to control fruit flies, cockroaches, houseflies, and termites (Butterwick et al., 1989).

Boron in the diet at concentrations of 0.025–5% caused sterilization of house flies (*Musca domestica*) when both sexes were fed the diet (Borkovec et al., 1969). Boron toxicity in honey bees has also been observed; a concentration of 50 mg boric acid/litre (8.7 mg boron/litre) in syrup had no effect on survival, whereas 100 mg boric acid/litre (17.5 mg boron/litre) caused 50% mortality (Ostrovskij, 1955).

Lang & Treece (1972) conducted a study to determine if boric acid would induce sterility in the face fly (*Musca autumnalis*). Adult male and female flies (50 each/concentration) were exposed to boric acid concentrations of 0.5%, 0.8%, or 1.0% in each of three media (water, malt, and dry food) for the first 4 days after eclosion (hatching from the pupal stage). Complete sterility (100%) was observed in flies fed the two highest concentrations in dietary malt; however, a high degree of recovery was observed within 5 days after cessation of treatment. Many eggs from the females fed 1.0% boric acid were transparent and watery in appearance; this was possibly due to the interference of boric acid with egg chorion formation. Almost 100% mortality occurred in the flies exposed to boric acid concentrations of 0.5% and 0.8% in water within the first 4 days of treatment. In a subsequent test, erratic sterility with recovery of fertility was observed in face flies exposed to boric acid concentrations of 0.1% and 0.3% in water.

9.1.3.3 Vertebrates

In order to determine the impact of high levels of boron on waterfowl in Kesterson Reservoir (located within the Kesterson National Wildlife Refuge in the San Joaquin Valley of California, USA), a
number of investigators have studied the effects of controlled boron exposure to mallard ducks. Smith & Anders (1989) studied the effects on reproduction in mallards fed diets supplemented with 0, 30, 300, or 1000 mg boron/kg as boric acid (concentrations known to be found in the field). The adults were fed this diet prior to mating and during egg incubation, and the ducklings were fed this diet after hatching. In the 1000 mg/kg group, hatching success of fertile eggs and duckling survival were significantly reduced, and embryo mortality was significantly higher. The body weight of hatchlings was lower in the 300 and 1000 mg/kg groups than in controls. Growth rate of ducklings was significantly reduced at all three dose levels. No effect on egg fertility, eggshell thickness, or eggshell quality was observed at any dose level. In addition, boron did not produce any overt signs of toxicity in young or adult mallards. The researchers were unable to determine whether duckling mortality and impaired growth were due to pre-hatching or post-hatching exposure or the combined effect.

Hoffman et al. (1990) examined the effect of dietary boron exposure on the survival, growth, and physiology of ducklings hatched from uncontaminated eggs. Day-old mallards were exposed to 0, 100, 400, or 1600 mg boron/kg diet as boric acid for 10 weeks. No significant effect on survival was found. The highest dietary concentration of boron significantly decreased overall growth and the rate of growth (sexes combined), whereas lower concentrations altered growth only in female ducklings. Significantly decreased food consumption was observed in the high-dose group during the first 3 weeks and in all dose groups during the 2nd week. Effects on blood, brain, and liver biochemistry were also observed in the high-dose group. Overall, dietary boric acid proved to be less toxic to ducklings hatched from untreated eggs than to ducklings hatched from boron-contaminated eggs.

Boron has also been shown to affect the behaviour of mallard ducklings. Whitworth et al. (1991) analysed the activity schedules and behaviour durations of day-old ducklings that received diets containing 0, 100, 400, or 1600 mg boron/kg as boric acid. The highest dose level had significant effects on the activity schedules of the ducklings, including increased time at rest. Ducklings exposed to
1600 mg/kg in the diet spent less time in alert behaviours and in the water compared with controls.

These studies suggest that high dietary levels of boron can adversely affect normal duckling development and survival. In addition, interactive effects have been demonstrated in mallard ducklings given both boron and selenium in the diet. Hoffman et al. (1991) noted further growth reduction in ducklings fed diets with 60 mg selenium/kg (as seleno-methionine) and 1000 mg boron/kg (as boric acid) compared with ducklings fed diets with only 1000 mg boron/kg (as boric acid) over a 4-week period. These effects were magnified when dietary protein was restricted. Reduction of the dietary protein content from 22% to 7% in combination with the same selenium and boron exposure scenario as above resulted in significant duckling mortality. These findings suggest that selenium and boron may interact to cause more severe toxicological effects in waterfowl than boron causes alone, especially in cases where dietary protein is restricted.

The liver boron content of mallards fed with dietary boron at 0, 30, 300, or 1000 mg/kg was found to range from 0 to 51 μg/g dry weight. The level of 33–51 μg boron/g in liver was associated with reproductive impairment in the 1000 mg/kg exposed group (Smith & Anders, 1989).

Boron levels in the livers of aquatic birds from the Grassland Water District of California, USA, were also examined during 1985–1988. The levels detected ranged from 1.7 to 40 μg boron/g dry weight; the highest level detected is in a range associated with reproductive impairment (Paveglio, 1992).

9.2 Field observations

9.2.1 Aquatic

Concentrations of boron in trout hatcheries of Germany, the United Kingdom, and the USA (California) have been determined. Mean concentrations of boron in feed waters to 20 United Kingdom rainbow trout hatcheries were 0.009–0.021 mg/litre (ECETOC, 1997).
A range of 0.002–0.107 mg boron/litre was noted in 18 hatcheries in Germany. A range of higher concentrations, 0.02–1.0 mg boron/litre, was reported for the 10 largest hatcheries in California (Bingham, 1982; EA, 1994).

Concentrations of boron in streams and lakes of the United Kingdom and USA capable of sustaining trout species were found to be similar to concentrations found in hatcheries. Median boron concentrations from nine different water regions within the United Kingdom ranged from 0.007 to 0.272 mg/litre, with maximum values in each of the regions ranging from 0.113 to 2.3 mg boron/litre (ECETOC, 1997). Boron concentrations in California surface waters that supported viable populations of wild rainbow trout ranged from <0.01 to 13.1 mg/litre (Bingham, 1982). An update to the Bingham report was provided by a survey of 37 fisheries biologists in the western USA (EA, 1994). No instances were found where rainbow trout populations were limited by boron. Several locations were found to have successful trout populations with aqueous boron concentrations near or above 1 mg/litre. Specific examples include East and Paulina lakes in Oregon (>0.9 mg boron/litre), Firehole River in Wyoming (>0.9 mg boron/litre), Napa River in California (>1.2 mg boron/litre), and Little Warm Springs in California (>3.2 mg boron/litre). The first two sites are renowned trophy trout waters. Important fish species other than trout, such as northern pike, sturgeon, and catfish, were reported to live in streams with higher boron concentrations, up to approximately 2 mg/litre, such as in the Poplar River in Montana and Souris River in North Dakota. Neither of these latter rivers was reported to contain rainbow trout owing to excessive temperatures and unsuitable habitat (EA, 1994).

9.2.2 Terrestrial

Boron deficiencies in terrestrial plants have been reported in many countries of the world (Kabata-Pendias & Pendias, 1984). For example, deficiency has been reported in Canada, New Zealand, Sweden, Nigeria, the United Kingdom, the USA, and some arid regions of India and Pakistan. Boron deficiency is more likely to occur in light-textured, acid soils in humid regions, because of boron’s susceptibility to leaching. Boron deficiency may also occur in heavy-textured soils with high pH, because boron is readily adsorbed under
these conditions. Boron deficiency is more widespread than the deficiency for any other micronutrient (Gupta et al., 1985).

When deficiency exists, boron applications increase yield and improve quality of many crops (Gupta et al., 1985). Hopmans & Flinn (1984) observed severe dieback in Monterey pine plantations during dry years in south-eastern Australia owing to boron deficiency. Borax applied in the spring at rates of 50, 100, or 150 kg/ha resulted in a significant improvement in height growth of fertilized trees.

Irrigation water is one of the main sources of high boron levels resulting in toxicity in the field. Few irrigation waters contain enough boron to injure plants directly. However, it is the continued use and concentration in the soil as a result of evapotranspiration that lead to the eventual toxicity problems (Gupta et al., 1985). In waters used for irrigation, Wilcox (1958) reported a critical boron concentration of 0.3–1.0 mg/litre for sensitive crops, such as citrus and other fruits. Semi-tolerant crops, such as potatoes, tomatoes, and oats, tolerate concentrations of 1–2 mg/litre; tolerant crops, such as sugar beets, onions, and carrots, can withstand concentrations of 2–4 mg/litre.

The symptoms of boron toxicity are predominantly manifested in the leaves and roots; however, Eaton et al. (1941) observed that these effects were frequently absent in stone fruit trees, with boron accumulation occurring in the bark and fruits rather than the leaves. Dye et al. (1984) reported that boron concentrations in bark of 31–120 μg/g dry matter and in fruit of 90–311 μg/g dry matter resulted in bud-drop and branch die-back in peach trees. In nectarine trees with boron tissue concentrations of 380–457 μg/g dry matter, the buds failed to swell and subsequently dropped in the spring. Dye et al. (1983) observed the same symptoms in apricot trees given about 2.4 g of borax per tree during planting. Buds on unhealthy trees that failed to break contained 40–100 μg boron/g dry matter.

Pollutant sources of boron, in the form of either airborne emissions or leachates from soil application, have been shown to produce toxic symptoms in endemic species. Smidt & Whitton (1975) studied the toxic responses in a stand of Monterey pine adjacent to a boiler house. The trees were exposed to boron as a result of dumping
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of furnace ash into an adjacent gully and from airborne ash emitted from the furnace chimney. The average boron concentration in the ash was 1900 mg/kg. Chlorosis and necrosis of the needles were most severe closest to the furnace chimney, with the effects decreasing with increased distance from the furnace. No evidence of toxicity was observed at needle boron concentrations of 13–70 µg/g, whereas toxic symptoms were observed at needle boron concentrations of approximately 200 µg/g. The authors concluded that foliar absorption of airborne boron, as well as root absorption from boron in soil solution, resulted in the injury to this stand of trees.

Temple & Linzon (1976) reported that atmospheric boron emissions from an appliance manufacturing plant and a fibreglass manufacturing plant resulted in >35% foliar necrosis on vegetation within 700 m of the plant, with 1–15% foliar necrosis occurring within 500 m in all directions from the plant. The amount of leaf damage was proportional to the boron concentration in the leaves. Species of maple (Acer sp.) appeared to be the most sensitive, with slight necrosis occurring at a concentration of 432 µg/g in unwashed foliage, moderate necrosis at foliar concentrations ranging from 707 to 1013 µg/g, and severe necrosis at foliar concentrations of 1207–1560 µg/g.

Lang et al. (1986) found that boron thresholds for detectable levels (10%) of visible injury due to boron toxicity were about 500 mg/kg of foliage for both bigleaf maple and digger pine growing near geothermal generating units.
10. EVALUATION OF HUMAN HEALTH RISKS AND EFFECTS ON THE ENVIRONMENT

10.1 Evaluation of human health exposures

Boron is a naturally occurring element found combined with other elements (primarily oxygen) throughout the environment. It is found in the Earth’s crust, with the majority of readily available forms occurring in the ocean. It is estimated that more boron is released into the environment by natural weathering than from anthropogenic sources. Boron is not present in the atmosphere at significant levels. Boron is present in surface water and groundwater and is readily adsorbed on the surfaces of soil particles. Boron is present in food, beverages, and drinking-water.

Boron has a wide variety of uses in the manufacture of glass, glass products, antiseptics, cleaning products, pharmaceuticals, biological growth control agents, wood and leather preservatives, and insecticides. It is also used in photographic chemicals, enamels and frits, and fire retardants.

Exposure to boron compounds can occur by inhalation, ingestion, and dermal contact. Boron compounds are absorbed from the respiratory and gastrointestinal tracts, as indicated by increased levels of boron in the blood, tissues, and urine. Dermal absorption of boron across intact skin is negligible.

Specific information on population exposures from different countries was discussed in chapter 5. This information was used to determine mean intakes in ambient air, drinking-water, soil, food, and consumer products. From these mean intakes, per cent allocations of the TIs can be developed, as shown in Table 22. In general, food and drinking-water form the greatest contributions to boron intake in humans, at about 65% and 30%, respectively.

Only a few human studies have been conducted to assess health effects associated with exposure to boron compounds. The available data suggest that exposure is associated with short-term and reversible irritant effects on the upper respiratory tract, nasopharynx, and eye.
Table 22. Estimation of exposures based on ranges of mean concentrations in several environmental media on a global basis, and allocation of the Tl among media

<table>
<thead>
<tr>
<th>Environmental media</th>
<th>Mean intake&lt;sup&gt;a&lt;/sup&gt; (mg/day)</th>
<th>% allocation of Tl</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ambient air</td>
<td>0.000 44</td>
<td>Nil</td>
</tr>
<tr>
<td>Drinking-water</td>
<td>0.6&lt;sup&gt;b&lt;/sup&gt;</td>
<td>~30</td>
</tr>
<tr>
<td>Soil</td>
<td>0.000 5</td>
<td>Nil</td>
</tr>
<tr>
<td>Food</td>
<td>1.2</td>
<td>~65</td>
</tr>
<tr>
<td>Consumer products</td>
<td>0.1</td>
<td>5</td>
</tr>
<tr>
<td>Total</td>
<td>1.9</td>
<td>100</td>
</tr>
</tbody>
</table>

<sup>a</sup> Mean intakes are estimated in chapter 5.

<sup>b</sup> Assuming an intake of 2 litres of water per day.

The sole long-term (7-year) follow-up study failed to identify any long-term health effects, although a healthy worker effect cannot be entirely ruled out, given the rate of attrition (47%). In two descriptive studies that assessed fertility and secondary sex ratios in relation to exposure, no detrimental effects on demonstrated fertility for the study samples were reported. Although an excess percentage of female births has been suggested, the absence of statistical significance and attention to other co-variates known to affect sex ratios warrants careful interpretation of this finding. No studies have been identified that assess the spectrum of reproductive outcomes, such as time-to-pregnancy, conception delays, spontaneous abortions, or semen quality. The role of other lifestyle or behavioural factors in relation to health and fertility requires further study to identify potentially sensitive populations and to evaluate reproductive effects more fully.

10.2 Choice of critical effect and application of uncertainty factors

The critical effect appears to lie within the area of developmental toxicity. Other effects, such as reproductive toxicity, also occur at slightly higher doses and were considered in the choice of critical
effects through a comparison of LOAELs (Table 17) or benchmark doses (BMDs) (Moore et al., 1997). Several developmental effects from boron exposure have been noted in rats, mice, and rabbits. Again, these effects are the most sensitive in a larger toxicity database that includes sub-chronic and chronic bioassays. The specific critical effect within these developmental toxicity studies is a decreased average fetal body weight per litter in the rat (Heindel et al., 1992; Price et al., 1996a).

In the Price et al. (1996a) study, boric acid was administered in the diet to CD rats from gestational day 0 to 20 at 3.3, 6.3, 9.6, 13.3, or 25 mg boron/kg body weight per day. For the low- to high-dose groups, fetal body weights were 99, 98, 97, 94, and 88% of controls. Fetal body weight was statistically significantly decreased only in the 13.3 and 25 mg/kg body weight per day dose groups on gestational day 20. The NOAEL for decreased fetal body weight was 9.6 mg boron/kg body weight per day, and the LOAEL was 13.3 mg boron/kg body weight per day. The results of this study provide a NOAEL and LOAEL that complement the LOAEL of 13.6 mg boron/kg body weight per day in the Heindel et al. (1992) study. This NOAEL is also similar to BMDs for developmental toxicity (see appendix).

For interspecies variation, a default value of 10 has often been applied in the absence of actual data showing less than the usual variation between species. For inter-individual (intraspecies) variation, a default value of 10 has often been applied in the absence of actual

---

\[ a \] The Weir & Fisher (1972) 2-year dog studies were not used directly for risk assessment for several reasons. The NOAEL and LOAEL were taken from two studies; one was 2 years long, and the high-dose group was a supplemental group terminated at 38 weeks. There were a limited number of animals (4/dose) per test group. One control group was used for both borax and boric acid, so that there were never more than 2 control animals sacrificed at one time. Some of the control animals showed some form of testicular damage.

\[ b \] In fact, the Price et al. (1996a) study was conducted specifically to address the lack of a NOAEL from the Heindel et al. (1992) study. Similarity in study designs and results from these two studies greatly strengthens the dose–response relationship for developmental toxicity as the critical effect.
data within a species. A scheme has been adopted by IPCS (1994) that allows for subdivision of each of these defaults to incorporate appropriate data on toxicodynamics or toxicokinetics. Where appropriate data exist, this scheme improves the extrapolation process and uses correction factors for toxicodynamic and toxicokinetic data instead of 10-fold uncertainty factors for inter- and intraspecies variation. For interspecies differences, the 10-fold factor is divided into a default factor of $10^{0.4}$ for toxicodynamics and $10^{0.6}$ for toxicokinetics in the absence of toxicodynamic or toxicokinetic data. Multiplying these subdivided default factors gives the default 10-fold uncertainty factor ($10^{0.4} \times 10^{0.6} = 10$).

For inter-individual (intraspecies) differences, the 10-fold factor is divided into a default factor of $10^{0.5}$ each for toxicokinetics and toxicodynamics in the absence of toxicodynamic or toxicokinetic data. Multiplying these subdivided default factors gives the default 10-fold uncertainty factor ($10^{0.5} \times 10^{0.5} = 10$).

The pharmacokinetics of boron appear to be quite similar across species in the following respects:

a) **Absorption** of borates is essentially complete (approximately 95% in humans and rats), and boron appears rapidly in blood and body tissues of several mammalian species following ingestion.

b) **Distribution** of boron in mammals appears to occur by passive diffusion throughout the body fluids. In contrast to soft tissues and blood, bone shows selective uptake of boron ($\geq 4$ times higher than serum) and significantly longer retention times.

c) **Metabolism** of boric acid is thermodynamically unfavourable in biological systems. Thus, the ionic species in systemic circulation are expected to be equivalent across mammals. This eliminates a major source of potential uncertainty for risk extrapolation, as interspecies differences in enzymatic pathways and/or metabolic rates do not need to be taken into consideration.

d) **Elimination** kinetics (especially route of elimination and terminal half-life) also appear to be similar for humans and rats.
The similarities in pharmacokinetic parameters between humans and rats, the species defining the NOAEL for laboratory studies, reduce the uncertainty for risk extrapolation between these two species.

10.3 Derivation of the tolerable intake

A TI is defined as an estimate of the intake of a substance that can occur over a lifetime without appreciable health risks. The TI is derived on the basis of the NOAEL of the critical effect, the adverse effects judged to be the most appropriate for determining the TI, using appropriate uncertainty factors. The use of the critical effect, judged here to be developmental toxicity, is expected to protect against other effects such as reproductive toxicity occurring at higher doses.

\[
\text{TI} = \frac{9.6 \text{ mg/kg body weight per day}}{[10^{0.4} \times 10^{0.1}] \times [10^{0.5} \times 10^{0.4}]}
\]

\[
= 0.4 \text{ mg/kg body weight per day}
\]

\[
= 400 \mu\text{g/kg body weight per day}
\]

where:

- 9.6 mg/kg body weight per day is the NOAEL from a well conducted developmental study with decreased fetal body weight occurring in a dose-related manner.

- \(10^{0.4} \times 10^{0.1} (=10^{0.5})\) is the uncertainty factor for interspecies differences:

**Dynamics:** Data do not exist to support a factor other than the default value of \(10^{0.4}\). Moreover, differences in LOAELs among rats, rabbits, and mice for the critical effect (Table 16) support the default value. The Task Group judged that \(10^{0.4}\) was appropriate.

**Kinetics:** Oral absorption of boron in rats and humans is quantitatively similar, with values of 94% for humans and 95%
for rats (section 6.1.1). The ratio of these absorption rates is approximately 1.

Distribution of boron in rats and humans appears quantitatively similar, as determined by a comparison of blood boron levels after doses in either diet or drinking-water (Fig. 1, section 6.2.2). Ratios of rat blood boron values to a regression line for human blood boron values are as low as 0.7 and as high as 6, with the majority of values in the range of 2–3. Comparative regression techniques should be pursued to confirm this trend. Pregnant rats appear to have lower blood boron values than non-pregnant rats when given similar doses. Comparative data for pregnant and non-pregnant humans are lacking.

Metabolism of boron is thought not to occur in humans or animals owing to the excessive energy required to break the boron–oxygen bond (section 6.3). As it is unlikely that there are any differences between species in the metabolism of boron, the ratio of metabolic parameters is 1.

Elimination of boron in rats and humans appears quantitatively similar, with half-life values in humans of 21 h in volunteers and approximately 13 h in poisonings, and values in rats of 14–19 h (section 6.4). The ratio of these elimination half-life values is approximately 1.3 when human volunteer data are compared with the rat data, or 0.8 when human poisoning data are compared with the rat data. The mean of these two ratios is about 1.

As a result, the Task Group judged that the default value of $10^{0.6}$ could be reduced to $10^{0.1}$.

- $10^{0.5} \times 10^{0.4} (=10^{0.9})$ is the uncertainty factor for inter-individual (intraspecies) differences:

**Dynamics:** Data in humans do not exist to support a value different from the default of $10^{0.5}$. Animal studies suggest that intraspecies variability in toxicodynamics exists. The Task Group judged that $10^{0.5}$ was appropriate.
Kinetics: Data exist in humans to suggest some limited variability in boron absorption and/or distribution (Nielsen, 1995). However, the lack of boron metabolism in humans and experimental animals suggests some reduction in the default value of $10^{0.5}$. The Task Group judged that $10^{0.4}$ was appropriate.

Other uncertainty factors for adequacy of database are not considered necessary, because the overall database includes sub-chronic and chronic studies on several species and several reproductive studies.

The total uncertainty factor\(^a\) is therefore:

$$10^{0.5} \times 10^{0.9} = 10^{1.4} \text{ (or 25)}$$

Data are inadequate to allow the development of a TI for inhalation exposure (TI).

**10.4 Derivation of guidance values**

Exposure to boron from various media varies with the locality. In areas where data on exposure are available, specific guidance values that are tailored to the local circumstances should be developed from the TI presented in this document.

For example, guidance values for specific media could be developed by first using the allocations shown in Table 22 with the TI derived in section 10.3. Table 23 shows the resulting allocation of the TI by media in mg/kg body weight per day.

\(^a\) After closure of the Task Group meeting, Dr M. Dourson, after additional consideration, dissented from the Task Group's recommendation on the uncertainty factor.

\(^b\) Subsequent to the Task Group meeting, a provisional guideline for boron in drinking-water was recommended by the Working Group Meeting on Chemical Substances in Drinking-Water, using a different uncertainty factor, based upon a different weighting attached to some toxico-kinetic studies for that area of application (WHO, 1998a,b).
The second step in the development of a guidance value would be to pick appropriate body weight and exposure assumptions. Two examples are given using allocations found in Table 23. The resulting guidance value (GV) for example A in drinking-water would be:

**Example A**

\[
GV = \frac{0.12 \text{ mg/kg body weight per day} \times 64 \text{ kg body weight}}{2 \text{ litres/day}} \\
\approx 4 \text{ mg/litre}
\]

where:

- 64 kg is the average human body weight (IPCS, 1994)
- 2 litres/day is one assumption of water intake (IPCS, 1994).

The resulting guidance value (GV) for example B would be:

**Example B**

\[
GV = \frac{0.04 \text{ mg/kg body weight per day} \times 64 \text{ kg body weight}}{2 \text{ litres/day}} \\
\approx 1.3 \text{ mg/litre}
\]

Assumptions of food intake and consumer product use could be used with allocations given in Table 23 to generate tolerances or other risk management standards. Individual countries are encouraged to develop guidance values using allocations, body weights, and exposure assumptions that are appropriate for their populations.
Table 23. Examples of allocation of Tl by media

<table>
<thead>
<tr>
<th>Environmental media</th>
<th>Example A</th>
<th>Example B</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Per cent</td>
<td>mg/kg body weight per day</td>
</tr>
<tr>
<td>Ambient air</td>
<td>Nil</td>
<td>0</td>
</tr>
<tr>
<td>Drinking-water</td>
<td>30</td>
<td>0.12</td>
</tr>
<tr>
<td>Soil</td>
<td>Nil</td>
<td>0</td>
</tr>
<tr>
<td>Food</td>
<td>65</td>
<td>0.26</td>
</tr>
<tr>
<td>Consumer products</td>
<td>5</td>
<td>0.02</td>
</tr>
<tr>
<td>Total</td>
<td>100</td>
<td>0.4</td>
</tr>
</tbody>
</table>

* Values from Table 22.

10.5 Evaluation of effects on the environment

10.5.1 Exposure

Boron is not present in the atmosphere at significant levels; however, the total amount present in the atmosphere at any one time is significant owing to the huge volume of the atmosphere. Boron concentrations in air range from <0.5 to approximately 80 ng/m³, with an average of 20 ng/m³.

Boron occurs naturally in rocks, with concentrations ranging from 5 mg/kg in basalts to 100 mg/kg in shales. Concentrations of boron in surface water are dependent on such factors as the geochemical nature of the drainage area, proximity to marine coastal regions, and inputs from industrial and municipal effluent discharges. Concentrations of boron range widely, from 0.001 to as much as 360 mg/litre. However, mean concentrations for waters of Europe, Pakistan, Russia, and Turkey are typically well below 0.6 mg boron/litre. Concentrations of boron in waters in Japan, South Africa, and South America are generally below 0.3 mg/litre. Typical concentrations in North American waters are below 0.1 mg boron/litre, with about 90% at 0.4 mg boron/litre or below.
Boron is adsorbed onto soil particles, with the degree of adsorption depending on the type of soil, pH, salinity, organic matter content, iron and aluminium oxide content, iron- and aluminium-hydroxy content, and clay content. Boron adsorption can vary from being fully reversible to irreversible, depending on the soil type and condition. Boron occurs in soils at concentrations ranging from 10 to 300 mg/kg (average 30 mg/kg), depending on the type of soil, amount of organic matter, and amount of rainfall.

Boron does not bioaccumulate in aquatic invertebrates and fish. Based on wet weights, boron concentrations in marine invertebrates and fish are similar to the levels found in the exposure media, between 0.5 and 4 mg/kg. Bioconcentration factors for two freshwater fish species were found to be 0.3. The results of studies of boron accumulation in plants, insects, and fish have shown that boron bioaccumulates in plants but does not biomagnify in aquatic food-chains. Concentrations of boron have been shown to range between 26 and 382 mg/kg in submerged aquatic freshwater plants, from 11.3 to 57 mg/kg in freshwater emergent vegetation, and from 2.3 to 94.7 mg/kg dry weight in terrestrial plants.

10.5.2 Effects

Boron is an essential micronutrient for cyanobacteria and diatoms. Considering all microorganisms, algae and protozoa appear to be equisensitive to boron and bacteria the most tolerant. Both algae and protozoa provide NOEC (including EC₃) values between 0.3 and 20 mg boron/litre.

Chronic studies with Daphnia magna provided consistent NOECs between 6 and 10 mg boron/litre. Long-term outdoor pond and field studies with microorganisms and invertebrates provided NOEC values up to 1.52 mg boron/litre.

Via acute tests, the rainbow trout and zebra fish were determined to be the most sensitive taxa, with acute values around 10 mg boron/litre. Further tests with embryo–larval stages of several fish species showed rainbow trout to be the most sensitive to boron. Tests conducted with early life stages of rainbow trout in reconstituted water overpredicted toxicity compared with tests conducted with natural
water. No adverse effects were found in natural water exposures containing up to 0.75 mg boron/litre. Consistent LOECs were between 1.1 and 1.7 mg boron/litre. These laboratory values were confirmed by several observations of successful trout populations thriving in hatcheries, streams, and lakes containing boron concentrations up to 1 mg/litre.

Boron is an essential micronutrient for higher plants, with interspecies differences in the levels required for optimum growth. The symptoms of boron deficiency in plants include cessation of root and leaf growth, necrosis, retardation of enzyme reactions, and reduced pollen germination. The initial symptoms of boron toxicity in plants are chlorosis, necrosis, and a subsequent loss of photosynthetic capacity, which reduces plant productivity.

Mallard duckling growth was adversely affected at dietary levels of 30 and 300 mg/kg, and survival was reduced at 1000 mg/kg.

10.5.3 Risk evaluation

Risk characterization is based on the comparison of the environmental concentration with a concentration protective for an ecosystem. Ambient concentrations of boron in surface waters have been reported for several countries covering four continents. The data indicate that mean or median levels are approximately 0.1 mg boron/litre and that 90th-percentile or greater values are approximately 0.5 mg boron/litre. Considerable data exist on the toxicity of boron to freshwater organisms and ecosystems. Acute tests with invertebrates and fish showed that rainbow trout and zebra fish were most sensitive to borate (LC\textsubscript{50} ~10 mg boron/litre). Chronic results for algae, higher plants, and fish clearly showed that the rainbow trout was the most sensitive species, with consistent NOECs and LOECs of about 1 mg boron/litre. Confirmed were several observations of healthy rainbow trout populations in US hatcheries and streams at or above 1 mg boron/litre. Not surprisingly, biocenoses (model ecosystems) covering all stages of the aquatic food-web (excluding fish) were more tolerant of boron than were rainbow trout (NOEC up to 1.52 mg boron/litre). Given all this information, the comparison of the environmental effects concentration with the general ambient environmental levels indicates that the risk of adverse effects of boron on the aquatic ecosystem is low. In a
few boron-rich environments, natural levels will be higher. It is reasonable to assume that aquatic organisms in such habitats may be adapted to the local conditions.

Boron deficiencies in terrestrial plants have been reported in many countries. Boron deficiency is more likely to occur in light-textured, acid soil in humid regions, because of boron’s susceptibility to leaching. In general, there is a small range between deficiency and toxicity. However, considerable variation exists between species in their resistance to boron. Species sensitive to boron are known to include citrus, stone fruits, and nut trees; semi-tolerant species include tubers and cereals; and tolerant species include most vegetables. Toxicity due to excess boron is much less common in the environment than boron deficiency. Irrigation water is one of the main sources of high boron levels that result in toxicity in the field. However, few irrigation waters contain enough boron to injure plants directly; it is the continued use and concentration in the soil resulting from evapotranspiration that lead to the eventual toxicity problems. Pollutant sources of boron, in the form of either airborne emissions or leachates from soil application, have also been shown to produce toxic symptoms in endemic plant species growing in the immediate vicinity.

Levels of boron measured in aquatic plants from Kesterson National Wildlife Refuge, California, USA (an evapotranspiration sink that receives boron-rich run-off from irrigated agricultural fields) are higher than those found to cause effects on mallard ducklings in the laboratory. Therefore, there appears to be a risk to waterfowl in this area. However, the bioavailability of such boron levels is uncertain. The extent of risk to waterfowl in most geographical areas is expected to be low.
11. CONCLUSIONS AND RECOMMENDATIONS FOR PROTECTION OF HUMAN HEALTH AND THE ENVIRONMENT

11.1 Conclusions

Boron is a naturally occurring element that is found in nature in the form of borates in the oceans, sedimentary rocks, coal, shale, and some soils. Natural sources of borates released into the environment are the oceans, geothermal steam, and natural weathering of clay-rich sedimentary rocks. Boron is also released from anthropogenic sources to a lesser extent.

Boron is an essential micronutrient for higher plants, with interspecies differences in the levels required for optimum growth. Boron deficiency has been observed in many countries throughout the world. There is a small range between deficiency and toxicity in some plants.

Comparison of the environmental no-effect concentration (1 mg/litre) with the general ambient environmental boron levels indicates that the risk of adverse effects of boron on the aquatic ecosystem is low. In a few boron-rich environments, natural levels will be higher. It is reasonable to assume that aquatic organisms in such habitats may be adapted to the local conditions.

For humans, boron exposure occurs primarily through the diet and drinking-water. The mean global boron concentration in drinking-water was considered to be between 0.1 and 0.3 mg boron/litre. For the general population, the greatest boron exposure comes from the oral intake of food. The mean daily intake of boron in the diet is estimated to be near 1.2 mg/day.

In humans and animals, boric acid and borate are absorbed from the gastrointestinal and respiratory tracts. Greater than 90% of administered doses of these compounds are absorbed, as evidenced by excretion in the urine, which is rapid, occurring over a few to several days.
Conclusions and Recommendations

Animal experiments have shown that boron in the form of boric acid and borate demonstrates reproductive and developmental toxicity at levels that are approximately 100- to 1000-fold greater than normal exposure levels. There is a lack of sufficient toxicity data on humans. The TI of boron was set as 0.4 mg/kg body weight per day. The allocation of the TI in various media should be based on the exposure data of individual countries.

11.2 Recommendations

a) Water and food guideline values should be based on the TI provided by this document.

b) The TI should be applied with the understanding that boron may provide a physiological benefit for human health.

c) It should be recognized in applying standards that boron is essential for some constituents of the environment (e.g. boron is an essential micronutrient for higher plants).

d) Dietary supplements that exceed the TI should be avoided.
12. FURTHER RESEARCH

a) Further studies regarding global cycling of boron.

b) Determine whether boron is required for normal fetal and postnatal development for higher animals.

c) Define a biochemical function that confirms the essentiality of boron for higher animals.

d) Determine the homeostatic mechanism through which boron concentrations are maintained during low dietary intakes.

e) Further studies on the absorption, distribution, and clearance of boron at oral doses in the range of 0.01–1 mg boron/kg body weight per day.

f) A modern rat reproduction study to determine the potential for developmental effects of borates in succeeding generations in a sensitive animal species.

g) Analytical epidemiology studies to assess the spectrum of reproductive and developmental outcomes to assess boron toxicity in targeted human populations.

h) Epidemiological studies that incorporate toxicological and physiological components to enhance an understanding of the toxicokinetics and physiology of boron in populations, including potentially sensitive ones.

i) Further quantitative definition of the maximum tolerable concentration for sensitive aquatic species.

j) A refined understanding of the relationship of water and dietary uptake of boron into waterfowl.

k) Development of an approach that integrates essentiality and toxicity for the establishment of acceptable boron concentrations in aquatic and terrestrial environments.
13. EVALUATIONS BY INTERNATIONAL BODIES

The EC Cosmetics Directive 76/768/EEC (and its subsequent amendment) sets an upper limit of boric acid in cosmetic products, which must not contain more than 5% in talc, 0.5% in oral hygiene products, and 3% in other products. Only the talc containing boric acid must, in addition, not be used on children less than 3 years of age.

In 1997, subsequent to the Task Group meeting, a provisional guideline for boron in drinking-water was recommended by the Working Group on Chemical Substances in Drinking-Water, which updated the Guidelines for drinking-water quality (WHO, 1998a,b).
REFERENCES


References


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References


Clarke WB, Koekebakker K, Barr RD, Downing RG, & Fleming RF (1987a) Analysis of ultratrace lithium and boron by neutron activation and mass spectrometric measurement of 3He and 4He. Appl Rad Isot, 38(9): 735-743.


References


Juhnke I & Ludemann D (1978) [Results of the investigation of 200 chemical compounds for acute fish toxicity with the golden orfe test.] Z Wasser Abwasser Forsch, 11: 161-164 (in German with English summary).


Korenaga T, Motomizu S, & Toei K (1980) Improved extraction method for the spectrophotometric determination of trace amounts of boron in river water with 1,8-dihydroxynaphthalene-4-sulphonic acid and removal of the excess of reagent. Analyst, 105: 955-964.


References


Mann H (1973) [Study of the effect of boron compounds on fish and other aquatic organisms.] Arch Fisch Wiss, 24: 171-175 (in German with English summary).


References


References


Stelzer LH (1980) Baseline levels of selected trace elements in Colorado oil shale region animals. J Wildl Dis, 16: 175-182.


References


Unilever (1994) Summary of external research project on environmental levels of boron, especially in trout-sustaining waters. Unilever Research, Port Sunlight Laboratory, 3 pp (Unpublished report).


Verbitskaya GV (1975) [Experimental and field investigations concerning the hygienic evaluation of boron-containing drinking water.] Gig i Sanit, 7: 49-53 (in Russian with English summary).


Alternative Approaches — Benchmark Dose

A suggested alternative to the use of a NOAEL in the development of the TI is to use a BMD. Some advantages in using a BMD are as follows: 1) more data from the dose–response curve are used; 2) influence by background incidence rate is lessened; and 3) sensitivity to the spacing of doses in the assay is reduced. A BMD is derived by first calculating or estimating a dose that causes a critical effect in a small percentage (e.g. 5%) of test animals (effective dose). A BMD is then determined as the lower confidence limit of this effective dose (Barnes et al., 1995).

Using data from the Heindel et al. (1992) study in rats and a decreased fetal body weight as the critical effect, a BMD for boron of 9.3 mg/kg body weight per day was estimated using a polynomial model (see Fig. 2). This BMD was based on the 95% confidence limit on the dose that causes a 5% decrease in fetal body weight. Dividing by an uncertainty factor of 25 gives a TI of 0.4 mg/kg body weight per day. Another model (Weibull) was used (Allen et al., 1996) with study data from Heindel et al. (1992) and Price et al. (1996a) and with decreased fetal weight as the critical effect to derive a BMD of 9.8 mg/kg body weight per day based on the 95% confidence limit on the dose that causes a 5% decrease in fetal body weight. Dividing by an uncertainty factor of 25 also gives a TI of 0.4 mg/kg body weight per day. Both BMD-based TIs are identical to the one developed with the traditional approach. Although use of a BMD to derive a TI does have some advantages over the NOAEL method, there is as yet no consensus on the incidence of effect to be used as a basis for deriving the BMD.
Continuous Weibull  
95% CL  BMD (○)

Polynomial  
95% CL  BMD (■)

(9.3, 3.56)  
(9.8, 3.55)

Dose  
(Mg boron/kg body weight per day)

Fetal weight (g/litter)

Note: 5% decrease from control mean (3.70) is 3.51

WHO 98150

Fig. 2. BMD estimates from two models for boric acid in rats: critical effect — fetal weight decrease.
RÉSUMÉ, CONCLUSIONS ET RECOMMANDATIONS

1. Résumé

1.1 Identité, état naturel et méthodes d’analyse

Le bore est un élément naturel qui se trouve sous la forme de borates dans les océans, les roches sédimentaires, la houille, le schiste et certaines huiles minérales. Il est très répandu dans la nature, avec des concentrations de l’ordre de 10 mg/kg dans l’écorce terrestre (elles vont de 5 mg/kg dans les basaltes à 100 mg/kg dans les schistes) et d’environ 4,5 mg/litre dans les océans.

Les dérivés boriques les plus importants, qu’il s’agisse de minéraux ou de produits du commerce, sont le borax à cinq molécules d’eau, le borax, le perborate de sodium, l’acide borique, la colemanite et l’ulexite. Aux faibles concentrations et au pH pratiquement neutre qui caractérisent la plupart des liquides biologiques, c’est le monomère B(OH)$_3$, qui est l’espèce prédominante (avec un peu de B(OH)$_4^-$), que la source de bore soit l’acide borique ou un borate. Cela tient au fait que l’acide borique est un acide très faible (pKa = 9,15). Le perborate de sodium s’hydrolyse pour donner du peroxyde d’hydrogène et du métaborate ; il peut donc présenter des propriétés chimiques et toxicologiques un peu différentes de celles des autres borates.

Les méthodes utilisant un plasma à couplage inductif (ICP) sont les méthodes de choix pour le dosage des faibles quantités de bore présentes dans les échantillons biologiques et environnementaux ; les méthodes colorimétriques doivent être utilisées avec prudence.

1.2 Production, usages, destinée dans l’environnement et sources d’exposition

Les dépôts de borates économiquement exploitables sont rares et se trouvent dans des zones arides de Turquie, des Etats-Unis, du Chili, de Russie, de Chine et du Pérou. La production mondiale totale de minéraux contenant du bore — principalement de la colemanite, de l’ulexite, du tincal et de la kernite — a été d’environ 2 750 000 tonnes en 1994. Environ 800 000 tonnes (en équivalents de B$_2$O$_3$) de dérivés boriques commerciaux ont été produits à partir des minéraux.
Les borates sont, entre autres, principalement utilisés pour fabriquer des produits isolants, des fibres de verre de qualité textile, des agents de blanchiment (perborate de sodium), des verres au borosilicate, des retardateurs de flamme, des engrais et des herbicides (à l’état de traces), des émaux, des vernis pour céramiques, des frittés ainsi qu’une myriade d’applications diverses.

La pénétration du bore dans l’environnement se fait principalement par l’action des agents météorologiques sur les roches, la volatilisation de l’acide borique présent dans l’eau de mer et l’activité volcanique. L’apport de bore dû aux activités humaines est moindre. Parmi ces dernières sources figurent les brûlis agricoles, l’incinération des déchets, la combustion du bois de feu, la production d’énergie à partir du charbon et du pétrole, l’industrie du verre, les borates et perborates utilisés comme produits industriels et ménagers, l’exploitation des mines de borates, le traitement des borates et des bois et papiers imprégnés et enfin le rejet des effluents et des boues. Il est souvent difficile de chiffrer l’apport de ces sources.

L’émission de borates et d’acide borique dans l’atmosphère se fait sous la forme de particules et de vapeurs par suite de la volatilisation de l’eau de mer, de l’activité volcanique et, dans une moindre mesure, de l’exploitation des mines, de la fabrication de verre et de céramique, de l’usage agricole de certains dérivés et des rejets des centrales thermiques fonctionnant au charbon. Le bore n’est pas très abondant dans l’atmosphère, mais la quantité totale qui s’y trouve à un moment donné n’est pas négligeable du fait du volume énorme de l’atmosphère. Compte tenu de la solubilité des borates dans l’eau, ils ne devraient pas séjourner longtemps dans l’atmosphère en concentrations importantes.

L’action des phénomènes météorologiques peut provoquer la libération de bore dans le sol et dans l’eau de même que, encore qu’en proportion bien moindre, les déversements d’origine humaine tels que les rejets d’effluents. On pense que les phénomènes d’adsorption-désorption sont les seuls mécanismes importants qui soient susceptibles d’influer sur la destinée du bore dans l’environnement. Le taux d’adsorption du bore dépend de sa concentration en solution et du pH de l’eau.
Le bore s'adsorbe sur les particules du sol, le degré d'adsorption étant fonction du type de sol, du pH, de la salinité, de la teneur en matières organiques, en oxyde et hydroxyde d'aluminium, en hydroxyde de fer et en argile. Le phénomène peut être parfaitement réversible ou au contraire complètement irréversible, selon la nature et l'état du sol.

Les ions borate présents en solution aqueuse s'y trouvent essentiellement au degré d'oxydation maximum. Il n'y a pas de processus aérobie qui soit susceptible d'influer sur la formation des différentes espèces chimiques et on n'a pas fait état de biotransformations. Il ne devrait donc pas y avoir de différence dans les différentes espèces chimiques qui soit due à une biotransformation.

Le coefficient de partage octanol/eau de l'acide borique est de 0,175, ce qui indique que ce composé a un faible potentiel de bioaccumulation. Les expériences de laboratoire effectuées sur des organismes aquatiques ont confirmé l'existence d'un faible potentiel de bioaccumulation. Les végétaux ont tendance à accumuler du bore; toutefois la fixation du bore par les plantes dépend du pH de la solution de sol, de la température, de l'intensité lumineuse et de la concentration d'autres éléments (par ex. le calcium et le potassium). Les études relatives à l'accumulation du bore par les plantes, les insectes et les poissons montrent que cet élément s'accumule dans les végétaux mais qu'il ne s'amplifie pas de long de la chaîne alimentaire aquatique.

Le bore est présent dans les différents sols à des concentrations qui vont de 10 à 300 mg/kg (la moyenne est de 30 mg/kg) selon la nature du sol, sa teneur en matières organiques et l'importance des précipitations. Sa concentration dans les eaux superficielles dépend de plusieurs facteurs tels que la nature géochimique du bassin de drainage, la proximité de zones littorales et les apports dus aux décharges industrielles et municipales. Les valeurs sont très variables, allant de 0,001 à 360 mg/litre. Toutefois les concentrations moyennes dans les eaux de l'Europe, du Pakistan, de la Russie et de la Turquie se situent nettement en dessous de 0,6 mg/litre. Au Japon, en Afrique du Sud et en Amérique du sud elles sont généralement inférieures à 0,3 mg/kg. En Amérique du Nord, elles se caractérisent par des valeurs
inférieures à 0,1 mg/litre, dont 90% inférieures ou égales à 0,4 mg/litre.

Le bore s'accumule dans les plantes aquatiques et terrestres mais il ne s'amplifie pas le long de la chaîne alimentaire. On a trouvé des concentrations de bore comprises entre 26 et 382 mg/kg dans des plantes d'eau douces immergées, entre 11,3 et 57 mg/kg dans des plantes d'eau douce semi-immérgees et entre 2,3 et 94,7 mg/kg dans des plantes terrestres. En se basant sur le poids frais, on constate que les concentrations de bore trouvées dans les invertébrés marins et les poissons sont analogues à celles que l'on mesure dans les milieux correspondants, soit entre 0,5 et 4 mg/kg. Chez deux espèces de poissons, on a trouvé un facteur de bioconcentration de 0,3.

Dans l'air ambiant, la concentration du bore varie de < 0,5 à environ 80 ng/m³, avec une moyenne de 20 ng/m³ au-dessus des continents.

Le fait que la concentration du bore dans les eaux souterraines et les eaux douces de surface soit très voisine de sa concentration dans l'eau de boisson, indique que ce élément n'est pas éliminé par les traitements auxquels sont soumises les eaux souterraines et les eaux de surface destinées à la boisson.

L'apport de bore chez l'Homme devrait être de 0,44 µg/jour à partir de l'air ambiant, de 0,2–0,6 mg/jour à partir de l'eau de boisson et de 1,2 mg/jour à partir de l'alimentation. On estime que l'apport moyen de bore à partir du sol est de 0,5 µg/jour. On peut raisonnablement estimer que l'apport de bore par les produits de consommation est de 0,1 mg/jour.

1.3 Cinétique et suivi biologique

La pharmacocinétique du bore se révèle assez semblable d'une espèce à l'autre, notamment en ce qui concerne les aspects suivants:

a) Absorption. L'absorption des borates est pratiquement complète (environ 95% chez l'Homme et le rat) et après ingestion, le bore
apparaît rapidement dans le sang et les tissus de plusieurs espèces de mammifères.

b) Distribution. Chez les mammifères, elle se produit selon un mécanisme de diffusion passive par les liquides biologiques. Contrairement aux tissus mous et au sang, les os sont capables de fixer sélectivement le bore (teneur supérieure ou égale à 4 fois celle du sérum) et de le retenir sensiblement plus longtemps.

c) Métabolisme. Le métabolisme de l’acide borique est thermodynamiquement défavorable dans les systèmes biologiques. Les espèces ioniques présentes dans le courant sanguin devraient donc être les mêmes chez tous les mammifères. Dans ces conditions, on risque beaucoup moins de se tromper en procédant à des extrapolations, puisqu’il n’est pas nécessaire de prendre en considération les différences interspécifiques qui existent généralement au niveau des voies enzymatiques et de la vitesse de métabolisation.

d) Elimination. La cinétique d’élimination (en particulier la voie d’élimination et la demi-vie terminale) se révèle également analogue chez l’Homme et le rat.

Les analogies qui existent entre les paramètres pharmacocinétiques relevés chez l’Homme et chez le rat, l’espèce qui sert à définir la dose sans effet nocif observable (NOAEL) dans les études de laboratoire, permettent de réduire l’incertitude que comporte l’extrapolation à l’Homme des résultats obtenus sur le rat.

1.4 Effets sur l’Homme et les animaux de laboratoire

Les données relatives aux effets toxiques sur le développement et la reproduction montrent que l’effet déterminant consiste en une réduction du poids des foetus. On a estimé à 9, 6 mg de bore par jour et par kg de poids corporel, la NOAEL relative à cet effet. La dose la plus faible produisant un effet nocif observable (LOAEL) est, chez le rat, d’environ 13 mg/kg de poids corporel par jour, l’effet observé étant une légère différence dans le poids des foetus (~5%) et des
anomalies costales. A mesure que l’on augmente la dose, on observe les effets suivants, selon la dose:

a) autres anomalies costales et testiculaires (~25 mg de bore par jour et par kg de poids corporel);

b) réduction du poids des foetus et accroissement des malformations cardiovasculaires chez le lapin; graves anomalies testiculaires chez le rat (~40 mg de bore par jour et par kg de poids corporel);

c) atrophie testiculaire et stérilité chez le rat (~55 mg de bore par jour et par kg de poids corporel);

d) réduction du poids des foetus chez la souris (~80 mg de bore par jour et par kg de poids corporel).

Les études effectuées sur des rats et des souris ne révèlent aucun signe de cancérogénicité de l’acide borique. Comme les données humaines font défaut et que les données animales sont également limitées, on ne peut pas ranger le bore dans une classe précise de cancérogénicité.

Seules quelques études ont été consacrées à l’évaluation des effets résultant d’une exposition humaine aux dérivés du bore. Les données disponibles montrent que l’exposition à ces composés peut se traduire à brève échéance par une irritation des voies respiratoires supérieures, du rhinopharynx et des yeux. Ces effets sont cependant de brève durée et réversibles. La seule étude de suivi à long terme (7 ans) qui ait été consacrée à l’action toxique du bore n’a pas permis de mettre en évidence d’effets à long terme, encore que l’on ne puisse pas totalement exclure que ce résultat soit dû à la bonne santé des travailleurs étudiés, compte tenu du taux élevé d’attrition. Deux études descriptives ont porté sur la fécondité et le sex ratio secondaire en rapport avec une exposition. Aucune des deux études n’a révélé d’effet indésirable sur la fécondité observée dans l’échantillon. Il y aurait bien eu un excès de naissances féminines, mais il n’était pas statistiquement significatif et le fait qu’il existait d’autres facteurs connus pour influer sur le sex ratio incite à une interprétation prudente de ce résultat. On n’a pas retrouvé d’études portant sur l’ensemble des paramètres de la reproduction, par exemple le temps écoulé jusqu’à la grossesse, les retards dans la conception, les avortements spontanés et le comportement des spermatozoïdes. Il faut étudier plus à fond les autres
styles de vie et facteurs comportementaux dans leurs rapports avec la santé et la fécondité afin de mettre en évidence les populations potentiellement sensibles et évaluer dans le détail les effets sur la reproduction.

1.5 **Effets sur les êtres vivants dans leur milieu naturel**

Les bactéries ont une tolérance au bore relativement élevée. Les concentrations produisant des effets aigus ou chroniques vont de 8 à 340 mg de bore par litre, la plupart des valeurs se situant autour de 18 mg/litre. Ce sont les protozoaires qui sont les plus sensibles. Les épreuves effectuées sur des protozoaires du genre *Entosiphon* et *Paramecium* ont donné, pour la concentration sans effet observable sur 72 h (NOEC) et pour la CE₃, des valeurs comprises entre 0,3 et 18 mg de bore par litre.

Le bore est un micronutriments essentiel des cyanobactéries et des diatomées. Les épreuves habituelles pour l’évaluation de la toxicité chronique, ont donné une concentration sans effet observable comprise entre 10 et 24 mg de bore par litre pour les algues vertes dulçaquicoles. Les algues bleues ont une sensibilité analogue, avec une CE₃ à 8 jours de 20 mg de B par litre.

Si l’on se base sur les valeurs de la toxicité aiguë, les invertébrés sont moins sensibles au bore que les microorganismes. Pour un certain nombre d’espèces, les valeurs de la CE₅₀ à 24 et 48 h allaient de 95 à 1376 g de B par litre, la plupart des valeurs se situant dans l’intervalle 100–200 mg/litre. Les études de toxicité chronique effectuées sur *Daphnia magna* ont donné une NOEC allant de 6 à 10 mg de B par litre. Des valeurs un peu plus faibles ont été obtenues lors d’études en laboratoire ou dans des biocénoses naturelles. Une étude de 28 jours en laboratoire comportant six stades trophiques a donné une NOEC de 2,5 mg de B par litre. Des études à long terme sur des étangs et autres études en milieu naturel (à l’exclusion des poissons) ont donné des NOEC allant jusqu’à 1,52 mg de B par litre.

Des épreuves de toxicité aiguë portant sur plusieurs espèces de poissons ont donné des valeurs comprises entre 10 et près de 300 mg de B par litre. Ce sont des espèces telles que la truite arc-en-ciel
(Oncorhynchus mykiss) et Brachydanio rerio qui se sont révélées les plus sensibles, avec des valeurs d’environ 10 mg de B par litre.

La toxicité du bore pour les stades juvéniles des poissons est attestée par des études effectuées en eau reconstituée sur plusieurs espèces. C’est ainsi que l’on a exposé à du bore (acide borique ou borax) les embryons et les premiers stades larvaires de truites arc-en-ciel, de certaines perches (Micropterus salmoides), de poissons-chats (Ictalurus punctatus) et de poissons rouges (Carassius auratus), depuis le moment de la fécondation jusqu’à 8 jours après l’éclosion en eau douce ou dure. Ni la dureté de l’eau, ni la forme sous laquelle se trouvait le bore n’ont eu d’effets systématiques sur la survie embryo-larvaire des poissons. C’est la truite arc-en-ciel qui s’est révélée l’espèce la plus sensible. Pour ce poisson, la NOEC se situait entre 0,009 et 0,103 mg de B par litre.

L’effet de la dilution naturelle de l’eau sur la toxicité du bore a été déterminé en utilisant des eaux de surface prélevées en trois endroits, avec des concentrations de bore de 0,023, de 0,091 et de 0,75 mg/litre. Aucun effet indésirable n’a été noté jusqu’à la dose de 0,75 mg/litre. Les valeurs de la concentration la plus faible produisant des effets observables (LOEC) allaient de 1,1 à 1,73 mg/litre. L’une des épreuves, effectuée sur de l’eau de puits prélevée à grande profondeur (600 m), utilisée systématiquement pour les essais de toxicité en milieu aquatique et fournie par un laboratoire de Wareham (USA), a donné une NOEC > 18 mg de B par litre. Il semble donc que les épreuves effectuées en eau reconstituée surestiment la toxicité des eaux naturelles, peut-être du fait que les premières sont pauvres en certains nutriments.

On sait depuis les années 20 que le bore est un micronutriments essentiel pour les végétaux supérieurs, la quantité minimale nécessaire à la croissance dépendant de l’espèce. Le bore intervient dans la division cellulaire et le métabolisme ainsi que dans la structure et la fonction de la membrane. Il existe à l’état naturel sous forme de borates dans les fruits, les noix et les légumes. Chez les plantes, l’intervalle entre carence et fixation excessive (toxicité) est étroit. Dans de nombreux pays, on a constaté que les plantes présentaient une carence en bore. Cet déficit a plus de chances de se rencontrer dans les
sols acides à texture légère des régions humides, car le bore est facilement lessivé. En revanche, on trouve un excès de bore dans les solutions de sols provenant de dépôts géologiques récents, dans les sols arides, les sols issus de sédiments marins et ceux qui sont contaminés par diverses sources de pollution, comme les émissions des centrales thermiques à charbon et celles qui proviennent des exploitations minières. L'eau d'irrigation est l'une des principales causes des fortes teneurs en bore qui contaminent les terrains agricoles.

On a observé qu'à des doses dans l'alimentation de 30 et 300 mg de bore par kg, des colverts (Anas plathyrynchos) présentaient des troubles et qu'à la dose de 1000 mg/kg leur survie était réduite.

2. Conclusions

Le bore est un élément naturel qui existe à l'état de borates dans les océans, les roches sédimentaires, la houille, le schiste et certains sols. Certaines sources naturelles sont à l'origine de rejets de bore dans l'environnement comme les océans, la vapeur géothermique et l'action des agents climatiques sur les roches sédimentaires riches en argile. Les activités humaines libèrent également du bore dans l'environnement, mais dans une moindre proportion.

Le bore est un micronutriments essentiel des plantes supérieures, la concentration nécessaire à une croissance optimale étant variable suivant les espèces. Pour certaines plantes, il y a une faible marge entre carence et toxicité.

Si l'on compare la concentration environnementale qui ne produit pas d'effet (1 mg/litre) et les teneurs en bore généralement rencontrées dans le milieu, on peut en déduire que le risque d'effets indésirables sur l'écosystème aquatique est faible. Il est possible toutefois que dans certains milieux riches en bore, les teneurs naturelles soient plus élevées. On peut raisonnablement penser qu'en pareil cas, les organismes aquatiques se sont adaptés aux conditions locales.

Chez l'Homme, l'exposition au bore provient principalement de l'alimentation et de l'eau de boisson. On estime que la concentration du bore dans l'eau de boisson est, en moyenne mondiale, de l'ordre de
0,1 à 0,3 mg/litre. Pour la population générale, c’est la nourriture qui apporte le plus de bore. La dose moyenne ingérée avec la nourriture est d’environ 1,2 mg par jour.

Chez l’Homme et l’animal, l’acide borique et les borates sont absorbés au niveau des voies digestives et respiratoires. La résorption dépasse 90% de la dose administrée et on peut s’en rendre compte en mesurant l’excrétion urinaire, qui est rapide, puisqu’elle s’effectue en quelques jours.

L’expérimentation animale montre que sous forme d’acide borique et de borate, le bore a des effets toxiques sur le développement et la reproduction à des concentrations qui sont 100 à 1000 fois supérieures à celles que l’on rencontre dans l’environnement. On ne possède pas suffisamment de données toxicologiques sur l’Homme. On a fixé à 0,4 mg par kg de poids corporel la dose journalière tolérable de bore. Pour tenir compte des divers milieux lors de la fixation de cette dose, il faut connaître l’exposition dans les différents pays.

3. **Recommandations**

a) Les valeurs guides pour l’eau et les aliments doivent être basées sur la dose tolérable indiquée dans le présent document.

b) Dans l’application de la dose tolérable, il faut tenir compte du fait que le bore peut avoir un effet physiologiquement bénéfique pour l’Homme.

c) Dans l’application des normes, on tiendra compte du fait que le bore est essentiel pour certains composants de l’environnement (par exemple, le bore est un micronutriment essentiel pour les plantes supérieures).

d) Les suppléments alimentaires qui dépassent la dose tolérable sont à éviter.
RESUMEN, CONCLUSIONES Y RECOMENDACIONES

1. Resumen

1.1 Identidad, presencia en la naturaleza y métodos analíticos

El boro es un elemento presente en la naturaleza que se encuentra en forma de boratos en los océanos, las rocas sedimentarias, el carbón, el esquisto y algunos suelos. Está ampliamente distribuido en la naturaleza, con concentraciones de alrededor de 10 mg/kg en la corteza terrestre (margen de variación: de 5 mg/kg en los basaltos a 100 mg/kg en los esquistos) y de unos 4,5 mg/litro en el océano.

Los productos y minerales comerciales de borato más importantes son el pentahidrato de bórxax, el bórax, el perborato de sodio, el ácido bórico, la colemmanita y la ulexita. En las bajas concentraciones y el pH casi neutro en que está presente en la mayoría de los fluidos biológicos, la especie predominante es el B(OH)₃ (con algo de B(OH)₄⁻), con independencia de que la fuente de boro sea el ácido bórico o uno de los boratos. Esto se debe a que el ácido bórico es un ácido muy débil (pKₐ 9,15). El perborato de sodio se hidroliza para dar peróxido de hidrógeno y metaborato; por consiguiente, puede mostrar propiedades químicas y toxicológicas algo distintas de las de los otros boratos.

Para el análisis de los bajos niveles de boro presente en las muestras biológicas y del medio ambiente se prefieren los métodos de plasma acoplado por inducción (PAI); los métodos colorimétricos se deben utilizar con cautela.

1.2 Producción, aplicaciones, destino en el medio ambiente y fuentes de exposición

Los depósitos económicos de borato son raros y se encuentran en regiones áridas de Turquía, los Estados Unidos, la Argentina, Chile, Rusia, China y el Perú. La producción mundial total de minerales de
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boro—sobre todo colemanita, ulexita, tincal y kernita—fue de alrededor de 2 750 000 toneladas en 1994. Unas 800 000 toneladas de productos comerciales de borato, expresados como B₂O₃, se fabricaron a partir de minerales del boro.

Las principales aplicaciones finales del borato son la fibra de vidrio de calidad de aislamiento o textil, la lejía para lavar (perborato de sodio), el vidrio de borosilicato, pirorretardantes, fertilizantes y herbicidas agrícolas (como elemento traza) y esmaltes, fritas y vidriados cerámicos, así como innumerables aplicaciones diversas.

El boro entra en el medio ambiente sobre todo mediante la meteorización de las rocas, la volatilización de ácido bórico del agua del mar y la actividad volcánica. También se desprende boro de fuentes antropogénicas en menor medida. Entre las fuentes antropogénicas figuran la quema de productos agrícolas, de basuras y de leña, la producción de energía utilizando carbón y petróleo, la fabricación de productos de vidrio, la utilización de boratos/perboratos en el hogar y en la industria, la extracción/elaboración de borato, la lixiviación de madera/papel tratados y la eliminación de aguas residuales/fangos de alcantarillado. Muchas de estas fuentes son difíciles de cuantificar.

Se producen emisiones a la atmósfera de boratos y de ácido bórico en forma de partículas y de vapor como consecuencia de la volatilización desde el agua del mar, la actividad volcánica y, en menor medida, las operaciones de extracción, la fabricación de vidrio y cerámica, la aplicación de productos químicos agrícolas y las centrales eléctricas de carbón. El boro no está presente en la atmósfera en concentraciones significativas; sin embargo, la cantidad total que hay en ella en cualquier momento es significativa debido al enorme volumen de la atmósfera. Teniendo en cuenta su solubilidad en el agua, no es previsible que los boratos persistan en la atmósfera en una medida significativa.

Se puede incorporar boro al agua libre y a la del suelo mediante procesos de meteorización, y en una medida mucho menor por vertidos antropogénicos, como desagües de aguas residuales. Se supone que las reacciones de adsorción–desorción son el único mecanismo importante que influye en el destino del boro en el agua.
El grado de adsorción de boro depende del pH del agua y de su concentración en la solución.

El boro se adsorbe en las partículas del suelo, dependiendo el grado del tipo de suelo, el pH, la salinidad, el contenido de materia orgánica, el contenido de óxido de hierro y de aluminio, el contenido de hidróxido de hierro y de aluminio y el contenido de arcilla. La adsorción de boro puede variar entre totalmente reversible e irreversible, en función del tipo y de la condición del suelo.

Los iones borato presentes en solución acuosa están básicamente en estado totalmente oxidado. No es probable que ningún proceso aeróbico influya en su especiación y no se han notificado procesos de biotransformación. Por consiguiente, no es probable que haya ninguna diferencia en las especies de boro debida a la biotransformación.

El coeficiente de reparto octano/agua del ácido bórico medido es de 0,175, lo cual indica un potencial de bioacumulación bajo. Los experimentos de laboratorio con organismos acuáticos han confirmado este potencial. Las plantas acumulan boro; sin embargo, la absorción se ve afectada por el pH de la solución del suelo, la temperatura, la intensidad de la luz y la concentración de otros elementos (por ejemplo, calcio y potasio). Los estudios de la acumulación de boro en plantas, insectos y peces han puesto de manifiesto que el boro se bioacumula en las plantas, pero no se bioamplifica en la cadena alimentaria de los organismos acuáticos.

El boro está presente en los suelos en concentraciones que van de 10 a 300 mg/kg (promedio de 30 mg/kg), en función del tipo de suelo, la cantidad de materia orgánica y la cantidad de precipitación. Las concentraciones de boro en el agua superficial dependen de factores como la naturaleza geoquímica de la superficie de drenaje, la proximidad a regiones costeras marinas y la incorporación de vertidos de efluentes industriales y urbanos. Las concentraciones de boro en el agua superficial varían ampliamente, desde 0,001 hasta llegar a 360 mg/litro. Sin embargo, las concentraciones medias en las aguas de Europa, el Pakistán, Rusia y Turquía suelen ser inferiores a 0,6 mg/litro. Las concentraciones de boro en el agua del Japón, Sudáfrica y América del Sur están en general por debajo de
0,3 mg/litro. En las aguas de América del Norte son normalmente menores de 0,1 mg/litro, con 0,4 mg/litro o menos en alrededor del 90%.

El boro se acumula en las plantas acuáticas y terrestres, pero no se amplifica a través de la cadena alimentaria. Se ha comprobado que las concentraciones de boro oscilan entre 26 y 382 mg/kg en las plantas acuáticas de agua dulce sumergidas, entre 11,3 y 57 mg/kg en la vegetación de agua dulce que crece fuera del agua y entre 2,3 y 94,7 mg/kg de peso seco en las plantas terrestres. Tomando como base el peso fresco, las concentraciones de boro en los invertebrados y los peces marinos son semejantes a los niveles presentes en los medios de exposición, entre 0,5 y 4 mg/kg. Para dos especies de peces de agua dulce se observó un factor de bioconcentración de 0,3.

Las concentraciones de boro en el aire del medio ambiente oscilan entre <0,5 y alrededor de 80 ng/m³, con un promedio en todos los continentes de 20 ng/m³.

La estrecha semejanza entre las concentraciones de boro en el agua frágil, el agua dulce superficial y el agua potable indica que el boro no se elimina en el tratamiento del agua frágil y del agua dulce superficial utilizadas para beber.

Se supone que la ingesta de boro por el ser humano es de 0,44 µg/día a partir del medio ambiente, de 0,2–0,6 mg/día con el agua de beber y de 1,2 mg/día en la alimentación. Se considera que la ingesta media de boro a partir del suelo es de 0,5 µg/día. Una estimación razonable de la exposición al boro en los productos de consumo es de 0,1 mg/día.

1.3 Cinética y vigilancia biológica

La farmacocinética del boro parece ser bastante parecida en todas las especies en los siguientes aspectos:

a) La absorción de boratos es básicamente completa (alrededor del 95% en el ser humano y en ratas), y tras la ingestión aparece con
rapidez boro en la sangre y los tejidos corporales de varias especies de mamíferos.

b) La distribución del boro en los mamíferos parece producirse por difusión pasiva en todos los líquidos del cuerpo. Al contrario que los tejidos blandos y la sangre, los huesos muestran una absorción selectiva de boro (>4 veces mayor que en el suero) y tiempos de retención considerablemente más largos.

c) El metabolismo del ácido bórico es termodinámicamente desfavorable en los sistemas biológicos. Por consiguiente, se supone que las especies iónicas en la circulación sistémica son equivalentes en todos los mamíferos. Así se elimina una fuente importante de posible incertidumbre para la extrapolación del riesgo, puesto que no es necesario tener en cuenta diferencias interespecíficas en las rutas enzimáticas y/o las tasas metabólicas.

d) La cinética de la eliminación (especialmente la vía de eliminación y la semivida terminal) también parece ser semejante para el ser humano y para las ratas.

Las semejanzas de los parámetros farmacocinéticos entre el ser humano y las ratas, especie que define la concentración sin efectos adversos observados (NOAEL) para estudios de laboratorio, reducen la incertidumbre en cuanto a la extrapolación entre estas dos especies.

1.4 Efectos en animales de laboratorio y en el ser humano

Los datos relativos a la toxicidad en el desarrollo y reproductiva indican que el efecto crítico en las ratas es el menor peso corporal del feto. La NOAEL para el menor peso corporal del feto es de 9,6 mg de boro/kg de peso corporal al día. La menor concentración con efectos adversos observados (LOAEL), en la que las ratas muestran ligeras (~5%) diferencias en el peso corporal del feto y anomalías en las costillas, es de unos 13 mg de boro/kg de peso corporal al día. A medida que aumenta la dosis, los efectos que se observan (y las dosis a las que se ven) son los siguientes:
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a) nuevos efectos en las costillas y patología testicular en ratas (~25 mg de boro/kg de peso corporal al día);

b) disminución del peso corporal del feto y aumento de las malformaciones cardiovasculares fetales en conejos, y patología testicular grave en ratas (~40 mg de boro/kg de peso corporal al día);

c) atrofia testicular y esterilidad en ratas (~55 mg de boro/kg de peso corporal al día); y

d) reducción del peso corporal del feto en ratones (~80 mg de boro/kg de peso corporal al día).

En los estudios de animales con ratones y ratas no se observaron pruebas de carcinogenicidad del ácido bórico. Debido a la falta de datos humanos y a lo limitado de los obtenidos de animales, el boro no se puede clasificar en cuanto a su carcinogenicidad humana.

Son pocos los estudios que se han realizado en el ser humano de evaluación de los efectos para la salud asociados con la exposición a compuestos de boro. Los datos disponibles indican que la exposición está asociada con efectos irritantes de corta duración en las vías respiratorias superiores, la nasofaringe y los ojos. Sin embargo, parece que esos efectos son breves y reversibles. En el único estudio de seguimiento de larga duración (siete años) no se consiguió identificar ningún efecto prolongado para la salud, aunque no se puede excluir del todo un efecto en trabajadores sanos debido a la tasa de desgaste (47%). En dos estudios descriptivos se evaluó la fecundidad y la razón secundaria de sexos en relación con la exposición. En ninguno de los dos se notificó un efecto perjudicial demostrado en la fecundidad de la muestra seleccionada. Aunque se ha indicado la posibilidad de un porcentaje de nacimientos de hembras superior al normal, la ausencia de significación estadística y la atención a otras covariantes que se saben que influyen en el sexo obliga a una interpretación cauta de este resultado. No se conoce ningún estudio en el que se evalúe el espectro de resultados reproductivos, como el tiempo hasta la gestación, los retrasos en la concepción, los abortos espontáneos y los análisis del esperma en los machos. La función de otros factores relativos al tipo
de vida y al comportamiento en relación con la salud y la fecundidad requiere un ulterior estudio para identificar poblaciones posiblemente sensibles y evaluar los efectos reproductivos de manera más completa.

1.5 **Efectos en los organismos del medio ambiente**

Las bacterias tienen una tolerancia hacia el boro relativamente grande. Las concentraciones con efectos agudos y crónicos oscilan entre 8 y 340 mg de boro/litro, siendo la mayoría de los valores superiores a 18 mg de boro/litro. Los protozoos son más sensibles. En pruebas realizadas con *Entosiphon* y con *Paramecium* se obtuvieron concentraciones sin efectos observados (NOEC) en 72 horas y valores de CE₃ de 0,3 a 18 mg de boro/litro.

El boro es un micronutriente esencial para las cianobacterias y las diatomeas. En pruebas crónicas normales con algas verdes de agua dulce se observaron concentraciones sin efectos comprendidas entre 10 y 24 mg de boro/litro. Las algas verdeazuladas parecen tener una sensibilidad semejante, con una CE₃ en ocho días de 20 mg de boro/litro.

Tomando como base los valores de la toxicidad, los invertebrados son menos sensibles al boro que los microorganismos. Para varias especies, los valores de la CE₅₀ en 24-48 horas oscilaron entre 95 y 1376 mg de boro/litro, con la mayoría de los valores del orden de 100-200 mg de boro/litro. En estudios de toxicidad crónica con *Daphnia magna*, los valores de la NOEC oscilaron entre 6 y 10 mg de boro/litro. Se obtuvieron valores de la NOEC ligeramente más bajos en estudios de biocenosis de laboratorio y de campo. En el estudio de laboratorio de 28 días, consistente en seis etapas tróficas, se obtuvo una NOEC de 2,5 mg de boro/litro. En estudios prolongados realizados en un estanque al aire libre y en el campo (sin incluir peces) las NOEC fueron de hasta 1,52 mg de boro/litro.

En pruebas de toxicidad aguda con varias especies de peces se obtuvieron valores comprendidos entre alrededor de 10 y cerca de 300 mg de boro/litro. La trucha irisada (*Oncorhynchus mykiss*) y *Brachydanio rerio* fueron los más sensibles, con valores aproximados de 10 mg de boro/litro.
La toxicidad del boro en las primeras fases de la vida de los peces está documentada para varias especies en agua reconstituida. Se expusieron a boro, en forma de ácido bórico o de bórx, fases embrionarias o larvarias iniciales de trucha irisada, perca atruchada (*Micropterus salmoides*), coto punteado (*Ictalurus punctatus*) y *Carassius auratus* desde la fecundación hasta ocho días después de la eclosión en agua blanda o dura. Ni la dureza del agua ni la forma del boro influyeron de manera uniforme en la supervivencia de los embriones-larvas de los peces. La trucha irisada fue la especie más sensible. Las NOEC para la trucha irisada oscilaron entre 0,009 y 0,103 mg de boro/litro.

El efecto de la dilución natural en el agua sobre la toxicidad del boro se determinó utilizando agua superficial recogida en tres lugares, con concentraciones de boro de 0,023, 0,091 y 0,75 mg/litro. No se detectó ningún efecto adverso hasta los 0,75 mg de boro/litro. Las concentraciones más bajas con efectos observados (LOEC) oscilaron entre 1,1 y 1,73 mg de boro/litro. En una prueba con agua de un pozo profundo (600 m), utilizada habitualmente para pruebas de toxicidad acuática en virtud de un contrato con un laboratorio situado en Wareham, Massachusetts, Estados Unidos, se obtuvo una NOEC de >18,0 mg de boro/litro. Así pues, al parecer en la exposición a agua reconstituida se sobreestimaba la toxicidad determinada en aguas naturales, posiblemente como consecuencia de la deficiencia de nutrientes en la primera.

Desde los años veinte se sabe que el boro es un micronutriente esencial para las plantas superiores, con diferencias interespecíficas en cuanto a las concentraciones necesarias para un crecimiento óptimo. El boro interviene en la división, el metabolismo y la estructura y la función de las membranas de las células. En forma de borato está presente en las frutas, las nueces y las hortalizas. La diferencia entre la deficiencia y la absorción excesiva (toxicidad) es pequeña en las plantas. Se ha notificado deficiencia de boro en plantas terrestres en muchos países. Es más probable que se produzca deficiencia de boro en suelos ácidos de textura ligera en las regiones húmedas, debido a su susceptibilidad a la lixiviación. Suele haber exceso de boro en soluciones del suelo procedentes de depósitos jóvenes desde el punto de vista geológico, en suelos áridos, en los derivados de sedimentos.
marinos y en los afectados por fuentes de contaminación como los vertidos de centrales termoeléctricas de carbón y de operaciones de extracción. El agua de riego es una de las principales fuentes de concentraciones altas de boro que provocan toxicidad en el campo.

El crecimiento del pato real (*Anas platyrhynchos*) se vio afectado negativamente por concentraciones de 30 y 300 mg de boro/kg en los alimentos y con 1000 mg/kg se redujo la supervivencia.

2. Conclusiones

El boro es un elemento que se encuentra presente en la naturaleza en forma de boratos en los océanos, las rocas sedimentarias, el carbón, el esquisto y algunos suelos. Las fuentes naturales de los boratos que se liberan en el medio ambiente son los océanos, el vapor geotérmico y la meteorización natural de las rocas sedimentarias ricas en arcilla. También se desprende boro en menor medida de fuentes antropogénicas.

El boro es un micronutriente esencial para las plantas superiores, con diferencias interespecíficas en cuanto a las concentraciones necesarias para un crecimiento óptimo. Se ha observado deficiencia de boro en plantas terrestres en muchos países de todo el mundo. La diferencia entre la deficiencia y toxicidad es pequeña en algunas plantas.

La comparación de la concentración sin efectos en el medio ambiente (1 mg/litro) con los niveles generales en el medio ambiente indica que el riesgo de efectos adversos del boro en el ecosistema acuático es bajo. Los niveles naturales son más elevados en algunos medios ricos en boro. Es razonable suponer que los organismos acuáticos de dichos hábitats pueden adaptarse a las condiciones locales.

La exposición del ser humano al boro se produce sobre todo por medio de los alimentos y el agua potable. Se consideró que la concentración media mundial de boro en el agua potable estaba comprendida entre 0,1 y 0,3 mg de boro/litro.
Para la población general, la mayor exposición al boro procede de la ingesta oral con los alimentos. La ingesta diaria media de boro con los alimentos es de alrededor de 1,2 mg.

En las personas y en los animales, el ácido bórico y el borato se absorben del tracto gastrointestinal y de las vías respiratorias. Se absorbe más del 90% de las dosis administradas de estos compuestos, como se pone de manifiesto en la excreción en la orina, que es rápida, en unos pocos días.

En experimentos con animales se ha demostrado que el boro en forma de ácido bórico y de borato tiene toxicidad reproductiva y en el desarrollo en concentraciones de 100 a 1000 veces superiores a los niveles normales de exposición. Se carece de datos suficientes acerca de la toxicidad en el ser humano. La ingesta tolerable (IT) de boro se fijó en 0,4 mg/kg de peso corporal al día. La asignación de la IT en diversos medios debe basarse en los datos relativos a la exposición de cada país.

3. **Recomendaciones**

a) Los valores guía del agua y los alimentos deben basarse en la IT proporcionada por este documento.

b) La IT se debe aplicar quedando entendido que el boro puede aportar beneficios fisiológicos para la salud humana.

c) Hay que reconocer al aplicar las normas que el boro es esencial para algunos elementos constituyentes del medio ambiente (por ejemplo, el boro es un micronutriente esencial para las plantas superiores).

d) Se deben evitar los complementos de la alimentación que superen la IT.
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