CHAPTER 4

INFOTOX (Pty) Ltd

2001/000870/07

Retrieval and scientific interpretation of ecotoxicological information

PostNet Suite 112 Private Bag X25723 Monumentpark 0105 SOUTH AFRICA

Tel: 27(12) 346 4668 Fax: 086 513 5478 Cell: 082 416 5864

e-mail: Info@infotox.co.za www.infotox.co.za

Project conducted on behalf of the Fertilizer Association of Southern Africa

Health Risk Assessment and Management of Boron in Fertilizers

Report No 008-2024 Rev 2.0

WCA van Niekerk PhD QEP(USA) Pr Sci Nat (Environmental Science)

MH Fourie PhD MSc Pr Sci Nat (Toxicological Science)

4 June 2024

Copyright Warning

Copyright of all text and other matter in this document, including the manner of presentation, is the exclusive property of INFOTOX (Pty) Ltd. It is a criminal offence to publish this document or any part of the document under a different cover, or to reproduce and/or use, without written consent, any technical procedure and/or technique contained in this document. The intellectual property reflected in the contents resides with INFOTOX (Pty) Ltd and shall not be used for any project or activity that does not involve INFOTOX (Pty) Ltd, without the written consent of INFOTOX (Pty) Ltd.

This report has been prepared by INFOTOX (Pty) Ltd with all reasonable skill, care and diligence within the terms of the Agreement with the Client. The report is confidential to the client and INFOTOX (Pty) Ltd accepts no responsibility of whatsoever nature to third parties whom this report, or any part thereof, is made known. Any such parties rely upon the report at their own risk.



WCA van Niekerk PhD QEP (USA) Pr Sci Nat (Environmental Science)
Managing Director

4 June 2024

Expertise and Declaration of Independence

This report was prepared by INFOTOX (Pty) Ltd ("INFOTOX"). Established in 1991, INFOTOX is a professional scientific company, highly focused in the discipline of ecotoxicological risk assessment. Both occupational and environmental human health risks, as well as risks to ecological receptors, are addressed.

Dr Willie van Niekerk, Managing Director of INFOTOX, has BSc, Hons BSc and MSc degrees from the University of Potchefstroom and a PhD from the University of South Africa. He is a Qualified Environmental Professional (QEP), certified by the Institute of Professional Environmental Practice (IPEP) in the USA (No 07960160), and a registered Professional Natural Scientist (Pr Sci Nat, Environmental Science, No 400284/04). Dr Van Niekerk has specialised in chemical toxicology and human health risk assessments, but he has experience in many other areas in the disciplines of analytical and environmental sciences.

Dr Marlene Fourie has BSc and Hons BSc degrees from the University of Stellenbosch and MSc and PhD degrees from the University of Pretoria. Her field of specialisation is reproductive biology/toxicology. Dr Fourie also has an MSc-degree in epidemiology from the University of Pretoria. Following positions as Medical Natural Scientist at the Andrology Unit, Department of Urology, University of Pretoria and the Pretoria Academic Hospital from 1987 to 2001, she joined INFOTOX as a Medical Biological Scientist. Dr Fourie has conducted many health risk assessments and projects relating to the health status of communities. She is registered as a Professional Natural Scientist (Pr Sci Nat, Toxicological Science, No 400190/14).

Dricky Simpson has a higher diploma in Quality Assurance as well as in Medical Technology. Dricky worked in pathology laboratories and she has done research in human toxicology and pharmacology. She also has experience in animal toxicology and pharmacology. During the last fifteen years as Director of INFOTOX she worked in human health risk assessment for a wide range of industries.

This specialist report was compiled for the Fertilizer Association of Southern Africa. We do hereby declare that we are financially and otherwise independent of the Fertilizer Association of Southern Africa

Signed on behalf of INFOTOX (Pty) Ltd, duly authorised in the capacity of Managing Director:



Willem Christiaan Abraham van Niekerk

4 June 2024

Internal review
Dricky Simpson

Table of Contents

1 Background 1

2 Deployment of this INFOTOX document 1

3 Hazard identification 3
3.1 The need for GHS classification 3
3.2 GHS classification of boric acid 3

4 Regulatory context 3

5 The health risk assessment paradigm 5

6 Scope of the risk assessment 6

7 Fundamentals of toxicology and health risks 8
7.1 Overview 8
7.2 Consideration of routes of human exposure 9

8 Toxicological review for human health risk assessment 10
8.1 Acute toxicity 10
8.2 Carcinogenicity 10
8.3 Developmental and reproductive toxicology 10

9 Generic quantification of boron in fertilized soils 12
9.1 Purpose of this section 12
9.2 Hot-water extraction method 13
9.3 Saturated paste boron extraction method 15
9.4 Boron partitioning 16
9.5 Estimation of boron concentration in groundwater and surface water 17
9.6 The bio-accessible fraction of boron in soil 18

10 Human dietary exposure to boron 18
10.1 Food chain exposure 18
10.2 Boron from supplements 21
10.3 Summary of dietary boron intakes and risk interpretation 22

11 Exposure to boron in drinking water 22

12 Ingestion of boron in house dust and outdoor soil 23

13 Occupational exposures 24

14 Health risk assessment for animals: overview 27

15 Estimated boron concentrations in crops and forages 27

16 Health risk assessment for livestock 28
16.1 Introduction 28
16.2 Food ingestion rates and risk assessment 29
16.3 Incidental soil ingestion 30
16.4 Livestock water ingestion rates and risk assessment 31
16.5 Cumulative exposure of livestock 31

17 Wildlife risk assessment 32
17.1 Introduction and selection of wildlife species 32
17.2 Toxicology review 33
17.3 Ingestion of boron from food 34
17.4 Ingestion of boron from water 34
17.5 Cumulative exposure of wildlife 35

18 Avian species 36
18.1 Introduction and selection of avian species 36
18.2 Toxicological review 36
18.3 Food consumption rates 37
18.4 Water ingestion rates 38
18.5 Summary of water and food consumption rates 39
18.6 Bioconcentration factors and boron concentrations in aquatic species 39
18.7 Total boron intake of avian species 39
18.8 Cumulative exposure of avian species 40
19 Ecotoxicity 41
19.1 Scope of the assessment 41
19.2 Screening risk assessment for soil invertebrates 41
19.3 Screening risk assessment for aquatic life 43
19.4 Honey bees 44
20 Level of confidence 45
20.1 Philosophy in selecting exposure parameters 45
20.2 Human dietary exposure to boron 46
20.3 Occupational exposure to boron 46
20.4 Toxicological parameters 46
20.5 Determining boron concentrations in environmental media 46
20.6 Human exposure to boron in drinking water, indoor house dust, and outdoor soil 47
20.7 Exposure assessments for livestock, terrestrial wildlife, and avian species 47
20.8 Ecotoxicity 48
21 Summary of conclusions 48
22 Recommendations 50
23 References 50

List of Tables

Table 8.3.1: Supporting data for deriving human toxicology values for boron. 12
Table 9.2.1: HWS boron levels regarded as deficient and toxic in various countries Brdar-Jokanović (2020). 13
Table 9.2.2: HWS B deficiency, optimal levels, and toxic levels (Brdar-Jokanović (2020) 14
Table 9.2.3: Optimum hot-water-extractable B levels in soil for growth of various crop species (Gupta et al. 1985). 14
Table 9.2.4: HWS B and plant tolerance levels (Hill Labs online). 14
Table 9.2.5: HWS B and tolerance levels (Horneck et al. online). 15
Table 9.2.6: Boron fertilizer recommendations (British Columbia online). 15
Table 9.4.1: Saturated paste B concentrations for selected soil textures at HWS boron at 2 mg/kg 17
Table 9.4.2: Boron in saturated soil paste extracts of South African soils. 17

Table 10.1.1: Boron health risk assessment for food intakes based on NHANES III Phase 1 (1988-1994). 20

Table 10.1.2: Boron health risk assessment for food intakes based on NHANES III Phase 2 (1994-1996). 21

Table 10.2.1: Boron health risk assessment for supplement intakes based on NHANES III Phase 1 (1988-1994). 21

Table 11.1: Drinking water exposure parameters for two life stages. 23

Table 12.1: Soil and house dust exposure parameters for two life stages. 24

Table 13.1: Published studies on reproductive effects in humans. 25

Table 15.1: Bioconcentration factors in annual crops and forage for HWS boron 2 mg/kg. 28

Table 16.2.1: Body weights of livestock species. 29

Table 16.2.2: Food intake rates and dose calculations for livestock. 30

Table 16.3.1: Intake rates of boron from soil for livestock. 30

Table 16.4.1: Intake rates of boron from water for livestock. 31

Table 16.5.1: Cumulative exposure of livestock to boron. 32

Table 17.3.2: Summary of body weights of wildlife species. 34

Table 17.3.3: Food intake rates and dose calculations for wildlife. 34

Table 17.4.1: Intake rates of boron from water for wildlife. 35

Table 17.5.1: Cumulative exposure of wildlife to boron. 35

Table 18.6.1: Boron concentrations in freshwater species. 39

List of Figures

Figure 5.1: The holistic health risk assessment paradigm. 6

Figure 6.1: Diagram of environmental pathways and receptors that were considered in the risk assessment. 7

List of Abbreviations

GHS	Globally Harmonized System of Classification and Labelling of Chemicals
CMR	Carcinogenicity, mutagenicity, and reproductive toxicity
USA	United States of America
EU	European Union
USEPA	United States Environmental Protection Agency
ECHA	European Chemicals Agency
OHASA	Occupational Health and Safety Act
HCA Regulations	Regulations for Hazardous Chemical Agents
OELs	Occupational exposure limits
OMP	Occupational Medicine Practitioner
OHP	Occupational Health Practitioner
ATSDR	US Agency for Toxic Substances and Disease Registry
HHRA	Human health risk assessment
IARC	International Agency for Research on Cancer
IRIS	Integrated Risk Information System
USEPA	United States Environmental Protection Agency
WHO	World Health Organization
AIA	Approved Inspection Authority
SDS	Safety data sheet
NWA	National Water Act
NEMA	National Environmental Management Act
NEM:WA	National Environmental Management: Waste Act
STOT RE	Specific target organ toxicity (repeated exposure)
REACH	Registration, evaluation and authorization of chemicals
ECETOC	European Centre for Ecotoxicology and Toxicology of Chemical's
TRA	Targeted Risk Assessment
NOAELs	No-observed-adverse-effect levels
LOAELs	Lowest-observed-adverse-effect levels
UL	Upper Limit
TDI	Tolerable daily intake
POD	Point of departure
LOC	Level of concern
RfD	Reference dose
RfC	Reference concentration
UF	Uncertainty factors
UFH	Variation in susceptibility among the members of the human population
UFA	Uncertainty in extrapolating animal data to humans
UFC	Uncertainty in extrapolating from data obtained in a study with less-than-lifetime exposure
UFL	Uncertainty in extrapolating from a LOAEL rather than from a NOAEL
UFD	Uncertainty associated with extrapolation when the database is

MOE	Margin of exposure
DHHS	The US Department of Health and Human Services
pKa	pK_a is the negative base-10 logarithm of the acid dissociation constant (K_a) of a solution ($pK_a = -\log_{10}K_a$).
PRO	Pesticide Re-evaluation Division
AD	Antimicrobials Division
OPP	Office of Pesticide Programs of the USEPA
MRIDs	Master Record Identifiers
$BMDL_{05}$	Dose where the change in response is likely to be smaller than 5 per cent
TK	Toxicokinetic
TD	Toxicodynamic
BCFs	Bioconcentration factors
HWS	Hot water soluble
K_d	Distribution coefficient
DF	Dilution factor
NHANES III	The Third National Health and Nutrition Examination Survey
EFH	USEPA Exposure Factors Handbook
HQ	Hazard quotient
ADD	Average daily dose
UL	Upper intake limit (mg/day)
UF	Uncertainty factor
BW	Body weight (kg)
IR	Daily water intake rate (ml/day or litres/day)
CF	Conversion factor
EF	Exposure frequency (days/year)
ED	Exposure duration (days or years)
AT	Averaging time (days)
BCFs	Bioconcentration factors
DWAF	Department Water Affairs and Forestry
FIR	Food intake rate
WIR	Water ingestion rate
E	Exposure
NOECs	No observed effect concentrations
CWQG	Canadian Water Quality Guideline

List of Terms

95th percentile	The value where 95% of all data points will be lower, and 5% of the data points will be higher
Allometric equation	Equations that estimate food and water intake rates from body weights
Atrophy	Decrease in size of a body part, cell, organ, or other tissu
Bio-accessibility	The increase in concentration of a substance in the tissues of organisms at successively higher levels in a food chain
Bioaccumulation	The accumulation of a toxic chemical in the tissue of a particular organism
Biomagnification	Increased concentration of a toxic chemical the higher an animal is on the food chain
Carcinogenicity	Substance that causes cancer
Carnivores	Animals that eat virtually no plants, only meat
Developmental toxicity	Any developmental malformation that is caused by the toxicity of a chemical or pathogen
Epidemiology	Study of the determinants, occurrence, and distribution of health and disease in a defined population
Gestational	Common term used during pregnancy
Haematological	Effects on blood and blood disorder
Herbivorous	Feeding mostly on plants
Insectivorous	Feeding on insects
Mutagenicity	Property of chemical agents to induce genetic mutation
Omnivorous	Feeding on a variety of food of both plant and animal origin
Passerine	Any bird of the order *Passeriformes*, which includes more than half of all bird species
Registrar	Registrar of the Department of Agriculture, Land Reform and Rural Development, responsible for applying Act 36 of 1947
Reproductive toxicity	A substance or agent that can cause adverse effects on the reproductive system
Spermatozoal cells	The male sex cells that carry genetic material.
Spermiation	The process of sperm release

Executive Summary

In a document circulated to "*All Regulatory Holders*" on 14 April 2022, the Registrar of the Department of Agriculture, Land Reform and Rural Development ("Registrar" and "The Department") refers to an assessment that was carried out at the international level to determine risks to human health due to exposure to active ingredients and their formulations that meet the criteria of carcinogenicity, mutagenicity, and reproductive toxicity ("CMR") categories 1A or 1B according to the Globally Harmonized System of Classification and Labelling of Chemicals ("GHS"). The Department then stated that "*the assessment identified the need to reduce risks to human health associated with such products*".

Category 1A covers substances that are known to be CMR, mainly according to human evidence. Category 1B covers substances presumed to be CMR based on data from animal studies.

GHS classification of boric acid CAS # 11113-50-1.

Hazard class and category code	Hazard Statement Code	Hazard statement	Signal word	Pictogram
Repr. 1B	H360FD	May damage the unborn child Suspected of damaging fertility	Danger	 Health Hazard

Category 1B Presumed human reproductive toxicants - largely based on animal studies

- Clear evidence of adverse effects on sexual function and fertility or on development in absence of other toxic effects has been identified; or
- If occurring with other toxic effects, the reproductive toxicity is not considered to be a second non-specific consequence of the other toxic effects.

The Registrar stated his intention to "prohibit the use of ingredients and their formulations that meets (sic) the criteria of CMR categories 1A or 1B of the GHS as from 01 June 2024".

In a letter from the Registrar to FERTASA on 14 August 2023, it is stated that

"The Department position is that in exceptional circumstances, where there is not other fertilizer product(s) for the intended use, the Registrar Act 36 of 1947 may grant registration of an implicated fertilizer product(s)/remedy when the following conditions are met:

a. *The risk to humans, animals, or the environment from exposure to such fertilizer product(s), under realistic worst-case conditions of use, is negligible*"

(and other conditions not relevant to this INFOTOX report).

This INFOTOX report thus deals with health risk assessment for humans, animals, and the environment. This is quite a wide scope required by the Registrar, which is aligned with the general requirements that are set for registration dossiers under Act 36. This INFOTOX report is structured to address all requirements set by the Registrar.

Summary of studies covered in this INFOTOX risk assessment, supporting information, and conclusions

Study	Risk basis	Confidence	Conclusion
Human dietary	NHANES III	95th percentile data RME, conservative	Insignificant risk
Boron supplements	NHANES III	95th percentile data, RME, conservative	Insignificant risk
Drinking water	Childhood exposures	Highest exposed individuals, conservative	Insignificant risk
House dust/outdoor soil	Childhood exposures	Highest exposed individuals, conservative	Insignificant risk
Occupational exposures	Refer to 15 publications, including review articles, 1994 to 2023	High level, credible references	Insignificant evidence of risk to human developmental and reproductive effects
Livestock	Cattle, goats, horses, sheep, pigs. Boron intake from food and water	Intake of highest boron in food, conservative	Insignificant risk
Wildlife	Rats, mice, rabbits. Boron intake from food and water	Intake of highest boron in food, conservative	Insignificant risk
Avian species	Grey heron, great egret, little egret, red-billed teal. Boron intake from food and water	Intake of fish, invertebrates, and aquatic plants. Considered BCFs from boron in water, conservative	Insignificant risk
Soil invertebrates	Refer to 16 publications. Refer to LC25 and EC25	Based on saturated paste boron concentrations, compare to INFOTOX' derived saturated paste value, reasonable estimate	Insignificant risk
Aquatic species	Refer to 22 studies, EC10, IC19, NOEC	Based on surface water concentration 0.09 mg/litre, reasonable estimate	Insignificant risk
Honey bees	Literature studies	High level of confidence	Application of boron fertilizer did not have any impacts on the honeybees.

Abbreviations

NHANES III	The Third National Health and Nutrition Examination Survey in the USA, Phase 1 (1988 to 1991) and Phase 2 (1991 to 1994), 39 695 people
RME	Reasonable maximum exposure
BCF	Bioconcentration factor
LC25	Concentration at which exposure for a specific length of time is expected to cause death in 25% of a defined experimental animal population
EC25	EC25 is a point estimate of the toxicant concentration that would cause an observable adverse effect in 25 percent of the test organisms
EC10	The concentration of a substance in water or sediment that is estimated to produce a 10 % change in the response being measured
IC10	The concentration of a substance in water or sediment that is estimated to produce a 10 % inhibition of the response being measured in test organisms relative to the control response, under specified conditions
NOEC	No observed effect concentration. The highest concentration of a material used in a toxicity test that has no statistically significant adverse effect on the exposed population of test organisms as compared with the controls

Recommendations

A comprehensive risk assessment, as summarised above, confirmed insignificant health risks for the CMR categories associated with boron in fertilizers.

Boron is an essential micronutrient for growth and development of healthy plants in agriculture. Since the early 1920s, the importance of boron has been recognised and it has been applied in fertilizers since that time.

INFOTOX has not identified any health risks to humans, terrestrial animals, avian species, honey bees or ecosystems, due to the use of boron in fertilizers. It is thus not necessary to implement precautionary measures in addition to the normal procedures that are applied in fertilization of plants at farmlands.

There is thus no scientific basis to prohibit or restrict the use of boron in fertilizers because of hazards identified in animals for boron in the CMR categories.

1 Background

In a document circulated to "*All Regulatory Holders*" on 14 April 2022, the Registrar of the Department of Agriculture, Land Reform and Rural Development ("Registrar" and "The Department") refers to an assessment that was carried out at the international level to determine risks to human health due to exposure to active ingredients and their formulations that meet the criteria of carcinogenicity, mutagenicity, and reproductive toxicity ("CMR") categories 1A or 1B according to the Globally Harmonized System of Classification and Labelling of Chemicals ("GHS"). The Department then stated that "*the assessment identified the need to reduce risks to human health associated with such products*".

Category 1A covers substances that are known to be CMR, mainly according to human evidence. Category 1B covers substances presumed to be CMR based on data from animal studies.

The Registrar stated his intention to "prohibit the use of ingredients and their formulations that meets (sic) the criteria of CMR categories 1A or 1B of the GHS as from 01 June 2024".

In a letter from the Registrar to FERTASA on 14 August 2023, it is stated that

"The Department position is that in exceptional circumstances, where there is not other fertilizer product(s) for the intended use, the Registrar Act 36 of 1947 may grant registration of an implicated fertilizer product(s)/remedy when the following conditions are met:

b. *The risk to humans, animals, or the environment from exposure to such fertilizer product(s), under realistic worst-case conditions of use, is negligible*"

(and other conditions not relevant to this INFOTOX report).

This INFOTOX report thus deals with health risk assessment for humans, animals, and the environment. This is quite a wide scope required by the Registrar, which is aligned with the general requirements that are set for registration dossiers under Act 36. This INFOTOX report is structured to address all requirements set by the Registrar.

2 Deployment of this INFOTOX document

This INFOTOX report covers various aspects of the study in logical sections, as outlined below:

Section 1 states the intention of the Department to prohibit the use of ingredients and their formulations that meet the criteria for CMR categories in a notice dated 14 April 2022 ("Notice"). The Notice logically defines the point of departure for this INFOTOX study.

Section 2 outlines the deployment of this report, providing context of each section in the overall presentation.

Section 3 presents the hazard classification of boric acid according to the Globally Harmonized System of Classification and Labelling of Chemicals, indicating that boric acid poses developmental and reproductive hazards.

Section 4 provides an overview of regulatory aspects that govern the production and use of hazardous chemicals in South Africa.

Section 5 describes the health risk assessment paradigm, highlighting that exposure assessment and health risk quantification are essential steps in identifying and managing health risks associated with hazardous chemicals.

Section 6 provides an outline of the scope of this INFOTOX risk assessment.

Section 7 describes fundamental concepts in toxicology and the development of toxicological guidelines for risk assessment.

Section 8 reviews toxicology studies on boron and provides supporting data for deriving human toxicology values for boron.

Section 9 describes analytical methodologies and parameters to estimate boron concentrations in environmental media from published experimental boron fertilization data.

Section 10 summarises survey data on dietary exposure of communities, including exposure to boron from supplements. INFOTOX selected reasonable maximum exposure values for risk assessment.

Section 11 presents the methodology and calculation of the average daily boron dose calculated for the infant/pre-school and young-child life stages based on a groundwater boron concentration of 0.09 mg/litre, derived in Section 9.5.

Section 12 presents the methodology and quantification of exposure to boron in indoor house dust and outdoor soil at farmlands where boron is applied in fertilizers.

Section 13 lists a summary of publications in scientific journals presenting extensive evidence that the reproductive effects of boron observed in test animals have not been confirmed in humans.

Section 14 provides an overview of methodologies for assessing health risks to animals, and introduces the concept of allometric calculations for estimating food and water intake rates based on body weights.

Section 15 describes the use of boron bioconcentration factors ("BCFs") for a range of annual crops and forages, which values were applied in risk assessment of animals due to intake of boron in food.

Section 16 presents health risk assessments for livestock.

Section 17 presents health risk assessments for selected wildlife species.

Section 18 presents health risk assessment for selected avian species.

Section 19 reviews boron risks to soil invertebrates, aquatic life, and honey bees.

Section 20 presents an overview of the level of confidence in the health risk assessments, and provides examples where INFOTOX based exposure calculations on conservative assumptions and selection of reasonable maximum exposure concentrations.

Section 21 summarises conclusions of the INFOTOX evaluations, which form the basis for recommendations.

Section 22 covers a summary of recommendations.

Section 23 lists the scientific literature references that were consulted in compiling this document.

3 Hazard identification

3.1 The need for GHS classification

Internationally, there is a demand for safer chemicals and technologies, and it is appropriate to utilise information in the GHS as a starting point. This INFOTOX report relates specifically to active ingredients and their formulations that meet the criteria of CMR categories 1A or 1B in the GHS. Information in the GHS represents hazard data, not information on risk.

3.2 GHS classification of boric acid

This part summarises the classification of boric acid according to the GHS, as presented under the European Chemicals Agency ("ECHA").

The GHS classification contextualises the basis of the position of the Registrar, and the difference between hazard assessment and health risk assessment.

Table 3.2.1: GHS classification of boric acid CAS # 11113-50-1.

Hazard class and category code	Hazard Statement Code	Hazard statement	Signal word	Pictogram
Repr. 1B	H360FD	May damage the unborn child Suspected of damaging fertility	Danger	 Health Hazard

Category 1B Presumed human reproductive toxicants - largely based on animal studies

- Clear evidence of adverse effects on sexual function and fertility or on development in absence of other toxic effects has been identified; or
- If occurring with other toxic effects, the reproductive toxicity is not considered to be a second non-specific consequence of the other toxic effects.

4 Regulatory context

The overarching obligation of employers in South Africa is to provide and maintain, as far as is reasonably practicable, a working environment that is safe and without risk to employee health (section 8 of the Occupational Health and Safety Act, 85 of 1993 ("OHASA")). The yardstick of *"as far as is reasonably practicable"* is the requirement for the provision and maintenance of systems of work, plant and machinery that are safe and without health risks to health (section 8(2)(a)); eliminating or mitigating health and safety hazards (section 8(2)(b)) and establishing precautionary

measures regarding any substance which is produced, processed, used, handled, stored or transported (section 8(2)(d)).

More specifically, occupational exposure to hazardous substances is controlled in South Africa under the Regulations for Hazardous Chemical Agents, 2021, as governed by the Occupational Health and Safety Act no 85 of 1993, Government Gazette No 44348 of 29 March 2021 ("HCA Regulations"). The Regulations apply to an employer or self-employed person who carries out tasks at a workplace, which may expose any person to the intake of a hazardous chemical substance. The Regulations apply to the chemical production of boron fertilizers and to the handling and application processes.

Note that boron is not prohibited in terms of the Regulations. Prohibited chemical agents are listed in Table 1, Annexure 2 to the Regulations. Instead, boron compounds are listed in Table 3 of the Regulations for non-carcinogens, where they are assigned occupational exposure limits ("OELs").

Each worker must undergo a pre-employment medical examination designed to cover health symptoms relating to the hazardous chemical agents to which a worker may be exposed. Follow-up scheduled medicals may have to be performed, as determined by the appointed Occupational Medicine Practitioner ("OMP"). Medical examinations may be performed by an Occupational Health Practitioner ("OHP").

An exposure assessment (also referred to as an occupational risk assessment) must be performed by an Approved Inspection Authority ("AIA") in accordance with the requirements of the Department of Employment and Labour under the Regulations. If an assessment indicates that an employee may be exposed, the employer is expected to ensure that adequate protection of the employee is provided, and that monitoring is carried out in accordance with the provisions of the Regulations regarding air monitoring, biological monitoring, and medical surveillance.

External exposures may be assessed by sampling and analysing workplace air, and measured values are compared to OELs, listed in the Regulations. Exceedance of OELs would require intervention to reduce exposures, or appropriate personal protective equipment may have to be made available to employees. Physical hazards such as temperature and noise, where relevant, also have to be monitored.

Since South Africa has adopted the GHS, all hazardous substances must be classified according to the GHS, and safety data sheets ("SDSs") prepared to assist in managing exposure to hazardous substances and potential occupational risks.

Pollution of the environment by hazardous chemicals and human exposure to that pollution is regulated by the National Water Act, 36 of 1998 ("NWA"); National Environmental Management Act, 107 of 1998 ("NEMA") and the National Environmental Management: Waste Act, 59 of 2008 ("NEM:WA"). These laws govern the incorrect management of boron-containing fertilizers, for example where it is stored or applied without proper controls and spills can occur into sensitive environmental areas such as waterways (in large quantities in a significant spill or in small quantities over a long period of poor operational practices).

The NWA governs the pollution of water; it criminalises an intentional or negligent act or omission which pollutes or is likely to pollute or detrimentally affect a water resource (section 151(1)(i)) and (j)). It also requires landowners and land users to take reasonable measures to prevent pollution of a water resource from occurring, continuing, or recurring (section 19(1)). This is referred to as the "*duty of care*". It also gives competent authorities powers to direct landowners and users to take

measures to prevent pollution from occurring, continuing or recurring (section 19(3)) and to take those measures and recover the costs of implementing them from anyone who fails to comply with the directive adequately or at all (section 19(5)). Standards are also set under regulations for water quality for different uses, such as drinking water.

As in the case of the NWA, NEMA imposes a duty of care on landowners and users to prevent pollution of the environment from occurring, continuing or recurring. Directive and cost recovery powers are also conferred on competent authorities under NEMA. These provisions, collectively, require the manufacturer of a substance that may cause pollution of the environment to take reasonable measures to prevent it from doing so.

NEM:WA regulates contaminated land. It imposes notification and investigation obligations where land is contaminated. Regulations made under NEM:WA impose soil screening threshold values for the remediation of contaminated soil on land intended for different kinds of uses.

The extensive pieces of legislation presented above provide a framework for safe management of chemicals in production facilities, and throughout use of chemicals in the value chain. This also applies to boron in fertilizers.

5 The health risk assessment paradigm

Considering that there are no viable alternative fertilizer options for boron, exposure to boron through the fertilizer value chain should be managed to ensure protection of human health, animals, and the environment.

A significant factor in the Organisation for Economic Co-operation and Development (OECD 2021) guidance document on key considerations for the identification and selection of safer chemical alternatives assessment, deals with the likelihood of exposure (human and ecological). OECD recommended that routes of exposure to a hazardous chemical that are unlikely, based on measured exposure data or physical-chemical properties of the substance of concern, should be excluded from the assessment. More correctly, the statement should refer to pathways of exposure (air, soil, water, and sediment), and routes of exposure (inhalation, ingestion, and dermal contact).

This recommendation of the OECD (2021) takes the assessment a step further from the hazard data of chemicals represented in the GHS, to the level where the potential for exposure of humans and ecological receptors is assessed, and through accounting for the toxicology of a substance or formulation, the level of risk is determined. This is aligned with the observations and recommendations of Karamertzanis et al. (2019).

Karamertzanis et al. (2019) evaluated the impact on classifications of carcinogenicity, mutagenicity, reproductive and specific target organ toxicity after repeated exposure in the first ten years of implementation of the REACH[1] regulation. The authors highlighted that classification for carcinogenicity, mutagenicity, reproductive toxicity, and specific target organ toxicity (repeated exposure) ("STOT RE") triggers several obligations for manufacturers, importers, and professional users.

[1] Registration, evaluation and authorization of chemicals.

Karamertzanis et al. (2019) then stated:

"In addition to such consequences under other legislations (sic), registrants are required to carry out exposure assessment and risk characterisation for substances that are classified and, hence, classification under REACH is a trigger for risk assessment for human health."

OECD (2021) refers to the European Centre for Ecotoxicology and Toxicology of Chemical's ("ECETOC")[2] Targeted Risk Assessment ("TRA") tool for calculating the risk of exposure from chemicals to workers, consumers, and the environment. This illustrates the logic of basing the final decision about the safety of a chemical or formulation on health risk assessment, rather than only on hazard identification, as represented in the GHS.

The original paradigm for regulatory human health risk assessment ("HHRA") in the USA was developed by the US National Research Council (NRC 1983). This model has been adopted and refined by the US Environmental Protection Agency ("USEPA") and other international agencies as published under the International Programme on Chemical Safety (IPCS 1999; IPCS 2010), and is widely used for quantitative human health risk assessments.

Figure 5.1 illustrates the health risk assessment paradigm in a simple diagram.

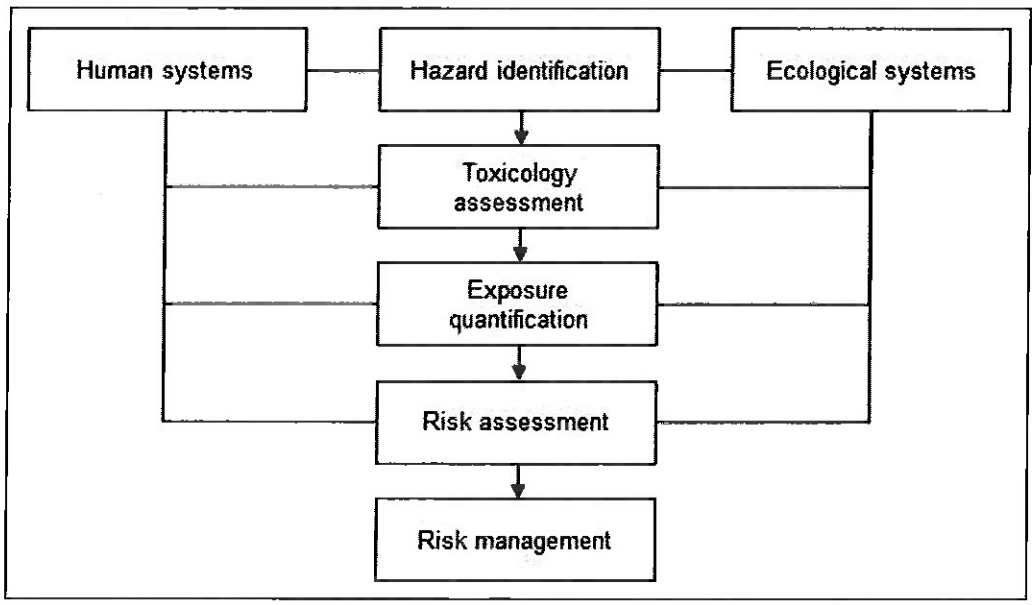

Figure 5.1: The holistic health risk assessment paradigm.

It is shown in this INFOTOX report that exposure assessment and health risk quantification are essential steps in managing health risks associated with hazardous chemicals.

6 Scope of the risk assessment

INFOTOX covered the risk assessment for pathways and receptors illustrated at a high level in Figure 6.1. The diagram does not show all receptor species, and provides only a broad overview of the assessment of exposure to boron through contact with environmental media. Detail is presented in relevant sections in the report.

[2] http://www.ecetoc.org/tools/targeted-risk-assessment-tra/.

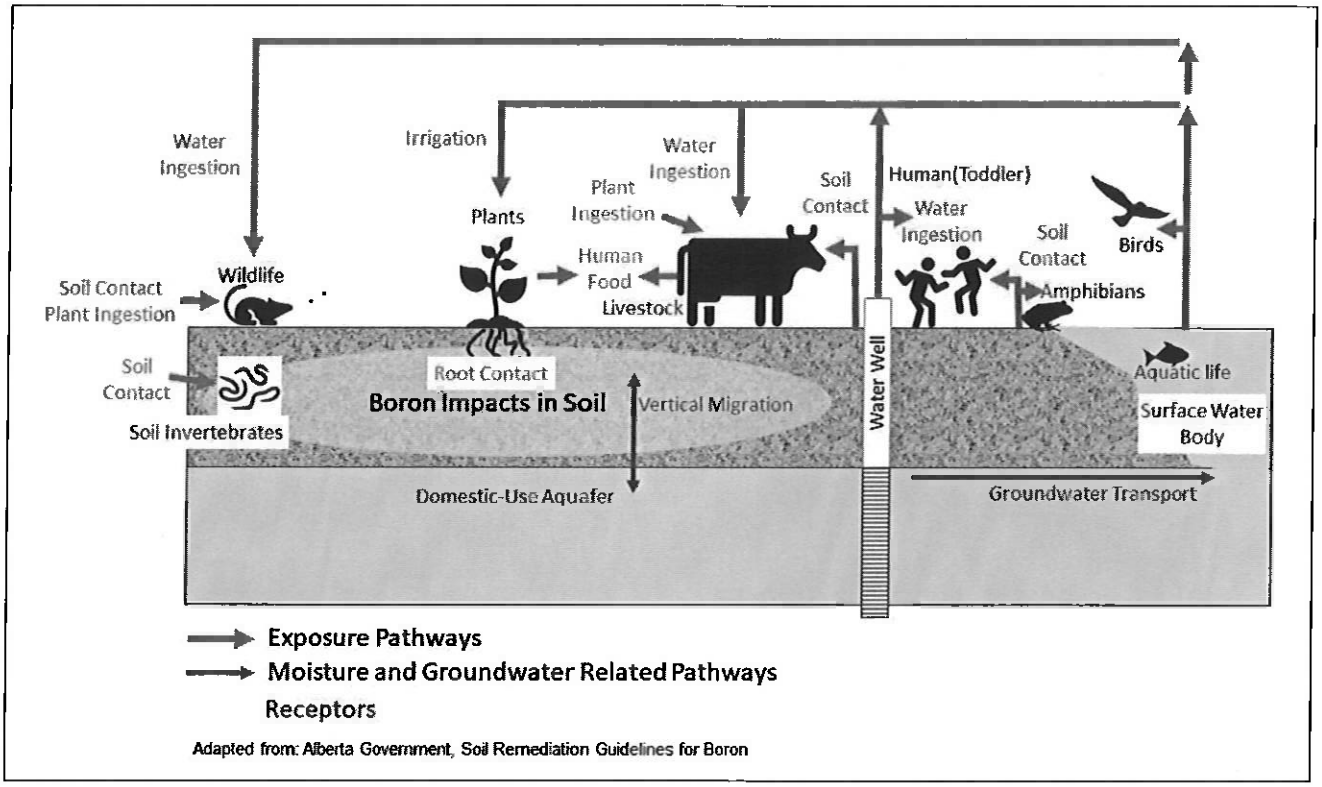

Figure 6.1: **Diagram of environmental pathways and receptors that were considered in the risk assessment.**

The following terms are relevant in the multi-pathway health risk assessment:

- Bioaccumulation refers to the accumulation of a toxic chemical in the tissue of a particular organism from all the sources (including water, air, and solid phases – food, soil, sediment, etc.). It is measured in laboratory (model ecosystem) experiments, or estimated from field studies.

- Biomagnification refers to the increased concentration of a toxic chemical the higher an animal is on the food chain.

Boron accumulates in aquatic and terrestrial plants, but it does not increase in concentration through the food-chain, i.e., it does not biomagnify along the food chain (EHC 1998).

7 Fundamentals of toxicology and health risks

7.1 Overview

Health risk assessors generally use decreased foetal weight (developmental effect) as an appropriate critical effect for assessment of exposure to boron. This is summarised in the USEPA Integrated Risk Information System (IRIS 2004), based on rat dietary gestational exposure to boric acid.

Toxicity data are expressed as no-observed-adverse-effect levels ("NOAELs") and lowest-observed-adverse-effect levels ("LOAELs") in the derivation of an oral reference dose for boron. Considering that the current INFOTOX study should deal with reproductive effects in humans, INFOTOX reviewed published scientific reports on reproductive effects to determine NOAELs and LOAELs for reproductive toxicity of boron. These studies are based on observations in laboratory test animals. Study designs were considered, e.g., acute, sub-chronic or chronic exposures, to determine appropriate uncertainty factors in deriving the tolerable upper limit of exposure ("UL").

The UL of exposure is the highest level of daily intake of a substance that is likely to pose no risk of adverse health effects for almost all individuals in the general population. As intake increases above the UL, the potential risk of adverse effects may increase (NAP 1998). The term tolerable daily intake ("TDI") may be preferred to avoid implying a possible beneficial effect. Instead, the term is intended to indicate a level of intake that can, with high probability, be tolerated biologically.

Uncertainty factors are applied to extrapolate from LOAELs to NOAELs, and to account for intraspecies and interspecies variations, to extrapolate from short-term studies to chronic exposures, and for limitations in the toxicological database. A NOAEL is used as a point of departure ("POD"), and through application of an overall uncertainty factor, a tolerable UL of exposure is derived. This is conceptually similar to the USEPA level of concern ("LOC") that is applied in health risk assessment of hazardous substances.

The USEPA chronic oral reference dose ("RfD") is "an estimate (with uncertainty spanning perhaps an order of magnitude) of a daily oral exposure for a chronic duration (up to a lifetime) to the human population (including sensitive subgroups) that is likely to be without an appreciable risk of deleterious effects during a lifetime. It can be derived from a NOAEL, LOAEL, or benchmark dose, with uncertainty factors generally applied to reflect limitations of the data used. Generally used in EPA's noncancer health assessments" (IRIS 2022).

The USEPA chronic inhalation reference concentration ("RfC") is "an estimate (with uncertainty spanning perhaps an order of magnitude) of a continuous inhalation exposure for a chronic duration (up to a lifetime) to the human population (including sensitive subgroups) that is likely to be without an appreciable risk of deleterious effects during a lifetime. It can be derived from a NOAEL, LOAEL, or benchmark concentration, with uncertainty factors generally applied to reflect limitations of the data used. Generally used in EPA's noncancer health assessments".

Uncertainty factors ("UFs") are used in non-cancer risk assessment when insufficient data are available to support the use of chemical-specific and species-specific extrapolation factors (IRIS 2022). These are, generally 10-fold, default factors used in operationally deriving the RfD and RfC from experimental data. The factors are intended to account for:

- Variation in susceptibility among the members of the human population (i.e., inter-individual or intraspecies variability) ("UFH")
- Uncertainty in extrapolating animal data to humans (i.e., interspecies uncertainty) ("UFA")
- Uncertainty in extrapolating from data obtained in a study with less-than-lifetime exposure (i.e., extrapolating from subchronic to chronic exposure) ("UFC")
- Uncertainty in extrapolating from a LOAEL rather than from a NOAEL ("UFL")
- Uncertainty associated with extrapolation when the database is incomplete ("UFD").

In accordance with USEPA science policy, if two uncertainty factors are applied (e.g., UFA and UFH), each uncertainty is given a value of 10, resulting in a total uncertainty factor of 100. Where uncertainty factors other than 10 are applied (e.g., 3), or where more than 2 uncertainty factors are applied, the overall UF is determined by the product of all UFs.

USEPA also applied the concept of margin of exposure ("MOE") in the health risk assessment. The MOE is the ratio calculated by determining a level of exposure at which harm to human health is not expected to occur, divided by an estimated level of human exposure. The point of departure ("POD") generally is a NOAEL. The LOC is derived by applying uncertainty factors to the NOAEL. The LOC for oral exposure can also be expressed as a RfD.

Although not a primary objective of the study, INFOTOX also reviewed scientific publications that evaluated the validity of extrapolations from reproductive effects in animals to humans. It is important to assess the weight of evidence for exposure to boron as causal in the manifestation of reproductive effects in humans, as this will contextualise the validity of regulatory and public concerns about this matter.

7.2 Consideration of routes of human exposure

The primary health effects associated with dermal exposure to boron and its salts are irritation of the eyes and reversible skin changes (ATSDR 2010). Dermal contact with soil that contains boron is not a significant route of exposure.

Data are inadequate to support derivation of an inhalation RfC for boron, because the available scientific publications do not include a well-conducted study that adequately evaluated the respiratory tract, and no NOAEL or LOAEL for inhalation could be established (IRIS 2004).

No developmental effects were observed in animals following inhalation exposures. (ATSDR 2010).

Studies of health effects in animals exposed by inhalation to boron compounds for chronic durations are not available.

Health risk assessment for exposure to boron is thus focused on ingestion (oral exposure).

8 Toxicological review for human health risk assessment

8.1 Acute toxicity

Acute-duration oral exposures of humans to high levels of boron (as boric acid) have resulted in little or no observable toxicity, as was seen in accidental poisonings of 10-to-88 g, of which 88 per cent of cases were asymptomatic (ATSDR 2010). However, gastrointestinal, cardiovascular, hepatic, renal, and central nervous system effects, dermatitis, erythema, and death have been observed in children and adults exposed to ≥ 84 mg boron/kg (ATSDR 2010).

Most of the available animal studies on the acute toxicity of boron have focused on developmental and reproductive toxicity end points

8.2 Carcinogenicity

The US Department of Health and Human Services ("DHHS"), the International Agency for Research on Cancer ("IARC"), and the USEPA have not classified boron as to its human carcinogenicity (ATSDR 2010). One animal study found no evidence of cancer after lifetime exposure to boric acid in food. No human studies are available.

8.3 Developmental and reproductive toxicology

Inorganic borates, when taken up by a human or animal organism, exist in the body almost exclusively in the form of undissociated boric acid. This is because boric acid is a weak acid (pKa[3] = 9.15), existing in aqueous solutions at or below pH 7 as undissociated boric acid. Therefore, inorganic boron compounds are commonly addressed in the toxicological literature as boron (B) (Bolt et al. 2020).

The Pesticide Re-evaluation Division ("PRO") and the Antimicrobials Division ("AD") of the Office of Pesticide Programs ("OPP") of the USEPA conduct scheduled registration reviews of pesticides. As part of this activity, a human health risk assessment was conducted for boric acid/sodium salts of boric acid (USEPA 2015). The toxicological studies that were considered by USEPA can be applied also for risk assessment of boron in non-pesticide products, such as in fertilizers.

[3] pK_a is the negative base-10 logarithm of the acid dissociation constant (K_a) of a solution ($pK_a = -\log_{10}K_a$).

Incidental oral exposure for subchronic and chronic exposure durations an endpoint was selected by USEPA (2015) from the 90-day and 2-year dog oral studies, considered together to provide the LOAEL and NOAEL for borax (MRID[4] 40692308 and 40692310).

The NOAEL for reproductive effects in dogs is 8.8 mg/kg-day. The UL for boron is calculated by dividing the NOAEL by an UF of 100, giving a value of 0.088 mg/kg. The NOAEL from the 2-year study was selected because it was higher than the NOAEL from the 90-day study (4.1 mg/kg-day) as a result of dose-spacing. The details are presented in Table 8.3.1.

For the purpose of recording health risk information in the Integrated Risk Information System ("IRIS"), the USEPA published a chemical assessment summary for boron and compounds (IRIS 2004). Decreased foetal weight (developmental effect) from a rat dietary gestational exposure to boric acid was used to derive an oral RfD. A $BMDL_{05}$ of 10.3 mg/kg-day was derived by Allen et al. (1996) using combined data from Price et al. (1996) and Heindel et al. (1992). $BMDL_{05}$ is the dose where the change in response is likely to be smaller than 5 per cent. These studies are again referred to in Section 17 that deals with wildlife risk assessment.

The animal-to-human and sensitive-human uncertainty factors ("UFA" and "UFH") were each split into toxicokinetic ("TK") and toxicodynamic ("TD") components to apply existing rat and human toxicokinetic data, leading to an uncertainty factor of 66 (IRIS 2004). The RfD of 0.2 mg/kg-day that applies to developmental effects is listed in Table 8.3.1.

Considering that the GHS is administered in the European Union, it is appropriate to consider toxicological studies considered in documentation of the European Chemicals Agency ("ECHA"). Various animal studies that were consulted confirmed that boric acid adversely effects fertility and development (ECHA 2010). Feeding studies in different animal species (rats, mice and dogs) reported in the scientific literature consistently demonstrated that the male reproductive system is the principal target, although effects on female fertility have also been observed. Effects on fertility occurred at lower dose levels compared to dose levels at which signs of general toxicity appeared. Testicular damage ranging from mildly inhibited spermiation to complete atrophy has been demonstrated following oral administration of boric acid. 17.5 mg/kg-day was derived as a NOAEL for male and female fertility [(Weir and Fisher 1972), cited in ECHA (2008)]. The data are summarised in Table 8.3.1.

The NOAEL for developmental effects in rats was determined as 9.6 mg/kg-day (WHO 1998; ECHA 2010). The Institute of Medicine (2001) applied uncertainty factors of 10x for UFA and 3x for UFH. The RfD for boron based on ECHA (2010) is 0.32 mg/kg-day (Table 8.3.1)

It is noted that neither boron-related male reproductive effects, nor developmental effects, have been confirmed in human populations exposed to high boron levels (Bolt et al. 2020).

[4] USEPA uses MRIDs (Master Record Identifiers) to track and manage information submitted to the pesticide program. An MRID is a unique eight-digit number assigned to each study submitted to USEPA. The first six digits are referred to as the 'root' MRID.
https://www.epa.gov/pesticide-registration/study-formatting-and-supplemental-information#establish%20MRID.

Table 8.3.1: Supporting data for deriving human toxicology values for boron.

Exposure scenario	POD mg/kg-day	UF	UL/RfD/TDI mg/kg-day	Critical study
Incidental oral (short-, intermediate-, long-term)	NOAEL = 8.8	UFA= 10x UFH=10x FQPA SF=1x	0.088	Subchronic (90-day) and chronic (2-year) feeding study (borax) – dog. LOAEL (90-day study) = 32 mg/kg-day, based on haematological effect and testicular atrophy MRID 40692308 (1967) MRID 40692310 (1967)
Rat dietary gestational exposure	$BMDL_{05}$: 10.3	66 IRIS 2004	0.2	Rat dietary gestational exposure to boric acid, developmental (IRIS 2004)
Male and female fertility	Male reproductive effects NOAEL =17.5	UFA= 10x UFH=10x FQPA SF=1x	0.17	Multigeneration study of rats (as the most susceptible species) (ECHA 2008; ECHA 2010)
	Developmental effects NOAEL=9.6	UFA= 10x UFH=3x FQPA SF=1x	0.32	

9 Generic quantification of boron in fertilized soils

9.1 Purpose of this section

A key consideration in this INFOTOX study is to estimate boron concentrations in environmental media from published experimental boron fertilization data. No site-specific information across farmlands in South Africa is available, and INFOTOX had to determine generalised best concentration estimates.

Boron is an essential plant micronutrient, but there is a narrow range between soil deficiency and toxicity. Plant species differ considerably in terms of boron requirements, which affects the optimal fertilizer application rates. Boron that is available in soil for uptake into plants depends on the soil texture, soil chemistry, and other nutrients.

Different plants have different bioconcentration factors ("BCFs"), which further complicates the matter. The BCF can be defined as the ratio of chemical concentration in the plant tissue to the concentration in the growth medium.

It has been reported that plants respond primarily to the soil solution boron, irrespective of the amount of boron that is adsorbed to soil (Gupta et al. 1985). However, it is difficult to extract the soil solution from soil at moisture contents within the range available to plants. Therefore, it is common practice to assess boron deficiency or toxicity from various methods of extracted soil boron, as discussed in Sections 9.2 and 9.3 below.

It is not the purpose of this INFOTOX report to conduct an in-depth assessment of mechanisms of boron uptake into plants, but order-of-magnitude tolerance levels of boron in agricultural plants are used to estimate maximum boron levels in soil that are available for plant uptake after fertilizer application. It is also not the purpose to critically review analytical methods in terms of appropriateness for determining boron tolerance levels. The objective has been to estimate a

generic boron concentration in fertilized soil that would serve as a conservative upper value in risk interpretation. Furthermore, a generic estimate of boron in soil pore water at fertilized land must be obtained to calculate groundwater and surface water boron concentrations as pathways for risk assessment. This is the only practical approach that can provide reasonable generic estimates of boron in soil that could be absorbed in the human system following exposure to boron in fertilized soil, and to estimate born levels in groundwater and surface water at fertilized farmlands.

9.2 Hot-water extraction method

The hot-water extraction method for boron in soil was developed originally by Berger and Truog (1939). Boron is extracted into water in a soil:water ratio of 1:2 at 80 °C. Analysis of the extract is conducted spectrophotometrically. The extracted boron is referred to as the hot-water soluble ("HWS") fraction, and is representative of boron that is adsorbed on soil particles and in soil solution (pore water). HWS boron, expressed on a dry soil basis in mg/kg, is a reasonable estimate of boron in soil that is available for uptake into plants.

Boron is an essential plant nutrient, but many crops are also susceptible to boron toxicity. HWS concentrations in soil are used as guidance to assess deficient and toxic boron levels. A conservative upper estimate of HWS boron is estimated and applied for assessing incidental ingestion of boron in house dust and outdoor soil, as described in Section 12.

Brdar-Jokanović (2020) refers to HWS boron concentrations that were considered deficient and toxic in various countries, listed in Table 9.2.1 below. Table 9.2.2 presents optimum hot-water-extractable B levels in soil for growth of various crop species

Table 9.2.1: HWS boron levels regarded as deficient and toxic in various countries Brdar-Jokanović (2020).

HWS B deficient levels		HWS B toxic levels	
Concentration (mg/kg)	**Country**	**Concentration (mg/kg)**	**Country**
0.19	Nepal	0.68	Pakistan
0.25	Zambia	1.02	Hungary
0.27	Nigeria	1.10	Turkey
0.28	Philippines	1.26	Mexico
0.37	Korea	1.51	Iraq
0.39	Sierra Leone		
0.42	India		

Brdar-Jokanović (2020) summarised findings of various authors about HWS boron in soils in relation to boron deficiency, optimal levels, and toxicity. These data are presented in Table 9.2.2.

Table 9.2.2: HWS B deficiency, optimal levels, and toxic levels (Brdar-Jokanović (2020).

Interpretation of HWS B concentrations in soil	HWS B (mg/kg)
Deficient	< 0.5
Low	0.0 0.2
Medium	0.21 - 0.6
Optimal	0.7
High	0.61 – 1.1
Very high	1.2 – 3.0

Optimum HWS boron concentrations for various crop species are listed in Table 9.2.3. (Gupta et al. 1985).

Table 9.2.3: Optimum hot-water-extractable B levels in soil for growth of various crop species (Gupta et al. 1985).

< 0.1	0.1-0.5	> 0.5
HWS B (mg/kg)		
Small grain	Tobacco	Apple
Corn	Tomato	Alfalfa
Soybean	Lettuce	Clovers
Pea and bean	Peach	Beets
Strawberry	Pear	Turnips
Potato	Cherry	Cruciferae
Grass	Olive	Asparagus
Flax	Pecan	Radish
	Cotton	Celery
	Sweet potato	Rutabaga
	Peanut	
	Carrot	
	Onion	

On an order of magnitude basis, HWS boron values can be correlated with tolerance values listed in Tables 9.2.4(Hill Labs online) and 9.2.5 (Horneck online).

Table 9.2.4: HWS B and plant tolerance levels (Hill Labs online).

Tolerance level	HWS B (mg/kg)
Low	< 1
Medium	1 - 2
High	2 - 5
Very high	> 5

Table 9.2.5: HWS B and tolerance levels (Horneck et al. online).

Tolerance level	HWS B (mg/kg)
Very low	< 0.2
Low	0.2-0.5
Medium	0.5-1.0
High	1.0-2.0
Excessive	> 2.0

Useful information is also obtained from boron fertilizing recommendations of British Columbia (online), as listed for example crops in Table 9.2.6. According to the publication, alfalfa and canola can withstand higher soil boron concentrations than clovers. Cereals and grass crops are the most sensitive for injury at high boron levels. Barley has the highest sensitivity to boron, followed by wheat, and then oats. Toxicity symptoms are most pronounced in barley.

Table 9.2.6: Boron fertilizer recommendations (British Columbia online).

HWS boron mg/kg	Boron rating	Grasses, cereals	Alfalfa, canola, clovers
		kg B/ha	
< 0.2	Very low	1	5
0.21 – 0.40	Low	1	4
0.41 – 0.60	Medium	0	3
0.61 – 0.80	Medium	0	3
0.81 – 1.00	High	0	2
> 1.0		0	0

The significance of the information in Table 9.2.6 is that at HWS boron concentrations above 1.0 mg/kg, no fertilization requirements are recommended by British Columbia (online).

HWS boron concentrations in a range of South African soils, unfertilized and fertilized, ranged between 0.02 – 1.0 mg/kg (Personal communication Omnia Nutriology). Only plants that have a relatively high boron tolerance level would not be injured by HWS boron around 2 mg/kg in soil.

The concentration of 2 mg/kg HWS boron was selected as an upper estimate of total sorbed boron in fertilized agricultural soils for the purpose of health risk assessment. This is the boron level at which some plants would be injured, but plants with a higher tolerance level would not be affected. It does not make logical science to select a HWS boron concentration where a high incidence of plant toxicity would be observed.

9.3 Saturated paste boron extraction method

Dissolved boron is determined at soil saturation. This saturated paste boron will depend upon the B desorption characteristics of the soil. The saturated paste boron extraction method involves adding incremental amounts of water to a dried soil sample at ambient air temperature until a semi-fluid saturated paste is obtained. The boron concentration is then measured in the extract using a standard analytical technique such as ICP-MS.

Boron deficiency is more likely assessed in a soil sample using HWS extract method, while the toxicity of B is assessed in the soil-water extract from a saturated soil paste (Alberta Environment and Parks 2016).

The saturated paste boron (mg/litre) is applied in this INFOTOX report as the best estimate for boron in soil pore water in fertilized farmlands, not in relation to assessing boron deficiency in soil. Determination of the saturated paste boron concentration was performed only to estimate a conservative highest boron concentration in soil pore water in fertilized soil that would migrate downwards to an aquifer, for the purpose of calculating groundwater and surface water concentrations of boron at farmlands

9.4 Boron partitioning

Alberta Environment and Parks (2016) evaluated analytical data of soils from various sites in Alberta, Canada. K_d values depend on such factors as soil texture and organic matter, and ranged from 0.9 to 42.8 litre/kg, with an average of 15.5 kg. Based on theoretical background in the scientific literature and interpretation of the available analytical data, Alberta Environment and Parks (2016) established the relationship between the boron distribution coefficient, HWS boron, and saturated paste boron, as described in Equation 9.4.1.

$$K_d = \frac{HWS}{Sat\ Paste} - \frac{Sat\ \%}{100} \qquad (9.4.1)$$

Where:

K_d	Soil/water distribution coefficient (litre/kg)
HWS	Hot-water soluble B (mg/kg)
Sat Paste	Saturated paste extract B (mg/litre)
Sat %	Percentage saturation (60 where K_d is 2.0)

Equation 9.4.1 can be rearranged in Equation 9.4.2 to calculate saturated paste boron concentrations for typical Alberta soils from the HWS boron, K_d values, and the moisture saturation percentage for various soil types.

$$Sat\ Paste = \frac{HWS}{K_d + \frac{Sat\ \%}{100}} \qquad (9.4.2)$$

Table 9.4.1 shows average K_d values and average saturation percentages for selected soil textures (Alberta Environment and Parks 2016) at a HWS boron concentration of 2 mg/kg (the value selected in Section 9.2 for application in this INFOTOX risk assessment). Boron K_d values reported by Janik et al. (2015) were in the range 0.36 to 52 litre/kg over a wide range of soil types, with a median value of 2.15 litre/kg.

Table 9.4.1: Saturated paste B concentrations for selected soil textures at HWS boron at 2 mg/kg.

Soil texture	Average Kd (litre/kg)	Soil saturation fraction	Approximate saturated paste B concentration (mg/litre)
Heavy clay or organic	8.5	3.74	0.16
Fine textured	2.1	0.61	0.74
Coarse textured or silty	0.8	0.34	1.75

Saturated paste boron concentrations for Canadian soils range from 0.05 mg/litre in a peat sample to 5.54 mg/litre in an impacted/polluted mineral soil sample (Alberta Environment and Parks 2016). For some crops, 0.2 mg/litre boron in water is essential, while 1 to 2 mg/litre may be toxic (FAO 2023).

It is reasonable to select an upper estimate of saturated paste boron concentration of 1.75 mg/litre, based on a HWS boron concentration of 2 mg/kg. At this HWS boron concentration only plants with a high tolerance to boron toxicity will not be injured. Note that 1.75 mg/litre is the highest saturated paste concentration derived for soils with different K_d values in Table 9.4.1. It is also higher than the range reported for different soil textures in South Africa, covering unfertilized and fertilized soils (Personal communication Omnia Nutriology), presented in Table 9.4.2.

Table 9.4.2: Boron in saturated soil paste extracts of South African soils.

Soil texture			
Sand	Silt	Clay	Overall range
mg/litre			
0.01 – 0.02	0.02 – 0.11	0.07 – 0.21	0.01 – 0.21

9.5 Estimation of boron concentration in groundwater and surface water

When pore water moves downwards through the soil it will be diluted when it reaches the laterally moving aquifer according to Equation 9.5.1:

$$DF = 1 + \frac{Z \times V}{I \times X} \qquad (9.5.1)$$

Where:

DF	Dilution factor in the aquifer
Z	Mixing depth (m)
V	Darcy velocity (flux) in the aquifer (m/year)
I	Infiltration drainage (m/year)
X	Length of contaminated soil

Chemical attenuation is assumed to be 1, and DFs of between 10 and 30 are commonly applied in South Africa (DEA 2010). The risk assessment is not site specific, and a typical DF of 20 is assumed for generic application. **This would lead to a typical groundwater boron concentration of 0.0875 (rounded to 0.09) mg/litre.** This calculation applied the highest saturated paste solution boron of

1.75 mg/litre for coarse textured or silty soil from Table 9.4.1. It is assumed that there is no attenuation of boron when groundwater feeds into surface water, and there is also no dilution. **The surface water concentration of boron is thus also 0.09 mg/litre.**

Background boron concentrations in groundwater and surface water in boron-deficient areas where fertilization is required are expected to be low and were disregarded in the health risk assessments.

9.6 The bio-accessible fraction of boron in soil

Boron in the HWS extract is representative of boron that is adsorbed on soil particles and in soil solution (pore water). This represents the available fraction of boron which, in human exposure assessment, would represent the bio-accessible fraction. This is the fraction of boron in soil that will be available for uptake into the circulatory system of the human body following incidental oral intake of soil.

This is a reasonable best estimate, because there are no generic data available for bio-accessibility of boron in stomach and intestine fluids for a variety of soil types. Bio-accessibility describes the fraction of a substance in a soil matrix that is available for uptake into the human system.

The largest proportion among all fractions of boron in soil is captured within crystal structures and is not mobile. This residual fraction of boron constitutes about 87 to 99 per cent of total boron (Padbhushan and Kumar 2017). It is expected that boron in mineral phases in soil will not be totally bio-accessible to humans following incidental ingestion of soil and house dust. It is thus considered inappropriate to use boron concentrations in soil determined from total dissolution in strong acid media as the bio-accessible fraction.

Health risk assessment for incidental ingestion of boron in outdoor soil and house dust is discussed in Section 12.

10 Human dietary exposure to boron

10.1 Food chain exposure

Food chain exposure to boron can be modelled from soil boron concentrations and transfer factors into food commodities. There are several difficulties in following this approach. Firstly, there are multiple food commodities with different boron uptake factors, making it difficult to comprehensively estimate food boron concentrations. Secondly, consumption rates of various food commodities are partly available for South Africa, but it can be expected that it would be an immense task to estimate reliable coverage of nation-wide food consumption rates. INFOTOX thus considered an alternative approach.

Extensive data on human consumption rates of boron in food in the USA are available, which should provide an adequately-representative generalised estimate of boron intake from the food chain. The Third National Health and Nutrition Examination Survey ("NHANES III"), was a nationwide probability sample in the USA of 39 695 persons aged 2 months and older. It was conducted from 1988-1994 in two phases, namely, Phase 1 (1988 to 1991) and Phase 2 (1991 to 1994). The NHANES III database represents the largest source of records of dietary reference intake values of substances in food. Data for boron are presented for different sexes and age groups of the population, including pregnant females, and are available for different percentiles of the data distribution. The studies

were coordinated by the Panel on Micronutrients, Subcommittees on Upper Reference Levels of Nutrients and of Interpretation and Uses of Dietary Reference Intakes, and the Standing Committee on the Scientific Evaluation of Dietary Reference Intakes, Food and Nutrition Board, Institute of Medicine. Results of the studies were documented by the National Academy Press (NAP 2000).

The daily intake values can be converted to dose by applying appropriate body weights. INFOTOX used body-weight data for males and females in different age groups from the latest USEPA Exposure Factors Handbook ("EFH"). The latest edition of the EFH was released in 2011 (USEPA 2011), but since October 2017, USEPA has started to release chapter updates individually. The chapter on body weights has not been updated.

The NHANES data are relevant to the matter under consideration, as boron-containing fertilizers had been used widely to supplement boron-deficient soils in the USA and elsewhere at the time of the NHANES study. The data would thus be representative of the current situation where boron-deficient soils are treated through boron fertilizing.

In calculating the UL of exposure to dietary boron, NAP (2000) applied the NOAEL for developmental effects in rats of 9.6 mg/kg-day (see Table 8.3.1). An UF of 30, was applied, resulting in an UL of 0.32 mg/kg-day. Because the dietary intake values of boron in the NHANES III studies were presented as daily intakes in mg/day, the UL in mg/kg-day was converted to mg/day by applying the body weight for an adult woman of 61 kg in Equation 10.1. Using the female body weight for adults gives the lowest UL when multiplying dose with the body weight.

$$UL = \frac{NOAEL}{UF} \times BW \qquad (10.1.1)$$

Where:

UL	Upper intake limit (mg/day)
NOAEL	No-observed-adverse-effect level (mg/kg-day)
UF	Uncertainty factor
BW	Body weight (kg)

INFOTOX refined the calculations by selecting the 95th percentiles of the NHANES III data and converted daily intake rates to doses for the various age groups by applying age-specific body weights from the USEPA EFH (USEPA 2011). Hazard quotients were calculated using Equation 10.1.2.

$$HQ = {}^{Dose}/_{RfD} \qquad (10.1.2)$$

Where:

HQ	Hazard quotient (dimensionless)
Dose	Boron dose (mg/kg-day)
RfD	Reference dose (mg.kg-day)

The RfD for developmental effects of 0.32 mg/kg-day was applied (Table 8.3.1, the same as applied in NAP 2000). Note that the studies reported in NAP (2000) set UL on developmental effects, whereas INFOTOX also considered reproductive effects. The RfD for reproductive effects of 0.088 mg/kg-day was applied (Table 8.3.1).

NAP (2000) concluded on an UL for developmental effects for adults ≥ 19 years as 20 mg/day of boron.

Because the UL was based on adverse developmental effects in animals, and because there were no reports on boron toxicity in lactating females, the UL for pregnant and lactating females was selected the same as that for the nonpregnant and nonlactating females.

No data were reported for infants and young children in the NHANES III Phase 1 (1988-1994) study (Table 10.1.1), but data for these age groups were reported for the NHANES III Phase 2 (1994-1996) study. These values have a low level of confidence. The UL was judged not determinable for infants (NAP 2000), because of insufficient data on adverse effects in this age group, and because of uncertainties about the infant's ability to handle elevated levels of boron.

Table 10.1.1: Boron health risk assessment for food intakes based on NHANES III Phase 1 (1988-1994).

Sex / age category	B intake (mg/day)	BW (kg)	B dose (mg/kg-day)	Developmental HQ	Reproductive HQ
Both sexes, 0 to 6 m	Not provided				
Both sexes, 7 to 12 m	Not provided				
Both sexes, 1 to 3 y	Not provided				
Both sexes, 4 to 8 y	1.45	22.40	0.06	1.44	0.74
M 9 to 13 y	1.59	45.14	0.04	0.93	0.40
M 14 to 18 y	1.93	64.30	0.03	0.36	0.34
M 19 to 30 y	2.25	79.73	0.03	0.18	0.32
M 31 to 50 y	2.34	85.79	0.03	0.10	0.31
M 51 to 70 y	2.32	87.03	0.03	0.09	0.30
M 71+ y	2.20	81.46	0.03	0.08	0.31
F 9 to 13 y	1.40	43.58	0.03	0.09	0.37
F 14 to 18 y	1.36	57.40	0.02	0.09	0.27
F 19 to 30 y	1.61	66.74	0.02	0.10	0.27
F 31 to 50 y	1.95	71.52	0.03	0.10	0.31
F 51 to 70 y	1.85	73.49	0.03	0.08	0.29
F 71+ y	1.66	68.44	0.02	0.07	0.28
Pregnant	2.00	66.70	0.03	0.08	0.34
All Individuals	1.70	70.00	0.02	0.09	0.28
All Indiv 6+ +P	1.70	70.00	0.02	0.08	0.28

Table 10.1.2: Boron health risk assessment for food intakes based on NHANES III Phase 2 (1994-1996).

Sex / Age Category	B intake (mg/day)	BW (kg)	B dose (mg/kg-day)	Developmental HQ	Reproductive HQ
Both sexes, 0 to 6 m	2.95	6.4	0.46	1.44	5.22
Both sexes, 7 to 12 m	2.7	9.1	0.30	0.93	3.37
Both sexes, 1 to 3 y	1.66	14.2	0.12	0.36	1.33
Both sexes, 4 to 8 y	1.29	22.4	0.06	0.18	0.65
M 9 to 13 y	1.43	45.14	0.03	0.10	0.36
M 14 to 18 y	1.79	64.3	0.03	0.09	0.32
M 19 to 30 y	2.05	79.7	0.03	0.08	0.29
M 31 to 50 y	2.42	85.8	0.03	0.09	0.32
M 51 to 70 y	2.52	87.0	0.03	0.09	0.33
M 71+ y	2.53	81.5	0.03	0.10	0.35
F 9 to 13 y	1.35	43.58	0.03	0.10	0.35
F 14 to 18 y	1.4	57.4	0.02	0.08	0.28
F 19 to 30 y	1.54	66.7	0.02	0.07	0.26
F 31 to 50 y	1.83	71.5	0.03	0.08	0.29
F 51 to 70 y	2.13	73.5	0.03	0.09	0.33
F 71+ y	1.86	68.4	0.03	0.08	0.31
F Pregnant	2.06	66.7	0.03	0.10	0.35
F Lactating	2.64	66.7	0.04	0.12	0.45
All Individuals	2.07	70	0.03	0.09	0.34
All Indiv (+P/L)	2.06	70	0.03	0.09	0.33

10.2 Boron from supplements

The NHANES III database also presents intakes of boron supplements for different percentiles of data. INFOTOX converted the daily intake rates to doses by applying body-weight data from the latest USEPA Exposure Factors Handbook.

Doses from intake of boron supplements must be added to the doses from food chain boron intakes.

Table 10.2.1: Boron health risk assessment for supplement intakes based on NHANES III Phase 1 (1988-1994).

Sex / Age Category	B intake (mg/day)	BW (kg)	B dose (mg/kg-day)	Developmental HQ	Reproductive HQ
Both sexes, 1 to 8 y	0.65	20.8	0.031	0.10	0.36
Both sexes, 9 to 18 y	0.47	51.6	0.009	0.03	0.10
M 19+ y	0.41	84.5	0.005	0.02	0.06
F 19+ y	0.47	66.7	0.007	0.02	0.08
Pregnant/lactating	0.15	66.7	0.002	0.01	0.03

Sex / Age Category	B intake (mg/day)	BW (kg)	B dose (mg/kg-day)	Developmental HQ	Reproductive HQ
All individuals	0.47	70	0.007	0.02	0.08
All individuals (+P/L)	0.47	70	0.007	0.02	0.08

10.3 Summary of dietary boron intakes and risk interpretation

Potential health risks associated with dietary exposure to boron are evaluated through interpretations of HQs for developmental and reproductive effects. Referring to Equation 10.1.2, if the boron daily dose through dietary intake exceeds the RfD, resulting in a HQ above 1, there is a potential for health effects to manifest. An HQ of 1 must not be interpreted as a fine dividing line between risk and no risk, as RfDs accommodate uncertainty factors based on limitations in experimental toxicological data, and toxicological values are generally selected to overestimate rather than underestimate risk. INFOTOX applied the low RfD of 0.088 mg/kg-day for interpreting reproductive health risks (Table 8.3.1), but in the same table there is also a RfD 0. 0.17 mg/kg-day, based on other experimental data. In addition to uncertainties in toxicological data for infants and young children, using different values for the RfD suggests that HQs in the range 1.33 to 5.22 should not be of risk concern. Also note that INFOTOX selected the 95th percentiles of the available boron intake data from the NHANES III studies, which is a conservative approach.

Exposure data for boron supplements are given for age categories other than for food intakes, and it is not a simple matter of adding HQs for food and supplements. Nevertheless, by just comparing HQs qualitatively, it is clear the intake of food supplement has very little effect on boron doses from food consumption.

11 Exposure to boron in drinking water

The NHANES III study (NAP 2000) included boron intakes from municipal and bottled water in the USA. Whereas INFOTOX can justify using the food chain and supplement boron intakes from the NHANES III study, there is a more appropriate way to assess health risks to drinking water in the South African context. It should be more conservative in this assessment to model scenarios from an agricultural field where boron-deficient soils were treated for crop growing, and where there is a potential for contamination of a residential borehole from boron in the soil.

Section 9.5 presents assumptions and derivation of a typical groundwater boron concentration of 0.09 mg/litre in areas where boron is applied to agricultural soils.

Although the adult life stage is a major fraction of a lifetime, the highest average daily dose (ADD) is associated with the childhood life stage. The exposures of the infant to pre-school child and the young child are averaged, as shown in Equation 11.1.

$$ADD_c = \left(ADD_{1-ps} + ADD_{yc}\right)/2 \qquad (11.1)$$

Where:

ADD_c	Average daily dose for the childhood life stage 0 to 12 years (mg/kg-day)
$ADD_{i\text{-}ps}$	Average daily dose for the infant and pre-school child 0 to 6 years (mg/kg-day)
ADD_{yc}	Average daily dose for the young child 6 to 12 years (mg/kg-day)

Considering exposures of the infant/pre-school and young-child life stages provides the highest estimates of boron doses from drinking water. This is because intake rates of contaminants per body weight are higher than for adults.

The age-weighted average daily intake rate of drinking water is calculated according to the generalised Equation 11.2.

$$ADD = (C \times IR \times CF \times EF \times ED)/(BW \times AT) \quad (11.2)$$

Where:

ADD	Average daily boron dose (mg/kg-day)
IR	Daily water intake rate (ml/day)
CF	Conversion factor (litre/ml)
EF	Exposure frequency (days/year)
ED	Exposure duration (years)
AT	The averaging time (days)

Exposure parameters are listed in Table 11.1 (USEPA 2019a, where applicable).

Table 11.1: Drinking water exposure parameters for two life stages.

Parameter	Symbol	Unit	Age 0 to <6	Age 6 to <12
Drinking water intake rate	IR	ml/day	368	473
Conversion factor	CF	litre/ml	0.001	0.001
Exposure frequency	EF_f	days/year	350	350
Exposure duration	ED	years	6	6
Body weight	BW	kg	14.3	33.5
Averaging time: period of exposure	AT	days	2 190	2 190

The average daily boron dose calculated for the infant/pre-school and young-child life stages based on a groundwater boron concentration of 0.09 mg/litre is 0.0017 (rounded 0.002 mg/kg-day).

12 Ingestion of boron in house dust and outdoor soil

Although the adult life stage is a major fraction of a lifetime, the highest average daily dose (ADD) is associated with the childhood life stage. The exposures of the infant to pre-school child and the young child are averaged, as shown in Equation 12.1 (as in Equation 11.1).

$$ADD_c = (ADD_{1-ps} + ADD_{yc})/2 \quad (12.1)$$

Where:

ADD_c	Average daily dose for the childhood life stage 0 to 12 years (mg/kg-day)
$ADD_{i\text{-}ps}$	Average daily dose for the infant and pre-school child 0 to 6 years (mg/kg-day)
ADD_{yc}	Average daily dose for the young child 6 to 12 years (mg/kg-day)

The average daily dose for ingestion of boron from house dust and outdoor soil for each life stage is calculated according to the generic Equation 12.2.

$$ADD_O = (C \times IR \times CF \times EF \times ED)/(BW \times AT) \quad (12.2)$$

Where:

ADD_O	Average daily dose (mg/kg-day)
C	Concentration of boron in HWS (mg/kg)
IR	Oral soil intake rate per day (mg/day)
CF	Unit conversion factor for intake rate of soil or house dust per event (10^{-6} kg/mg)
EF	Exposure frequency (days/year)
ED	Exposure duration (6 years)
BW	Body weight (kg)
AT	Averaging time (days = 6 years*365 = 2 190 days)

It is assumed that the infant and pre-school life stage is exposed primarily to indoor house dust, whereas the young child is exposed primarily to outdoor soil. The concentration of boron was conservatively assumed to be the same in indoor house dust and outdoor soil. The HWS boron concentration was assumed to be the bio-accessible fraction of boron, as discussed in Section 9.6. Exposure factors are listed in Table 12.1 (USEPA 2017, where applicable).

Table 12.1: Soil and house dust exposure parameters for two life stages.

Parameter	Symbol	Unit	Age 0 to <6	Age 6 to <12
Soil intake rate	IR_{soil}	mg/day	0	30
House dust intake rate	IR_{dust}	mg/day	38.3	0
Conversion factor	CF	kg/mg	1.0E-06	1.0E-06
Exposure frequency	EF_f	days/year	350	350
Exposure duration	ED	years	6	6
Body weight	BW	kg	14.3	33.5
Averaging time: period of exposure	AT	days	2 190	2 190

The average daily boron dose calculated for the infant/pre-school and young-child life stages based on ingestion of indoor house dust and outdoor soil at a bio-accessible boron concentration of 2 mg/kg is 3.43E-06 mg/kg-day. This is insignificant in relation the boron RfDs for developmental and reproductive health effects. Even at much higher estimates of boron bio-accessibility from soil, health risks would remain insignificant.

13 Occupational exposures

Several human epidemiological studies on boron exposures have been conducted since 1994. The studies that are regarded as significant in the overall assessment of reproductive effects in humans associated with exposure to boron are summarised in Table 13.1.

Table 13.1: Published studies on reproductive effects in humans.

Reference	Study	Comments
Whorton MD et al. 1994	Reproductive effects of sodium borates on male employees: birth rate assessment. US borax production facilities.	Fertility and the sex ratio at birth (ratio of boys to girls) were not affected by boron exposure in the study cohort.
Sayli et al. 1998	An assessment of fertility in boron exposed Turkish subpopulations. Boron-rich areas, high exposure levels, drinking water and occupational exposures.	Based on questionnaire surveys. Boron-mediated effects on stillbirth, spontaneous abortion, having children, and the sex ratio at birth were not observed. Boron-mediated adverse effects on the frequency of infertility were not observed.
Sayli. 1998	An assessment of fertility in boron-exposed Turkish subpopulations. 2. Evidence that boron has no effect on human reproduction. An assessment of fertility in boron exposed Turkish subpopulations. Boron-rich areas, high exposure levels, drinking water and occupational exposures.	Based on questionnaire surveys. Boron-mediated effects on stillbirth, spontaneous abortion, having children, and the sex ratio at birth were not observed. Boron-mediated adverse effects on the frequency of infertility were not observed.
Tuccar et al. 1998	Comparison of infertility rates in communities from boron-rich and boron-poor territories. An assessment of fertility in boron exposed Turkish subpopulations. Boron-rich areas, high exposure levels, drinking water and occupational exposures.	based on questionnaire surveys. Boron-mediated effects on stillbirth, spontaneous abortion, having children, and the sex ratio at birth were not observed. Boron-mediated adverse effects on the frequency of infertility were not observed.
Sayli. 2001	Assessment of fertility and infertility in boron-exposed Turkish subpopulations. 3. Evaluation of fertility among sibs and in "borate families".	Based on questionnaire surveys. Boron-mediated effects on stillbirth, spontaneous abortion, having children, and the sex ratio at birth were not observed. Boron-mediated adverse effects on the frequency of infertility were not observed
Sayli. 2003	Low frequency of fertility among workers in a borate processing facility. An assessment of fertility in boron exposed Turkish subpopulations. Boron-rich areas, high exposure levels, drinking water and occupational exposures.	Boron-mediated adverse effects on the frequency of infertility were not observed
Yazbeck et al. 2005	Health impact evaluation of boron in drinking water: a geographical risk assessment in Northern France. Three groups of municipalities (zones) with different levels of boron in drinking water.	A statistically significant difference in the male-to-female sex ratios and adverse effects on birth and mortality rate (between the three study zones) was not detected.
Chang et al. 2006	Boron workers in China: exploring work and lifestyle factors related to boron exposure. Boron mining and processing units located in Northeast China.	Delayed pregnancies between the B-exposed and comparison groups not confirmed. Difference in the male-to-female birth ratio between the B-exposed and comparison groups not due to boron exposures.

Reference	Study	Comments
Xing et al. 2008.	Biomarkers of environmental and workplace boron exposure. Boron mines or borax/boric acid-producing plants	The total daily boron exposure and the mean boron concentrations in biological fluids (urine, blood, and semen) of boron workers were significantly higher than those of the community and control groups in both sampling periods (2003 and 2004). Deals with biomarkers of exposure, did not report adverse health outcomes. However, the studies were conducted in boron workers in China where other authors did not find reproductive effects.
Duydu et al. 2011	. Reproductive toxicity parameters and biological monitoring in occupationally and environmentally boron-exposed persons in Bandirma, Turkey. Boric acid production plant and related workplaces.	Dose levels of boron associated with developmental and reproductive toxic effects in animals are by far not reachable for humans under conditions of normal handling and use
Başaran et al. 2012	Reproductive toxicity in boron exposed workers in Bandirma, Turkey. Boric acid production plant and related workplaces.	Adverse effects of boron exposure on the reproductive toxicity indicators were not observed.
Robbins et al. 2008	Y:X sperm ratio in boron exposed men. Boron mining and processing units located in Northeast China.	Boron-mediated effects on reproductive outcomes (elective pregnancy termination, spontaneous abortion, stillbirths, and birth defects in offspring) were not observed.
Robbins et al. 2010	Chronic boron exposure and human semen parameters. Boron mining and processing units located in Northeast China.	Boron-mediated effects on reproductive outcomes (elective pregnancy termination, spontaneous abortion, stillbirths, and birth defects in offspring) were not observed.
Duydu and Başaran. 2023.	Effects of boron exposure on human reproduction and development. Current Opinion in Toxicology.	The current epidemiological studies have proven that it will not be possible to reach the critical blood-boron concentrations in humans for the reproductive and developmental effects, especially in daily life.
Duydu et al. 2023	What can we learn from epidemiological studies on chronic boron exposure? Review Article.	Boron-mediated adverse effects on human reproduction and development have not been proved in any of the epidemiology studies that were reviewed

The most useful publications for the purpose of this INFOTOX report are the recent review articles by Duydu and Başaran (2023) and Duydu et al. (2023). The references listed in Table 13.1 are covered in the review articles, but are listed in the table to illustrate the extensive list of studies that confirmed that there is extensive evidence that the reproductive effects of boron observed in test animals have not been confirmed in humans. This does not suggest that the ECHA hazard classification of boron presented in Section 3.2 is incorrect. Considering the explanation about the human health risk assessment paradigm in Section 5, the hazard classification logically should trigger a health risk assessment, as is presented in this INFOTOX report.

14 Health risk assessment for animals: overview

Categories of animals are broadly divided into livestock and wildlife, which are further subdivided as described in Sections 16, 17 and 18 below.

Reptiles and amphibians are not considered, because few data exist with which to assess exposure to these organisms. In addition, because toxicological data are scarce for both classes, evaluation of the significance of exposure estimates is problematic. However, the general exposure estimation procedure developed for mammals and birds would be relevant to reptiles and amphibians (Sample and Suter II 1994).

In the absence of experimental data, water and food consumption values can be estimated from allometric regression models based on metabolic rate. Larger animals have lower metabolic rates than smaller animals, because smaller bodies have higher water and food consumption rates per unit body weight. Because metabolism and body weight are related, body weights may be used to estimate food and water consumption rates (Sample and Suter II 1994).

Allometric equations based on body weights, following regression analysis of large study data points, can be applied to estimate food intakes of different mammals. Allometric equations are also available for estimating food and water intake rates of different avian species.

Considering the wide variety of wildlife species, rats, mice, rabbits and mallards are often used as indicator species in wildlife risk assessment.

15 Estimated boron concentrations in crops and forages

Using HWS boron concentrations, Alberta Environment and Parks (2016) collated bioconcentration factors ("BCFs") of boron for a range of crops and forages in field studies near Armena, Alberta. The BCFs were determined by dividing the analytical vegetation boron by the HWS boron in the soil, both in mg/kg dry basis (Equation 15.1). Crops included corn, three varieties of barley, two varieties of wheat, oats, two varieties of canola, and peas. Forages included silage, hay, and ten varieties of pasture. Similar data are not available for South Africa, and the literature values were adopted as reasonable to apply in the health risk assessment.

$$BCF = \frac{Vegetation\ boron}{HWS\ boron} \qquad (15.1)$$

Where:

BCF	Bioconcentration factor (unitless)
Vegetation boron	Boron concentration in vegetation (mg/kg on dry basis)
HWS boron	Boron in hot water extract (mg/kg on dry basis)

The Alberta Environment and Parks (2016) studies dealt primarily with boron contamination of soils, and the derivation of boron soil remediation guidelines. It is indicated that there is a potential for using boron-tolerant plants with high boron BCFs to remediate (bio-extract) boron by plant uptake. The studies thus included boron-tolerant vegetation. This INFOTOX report does not deal with boron-contaminated soils. Instead, as explained in Section 9.2, an HWS boron concentration of 2 mg/kg in soil was selected as the reasonable maximum concentration that would adjust boron-deficient soils without injuring boron-sensitive plants. It is not possible, and it has not been the purpose of this study, to distinguish between different soil types and multiple crops and forage of animals.

INFOTOX thus used BCFs for a range of crops and forages (Alberta Environment and Parks 2016), and applied Equation 15.1 with HWS boron at 2 mg/kg to calculate typical boron concentrations in crops and forages at fertilized lands. HWS boron of 2 mg/kg is at the upper range of the tolerance level in vegetation (Tables 9.2.1 to 9.2.6). the highest boron concentrations for annual crops and forage were used in calculating boron doses for livestock and wildlife food intakes.

Table 15.1 lists the ranges and median values of boron BCFs in annual crops and forages.

Table 15.1: Bioconcentration factors in annual crops and forage for HWS boron 2 mg/kg.

Vegetation	BCF range	Median BCF	Vegetation B (mg/kg dry) Based on median BCF	Vegetation B (mg/kg dry) Based on BCF range
Annual crops	2.2 - 22	5.4	10.8	4.4 – 44.0
Forage	2.9 – 18.3	6.4	12.8	5.8 – 36.6

Alberta Environment and Parks (2016) also reported BCFs for carrots (root) of approximately 40. This is at the upper end of BCFs that may be applied to calculate boron concentrations in diets for livestock such as pigs, and for certain wildlife species such as rabbits that may eat carrots as preferred food. Using this BCF and HWS boron at 2 mg/kg, the estimated boron concentration in carrots would be 80 mg/kg.

16 Health risk assessment for livestock

16.1 Introduction

The natural grazing diet of cattle consists mainly of grasses, legumes, alfalfa, clover, and hay.

Sheep and goats are also grazers, which means they wander pastures and consume plants like grass, clover, forbs, and legumes. During winter, when grazing is insufficient, livestock are fed on stored hay, barley, corn, and other grains.

Eisler (1990) conducted a comprehensive review of ecological and toxicological aspects of boron in the environment, which covered, among others, environmental chemistry, background concentrations, effects, and recommendations for the protection of living resources. Eisler (1990) recommended that livestock diets should contain more than 0.4 mg B/kg dry weight, but less than

100 mg/kg, and drinking water less than 5 mg/litre. The South African boron target water quality range for no adverse effects in all livestock is 0-to-5 mg/litre (DWAF 1996). In the review conducted by Alberta Environment and Parks (2016), it is indicated that boron concentrations in water much higher than 5 mg/litre can be tolerated by livestock. The limit of 5 mg/litre is thus on the conservative side.

The estimated born concentrations in annual crops and forages, based on HWS boron of 2 mg/kg, fall within the range 0.4 to 100 mg/kg (dry weight) (Table 15.1). When the entire diet for pigs consists of carrots, which is likely to be an overestimate, the highest boron concentration in feed would be 80 mg/kg (dry weight), which is still within the range 0.4 to 100 mg/kg (dry weight). Alberta Environment and Parks (2016) referred to scientific publications where boron concentrations of 150 mg/kg in cattle feeds were considered safe. The limit of 100 mg/kg recommended by Eisler (1990) is thus on the conservative side.

16.2 Food ingestion rates and risk assessment

As outlined in Section 14, allometric equations for food ingestion rates based on body weights, following regression analysis of large study data points, can be applied to estimate food intakes of different mammals. The calculation for food ingestion rates for livestock (placental animals) is presented in Equation 16.2.1.

$$FIR_L = 0.0687 \times BW^{0.822} \qquad (16.2.1)$$

Where:

FIR_L	Food intake rate for livestock (kg/day dry weight)
BW	Body weight (kg live weight)

Body weights for typical livestock species are listed in Table 16.2.1 (Wolfram Research 2016). Food intake rates calculated using Equation 16.2.1 are listed in Table 16.2.2. It is not necessary to convert food from dry weight to wet weight, because the allometric calculations of food intake rates for livestock are expressed on a dry-weight basis, and the bioconcentration factors for uptake of boron in crops and forage are also expressed on a dry-weight basis (Alberta Environment and Parks 2016). The HWS boron concentrations in soils are also for dry weights.

Table 16.2.1: Body weights of livestock species.

Species	Body weight (kg)
Cattle	465
Goats	27.66
Horses	521
Sheep	55.5
Pigs	192

Table 16.2.2: Food intake rates and dose calculations for livestock.

Species	FIR_L	B intake (min)	B intake (max)	Maximum dose
	kg/day (dry weight)	mg/day	mg/day	mg/kg-day
Cattle	10.71	47.10	471.04	1.01
Goats	1.05	4.63	46.30	1.67
Horses	11.75	51.72	517.19	0.99
Sheep	1.87	8.21	82.08	1.48
Pigs	5.17	22.77	227.66	1.19
Pigs (carrots)	5.17	413.92	413.92	2.16

The calculated maximum boron dose for cattle must be compared to the NOAEL of 5.5 mg/kg-day for increased phosphate excretion (Weeth et al. 1982, cited in Alberta Environment and Parks 2016). Although the NOAEL applies only to cattle, it must be noted that the boron doses for all livestock species are below this NOAEL. The assessment should also consider that boron feed concentrations discussed in Section 16.1 are below the upper limit of 100 mg/kg in livestock diets recommended by Eisler (1990), and even lower against the Alberta Environment and Parks (2016) value of 150 mg/kg in cattle feeds that is considered safe.

16.3 Incidental soil ingestion

Livestock eating forage at farmlands also ingest soil from the roots of plants. Studies on ingestion of soil by cattle focused on pasture as the sole or a major source of feed. The significance of soil ingestion relative to ingestion of forage and drinking water in terms of exposure to boron from fertilized soils is not easy to quantify.

For the purpose of this INFOTOX health risk assessment it is not necessary to conduct a precise evaluation of soil ingestion by livestock under all possible conditions. It only requires a general understanding of maximum intakes likely under normal exposure conditions. Fries et al (1982) conducted studies on dairy cattle and estimated an upper estimate on soil intake. It was concluded that 6 per cent of dry feed intake was a reasonable upper estimate to apply in assessing the suitability of contaminated farmland for livestock production. INFOTOX applied this value in calculating boron intake by livestock from incidental ingestion of soil, using the HWS boron level of 2 mg/kg. The results are listed in Table 16.3.1.

Table 16.3.1: Intake rates of boron from soil for livestock.

Species	FIR_L	Soil intake rate	B dose from feed	B dose from soil
	kg/day (dry weight)	kg/day (dry weight)	mg/kg-day	mg/kg-day
Cattle	10.71	0.64	1.01	0.0028
Goats	1.05	0.06	1.67	0.0046
Horses	11.75	0.71	0.99	0.0027
Sheep	1.87	0.11	1.48	0.0040
Pigs	5.17	0.31	1.19	0.0032

The boron dose from intake of soil clearly is insignificant in comparison of the intake from forage.

Even if the availability of boron from soil is a hundred times higher than the HWS fraction of 2 mg/kg, the contribution of intake of boron from soil to health risks is still insignificant.

16.4 Livestock water ingestion rates and risk assessment

Estimated boron concentrations in groundwater and surface water at farmlands where boron-containing fertilizer had been applied would be approximately 0.09 mg/litre (rounded). This concentration is well within the boron target water quality range of 0-to-5 mg/litre for no adverse effects in all livestock is (DWAF 1996). The concentration of 5 mg/litre is the limit value recommended by Eisler (1990) for livestock.

The assessment can be further contextualised by calculating boron doses for the livestock species considered in Section 16.2 from drinking water using the allometric calculation in Equation 16.4.1, and then adding the doses from feeds and drinking water. The estimated boron value of 0.09 mg/litre in groundwater and surface water was used in calculating the boron dose. The results are summarised in Table 16.4.1.

$$WIR_L = 0.099 \times BW^{0.90} \quad (16.4.1)$$

Where:

WIR_L	Water ingestion rate for livestock(litre/day)
BW	Body weight (kg live weight)

Table 16.4.1: Intake rates of boron from water for livestock.

Species	WIR_L	Boron intake rate	Boron dose
	litre/day	mg/day	mg/kg-day
Cattle	24.91	2.24	0.005
Goats	1.96	0.18	0.006
Horses	27.59	2.48	0.005
Sheep	3.68	0.33	0.006
Pigs	11.24	1.01	0.005

16.5 Cumulative exposure of livestock

Cumulative exposure of livestock to boron from feed, soil and water is calculated using Equation 16.5.1. Results are presented in Table 16.5.1.

$$E_j = \sum_{i=1}^{m} \left(\frac{IR_i \times C_{ij}}{BW} \right) \quad (16.5.1)$$

Where:

E_j	Total exposure to contaminant (j) (mg/kg-day) j
m	Total number of ingested media (food, water, soil)
IR_i	Consumption rate for medium i (kg/day or litre/day)
C_{ij}	Concentration of contaminant j in medium i (mg/kg or mg/litre)
BW	Body weight of species (kg)

Table 16.5.1: Cumulative exposure of livestock to boron.

Species	B dose from feed (max)	B dose from soil	B dose from water	Total B dose
	mg/kg-day			
Cattle	1.01	0.0028	0.005	1.021
Goats	1.67	0.0046	0.006	1.685
Horses	0.99	0.0027	0.005	1.000
Sheep	1.48	0.0040	0.006	1.489
Pigs	1.19	0.0032	0.005	1.194
Pigs (carrots)	2.16	0.0032	0.005	2.164

As explained in Section 16.2, the cumulative boron dose for cattle must be compared to the NOAEL of 5.5 mg/kg-day for increased phosphate excretion (Weeth et al. 1982, cited in Alberta Environment and Parks 2016). As discussed previously in Section 16.2, the assessment should also consider the upper limit of 100 mg/kg in livestock diets recommended by Eisler (1990).

It must be pointed out that the highest boron concentration in annual crops (see Section 15, Table 15.1) was used in the intake calculations, which represents the highest potential boron intake from animal feeds. Boron concentrations in forages (silage, hay, and ten varieties of pasture) are lower than in crops.

17 Wildlife risk assessment

17.1 Introduction and selection of wildlife species

As wildlife species move through the environment, they may be exposed to contamination via three routes: oral, dermal, or inhalation. The total exposure experienced by an individual is the sum exposure from all three pathways, when applicable, as presented in Equation 17.1.1 (Sample and Suter II 1994):

$$E_{total} = E_{oral} + E_{dermal} + E_{inhalation} \qquad 17.1.1$$

Where:

E_{total}	Exposure from all routes
E_{oral}	Oral exposure
E_{dermal}	Dermal exposure
$E_{inhalation}$	Inhalation exposure

Dermal exposure is regarded as negligible for birds and mammals (Sample and Suter II 1994).

Due to the wide distribution of wildlife species and a lack of site-specific wildlife information, rats, mice and rabbits were used as indicator species for wildlife risk assessment in this study. INFOTOX did not include omnivores such as foxes, because no data on boron content of small mammals and birds that form part of the omnivores' diet are available. For the scenarios relating to agricultural application of boron in fertilizers, it can be expected that total boron body burdens of small mammals and birds would be low, and would not contribute significantly to the total boron intake of wildlife such as foxes. Furthermore, wild animals roam among and within habitats, and do not get food from the

same source every day. Focusing the wildlife health risk assessment on rats, mice and rabbits feeding from the same hypothetical food sources every day represents a reasonable estimate of risks to wildlife due to boron in agricultural fertilizers. Alberta Environment and Parks (2016) also used these species in the derivation of soil remediation guidelines for boron.

Rats and mice prefer to eat grains, vegetables, fruits, seeds and nuts. INFOTOX applied the highest boron contents of crops, using BCFs reported by Alberta Environment and Parks (2016), and a HWS boron content of 2 mg/kg. The crops included corn, three varieties of barley, two varieties of wheat, oats, two varieties of canola, and peas. The mean boron concentration is 10.8 mg/kg (dry weight). Rabbits are herbivores and would eat forage, crops, and also a proportion of carrots.

The median boron concentration for forage is 12.8 mg/kg (dry weight). Alberta Environment and Parks (2016) also reported BCFs for carrots (root) of approximately 40. This is at the upper end of BCFs that may be applied to calculate boron concentrations in diets for wildlife, and may be applied to an indicator species such as rabbits. Using this BCF and HWS boron at 2 mg/kg, the estimated boron concentration in carrots would be 80 mg/kg.

17.2 Toxicology review

Some of the information in this section was also used in the toxicological review for human health risk assessment (Section 8). In the absence of human epidemiological data, results of toxicological tests on species such as rats and mice are used as the points of departure, and through applying uncertainty factors, as described in Section 7.1, reference doses that apply to humans can be derived. In this section, where the assessment is about health effects of boron in wildlife, the focus is on exposure of the selected wildlife species to boron in food grown at farmlands where boron-containing fertilizers had been applied.

USEPA (IRIS 2004) derived a chronic reference dose (RfD) from rat dietary gestational exposure to boric acid (Heindel et al.1992; Price et al. 1996). A $BMDL_{05}$ of 10.3 mg/kg-day was applied, considering developmental (decreased foetal weights) the critical effect. A $BMDL_{05}$ is the dose where the change in response is likely to be smaller than 5 per cent. The term "likely" is defined by the statistical confidence level, usually 95 per cent confidence. The $BMDL_{05}$ of 10.3 mg/kg-day for boron is very close to the NOAEL of 9.6 mg/kg-day from the Price et al. (1996) study.

Heindel et al. (1994) reported health effects for boric acid exposure in pregnant rats, mice, and rabbits. Time-mated rats or mice were given boric acid in the feed continuously from the morning of gestation day 0 to the morning of gestation day 20 (rats), or gestation day 17 (mice) at doses of 0, 0.1, 0.2, or 0.4 per cent boric acid, or from gestation day 6 through 15 (0.8 per cent dose, rats only). A NOAEL for exposure of mice to boron was derived as 43 mg/kg-day, based on reduced foetal success, body weight, and malformations.

Rabbits were artificially inseminated and given boric acid by gavage (62.5, 125, or 250 mg/kg-day in distilled water) on gestation day 6 through 19. According to Heindel et al. (1994), administration of boric acid by gavage was chosen for the rabbit study because rabbits are erratic eaters. A NOAEL for exposure of rabbits to boron was derived as 22 mg/kg-day, based on reduced foetal success and malformations.

17.3 Ingestion of boron from food

The food ingestion rate calculation for rats and mice is presented in Equation 17.3.1 (Sample and Suter II 1994).

$$FIR_R = 0.0306 \times BW^{0.564} \quad (17.3.1)$$

Where:

FIR_R	Food intake rate for rats and mice (kg/day dry weight)
BW	Body weight (kg live weight)

The food intake rate for rabbits is presented in Equation 17.3.2 (Sample and Suter II 1994).

$$FIR_H = 0.0875 \times BW^{0.727} \quad (17.3.2)$$

Where:

FIR_H	Food intake rate for herbivores (kg/day dry weight)
BW	Body weight (kg live weight)

Body weights of the selected wildlife species are listed in Table 17.3.2 (Alberta Environment and Parks 2016).

Table 17.3.2: Summary of body weights of wildlife species.

Species	Body weight (kg)
Rat	0.24
Mouse	0.028
Rabbit	3.5

Table 17.3.3: Food intake rates and dose calculations for wildlife.

Species	FIR_R	B intake (min)	B intake (max)	Maximum dose
	kg/day (dry weight)	mg/day	mg/day	mg/kg-day
Rat	0.016	0.07	0.71	2.95
Mouse	0.005	0.02	0.21	7.53
	FIR_H	B intake (min)	B intake (max)	Maximum dose
	kg/day (dry weight)	mg/day	mg/day	mg/kg-day
Rabbit (forage)	0.218	1.26	7.96	2.27
Rabbit (carrots)	0.218		17.40	4.97

17.4 Ingestion of boron from water

Water ingestion rate for wildlife (mammals) is calculated according to Equation 17.4.1.

$$WIR_M = 0.099 \times BW^{0.90} \quad (17.4.1)$$

Where:

WIR_M	Water ingestion rate for mammals (litres/day)
BW	Body weight (kg live weight)

This equation is the same as was applied for livestock in Section 16.4.

Table 17.4.1: Intake rates of boron from water for wildlife.

Species	WIR_M	Boron intake rate	Boron dose
	litre/day	mg/day	mg/kg-day
Rat	0.027	0.002	0.010
Mouse	0.004	<0.001	0.013
Rabbit	0.306	0.028	0.008

17.5 Cumulative exposure of wildlife

Similar to the assessment of boron intake from soil for livestock, it was reasonable to assume that intake of boron from soil would be negligible for wildlife.

Cumulative exposure to boron is thus calculated from the intake from food and water, following the simple Equation 16.5.1. Results are summarised in Table 17.5.1.

Table 17.5.1: Cumulative exposure of wildlife to boron.

Species	FIR	WIR	Boron from food	Boron from water	Total boron intake
	kg/day	litre/day	mg/kg-day		
Rat	0.016	0.027	0.72	0.010	0.735
Mouse	0.005	0.004	1.85	0.013	1.861
Rabbit	0.218	0.306	0.80 (from forage)	0.008	0.803
			4.97 (from carrots)	0.008	4.980

As discussed in Section 17.2 above, a $BMDL_{05}$ of 10.3 mg/kg-day for exposure of rats to boron was applied in IRIS (2004), which is very close to the NOAEL of 9.6 mg/kg-day from the Price et al. (1996) study. The total boron intake for rats presented in Table 17.5.1 is thus well below the NOAEL determined in rat feeding studies.

A NOAEL for exposure of mice to boron was derived as 43 mg/kg-day, based on the assessment pf reduced foetal success, body weight, and malformations (Heindel et al. 1994). The NOAEL is much higher than the total boron intake for mice listed in Table 17.5.1.

A NOAEL for exposure of rabbits to boron was derived as 22 mg/kg-day, considering reduced foetal success and malformations (Heindel et al. 1994). This value is much higher than the total intake of boron for rabbits, even when basing the total intake from food on a diet of carrots, which have a high BCF for boron.

18 Avian species

18.1 Introduction and selection of avian species

A passerine is any bird of the order *Passeriformes*, which includes more than half of all bird species (Austin et al. online). Sometimes known as perching birds, passerine species are mainly insectivorous[5], but no data are available for boron uptake by insect species. It is therefore not possible to link boron uptake of passerines from insects to the application of boron-containing fertilizers at farmlands at any level of accuracy.

It was considered more appropriate to select avian species that frequent water as the highest exposed species. INFOTOX selected birds that are regarded as representative of species in South Africa. These are:

- Grey Heron (*Ardea cinerea*),
- Great Egret (*Ardea alba*),
- Little Egret (*Egretta garzetta*), and
- Red-billed Teal (*Anas erythrorhyncha*).

It is assumed that all food intake is from aquatic organisms, in which boron is accumulated from boron in water, considering bioconcentration factors ("BCFs"). BCF is defined as the ratio of the concentration of an element in an aquatic organism or its tissues to that in the surrounding water under equilibrium or steady-state conditions. A summary of BCFs for freshwater aquatic food species is presented in Section 18.6 (Thompson et al. 1972). No distinction is made between boron concentrations in different organs/parts of aquatic organisms.

It is assumed that the selected species consume water only from the surface water source that they frequent. Boron concentrations in surface water were estimated as described in Section 9.5.

18.2 Toxicological review

While methods are available to assess dermal exposure to humans, data required for estimating dermal exposure are generally not available for avian species (Sample et al. 1997). Feathers of birds further reduce the likelihood of significant dermal exposure by limiting the contact of skin with contaminated media. Considering that the focus is on boron in food and water, the inhalation route of exposure is not relevant.

Little data are available on health effects of boron on avian species that could be applied to determine a NOAEL. Data on feeding studies on broiler chickens, and a study on mallard ducklings, were found. These data were applied as best estimates for assessing boron health effects on avian species.

One-day-old broiler chicks ingested feed treated with 2 500 and 5 000 ppm of boric acid for 2 weeks (Dufour et al. 1992). Based on a dose-related feather abnormality, a NOAEL was determined at 20 mg/kg-day. Applying an uncertainty factor of 3 for extrapolation to account for intraspecies sensitivities should be conservative, because there is no documented evidence that chickens are

[5] Eating only insects

more hardened than wild avian species. A NOAEL of 7 mg/kg-day may thus be applied for avian species

Based on two boron feeding studies on chickens using boric acid and borax, respectively, (Rossi et al. 1993), some differences in effects were observed. At feeding rates of 250 mg boron/kg feed, effects were observed in hatchability and damage to spermatozoal cells. Using the average body weight of 3.73 kg and food intake rate of 0.163 kg/day, a NOAEL/LOAEL of 10.9 mg/kg-day was calculated by Alberta Environment and Parks (2016). When comparing these results with the findings of Dufour et al. (1992), on an order of magnitude basis it is reasonable to accept the value of 10.9 mg/kg-day as a NOAEL. Applying an uncertainty factor of 3 for extrapolation to account for intraspecies sensitivities gives an overall NOAEL of 3.6 mg/kg-day.

In a study conducted by Hoffman et al. (1990), day-old mallard (*Anas platyrhynchos*) ducklings received an untreated diet (as controls), and diets containing 100, 400 or 1 600 ppm boron as boric acid. Survival, growth, and food consumption rates were measured for 10 weeks. At termination, blood and tissue samples were collected for biochemical assays and histological examination. A NOAEL was found at 14.6 mg/kg-day. Day-old mallard ducklings should be regarded as sensitive subjects, and application of an uncertainty factor for intraspecies extrapolation is probably not warranted.

18.3 Food consumption rates

Food intake rates for the selected avian species were calculated using allometric calculations developed by Sample and Suter II (1994), the principles of which are summarised in Section 14.

Food consumption rates are calculated using Equation 18.3.1.

$$FIR = 0.0582 \times BW^{0.651} \qquad (18.3.1)$$

Where:

FIR	Food ingestion rate (kg/day dry weight)
BW	Body weight (kg live)

Body weights are summarised in Table 18.3.1.

Table 18.3.1: Average body weights of the avian species.

Avian species	Average body weight (kg live)	Reference
Grey Heron	1.5	Llewellyn online Hancock and Kushlan 1987
Great Egret	1.1	Wild life safari online
Little Egret	0.45	Hancock and Kushlan 1987
Red-billed Teal	0.65	Oiseaux-Birds online.

Note that the calculated food ingestion rates are on a dry weight basis. Food intakes for the selected avian species are in wet state, and conversion of food intake rates from a dry-weight basis to wet weight is calculated according to Equation 18.3.2.

$$FIR_{fresh} = \sum_{1}^{f} \left(P_i \times \frac{FIR_{dry}}{1 - WC_i} \right) \quad (18.3.2)$$

Where:

FIR_{fresh}	Food ingestion rate (kg/day wet weight)
f	Total number of food types in the diet
P_i	Proportion of the i_{th} food type in the diet
FIR_{dry}	Food ingestion rate (kg/day dry weight)
WC_i	Proportion of the water content (by weight) of the i_{th} food type

The water content of fish is listed by Sample and Suter II (1994) as 75 per cent. Sample and Suter II (1994) listed the moisture contents for aqueous invertebrates and plants as 78 and 85 per cent, respectively. The proportions of the food types consumed by the various birds are not known and it is thus not useful to do separate conversions of various foods from a dry-weigh basis to wet weight, in accordance with Equation 18.3.2. If the proportion of water content for all food species is taken at 0.75 (as for fish), the conversion from dry to wet weights will be a reasonable general estimate.

Grey Herons primarily consume fish, but also eat amphibians, crustaceans, small birds, mammals, worms, lizards, and some insects (Birdfact online a). For the purpose of this study, it was assumed that the entire diet consists of fish and invertebrates, a lower trophic aquatic species that have the potential to absorb boron. This is a conservative assumption, ignoring food species that do not have the potential to absorb boron from the surface water. A proportion of 80 per cent fish and 20 per cent invertebrates was assumed.

Due to their biological similarity to herons, egrets' diets are also similar. Egrets primarily eat fish, but also crustaceans, shellfish, insects, and invertebrates of various kinds. Overall, egrets can be considered carnivores, as they consume virtually no plant foods (Birdfact online b). Similar to the Grey Heron, INFOTOX assumed that the entire diet of egrets consists of fish and lower trophic aquatic species that have the potential to absorb boron. This is a conservative assumption, ignoring food species that do not have the potential to absorb boron from the surface water. A proportion of 80 per cent fish and 20 per cent invertebrates was assumed.

Red-billed Teals primarily feed on aquatic plants and invertebrates (Oiseaux-Birds online). A proportion of 80 per cent plants and 20 per cent invertebrates was assumed.

18.4 Water ingestion rates

Water ingestion rates for birds can be calculated using Equation 18.4.1.

$$WIR = 0.059 \times BW^{0.67} \quad (18.4.1)$$

Where:

WIR	Water ingestion rate (litre/day)
BW	Body weight (kg live weight)

18.5 Summary of water and food consumption rates

Table 18.5.1 presents the water and food consumption rates for the avian species, estimated from the equations presented in Sections 18.3 and 18.4.

Table 18.5.1 Summary of water and food consumption rates for the avian species.

Avian species	Water consumption rate (litre/day)	Food consumption rate (kg/day wet)
Grey Heron	0.0774	0.3031
Great Egret	0.0629	0.2477
Little Egret	0.0346	0.1384
Red-billed Teal	0.0442	0.1759

18.6 Bioconcentration factors and boron concentrations in aquatic species

Boron concentrations in aquatic food species were calculated using boron concentrations in surface (freshwater), and applying the respective BCFs. (Thompson et al. 1972). It is assumed that the boron concentrations distribute evenly to all parts of the aquatic species.

Table 18.6.1: Boron concentrations in freshwater species.

Species	BCF (litre/kg)	Boron concentration (mg/kg fresh weight)
Plants	2.2	0.198
Invertebrates	50	4.500
Fish	0.22	0.020

18.7 Total boron intake of avian species

For the Grey Heron and egrets, the total food consumption is the fraction of fish consumed, plus the fraction of other food, namely amphibians and crustacea. The total daily boron intake is the sum of intake of boron) from food and the boron intake from water.

For the Red-billed Teal, the entire food consumption was allocated to the lower trophic level aquatic species.

The total boron intake from food for each of the avian species is calculated using Equation 18.7.1.

$$D_{ft} = \left[\left(C_f \times FIR_t \times F_f\right) + \left(C_i \times FIR_t \times F_i\right) \times \left(C_p \times FIR_t \times F_p\right)\right]/BW \qquad (18.7.1)$$

Where:

Df_t	Total boron dose from food(mg/kg-day)
C_f	Boron concentration in fish (mg/kg wet)
FIRt	Food ingestion rate (kg/day fresh)

F_f	Fish fraction of food
C_i	Boron concentration in invertebrates (mg/kg wet)
F_i	Invertebrate fraction of food
C_p	Boron) concentration in aquatic plants (mg/kg wet)
F_p	Plant fraction of food
BW	Body weight (kg)

The total boron intake from water for each of the avian species is calculated using Equation 18.7.2.

$$D_{wt} = (C_w \times WIR)/BW \quad (18.7.2)$$

Where:

D_{wt}	Total boron dose from drinking water (mg/kg-day)
C_w	Boron concentration in water (mg/litre)
BW	Body weight (kg)

18.8 Cumulative exposure of avian species

Table 18.8.1 lists a summary of boron intakes from food and water.

Table 18.8.1: Summary of boron intake rates from food and water for the avian species.

Avian species	Boron intake rate from food	Boron intake rate from water	Total boron intake rate
	mg/kg-day		
Grey Heron	0.1851	0.0046	0.1897
Great Egret	0.2062	0.0051	0.2114
Little Egret	0.2817	0.0069	0.2886
Red-billed Teal	0.2864	0.0061	0.2925

Total boron doses must be assessed against available NOAELs for exposure of indicator avian species, as discussed in Section 18.2. The NOALS are summarised in Table 18.8.2. The total boron intake rates of the selected avian species are well below the NOAELs.

Table 18.8.2: NOAELs for boron intake rates for test avian species.

Test species	Health effects	NOAEL (mg/kg-day)	Reference
One-day-old broiler chicks	Dose-related feather abnormality	7	Dufour et al. 1992
Two boron feeding studies on chickens	Effects on hatchability and damage to spermatozoal cells	3.6	Rossi et al. 1993
Day-old mallard ducklings	Survival, growth and food consumption rates	14.6	Hoffman et al. 1990

19 Ecotoxicity

19.1 Scope of the assessment

Boron essentiality and toxicity for terrestrial plants are not covered in this INFOTOX risk assessment. This level of detail did not form part of the scope of work. INFOTOX did include estimated boron concentrations in annual crops and forage, for assessing intake rates of boron from food for livestock and wildlife.

The assessment of boron ecotoxicity in this section covers screening risk assessments for soil invertebrates and aquatic species.

19.2 Screening risk assessment for soil invertebrates

Soil invertebrates are crucial in the soil ecosystem. INFOTOX reviewed available data on boron invertebrate toxicity for earthworms, collembola (springtails) and mites of various sub-species as indicator species for soil invertebrates. Results of several studies are available for interpretation, both from spiked boron experiments and from soils where saturated paste boron data were available (Alberta Environment and Parks 2016).

The risk assessment is based on results of published studies based on saturated paste boron exposure concentrations. Toxicity estimates were determined for boron concentrations in the solutions, and must be compared to the saturated paste boron concentrations for selected soil textures at HWS boron at 2 mg/kg (Table 9.4.1). The upper estimate for boron is 1.75 mg/litre, which is lower than any of the concentrations in Table 19.2.1 that were associated with toxic effects in soil invertebrates.

Table 19.2.1: Screening risk assessment for soil invertebrates.

Common name	Species	Test	Duration days	Soil	Measure	Sat paste B mg/litre	Reference
Oribatid mite	*Oppia nitens*	Lethality	28	Artificial	LC25	51.1	Environment Canada 2006-2010
Earthworm	*Eisenia andrei*	Avoidance	2	Field clay loam	EC25	48.4	Environment Canada 2004
Springtail	*Folsomia fimetaria*	Lethality	7-14	Artificial	LC25	36.6	CECOTOX 2005
Oribatid mite	*Oppia intens*	Lethality	28	Loam with 2-7% OM	LC25	30.1	Princz et al. 2010
Earthworm	*Eisenia andrei*	Reproduction	63	Sandy loam	EC25	26.4	Exova 2013
Springtail	*Folsomia fimetaria*	Lethality	7-14	Field clay loam	LC25	25.5	CECOTOX 2005
Springtail	*Proisotoma minuta*	Lethality	21	Artificial	LC25	17.7	Environment Canada 2010-2012
Earthworm	*Dendrodrilus tubidus*	Reproduction	56	Artificial	EC25	13.5	Environment Canada 2008-2010
Oribatid mite	*Oppia nitens*	Reproduction	28	Artificial	EC25	12.0	Environment Canada 2006-2010
Springtail	*Proisotoma minuta*	Reproduction	21	Artificial	EC25	9.4	Environment Canada 2010-2012
Earthworm	*Eisenia andrei*	Reproduction	84	Artificial	EC25	7.5	Ingraldi 2004
Oribatid mite	*Oppia nitens*	Reproduction	28	Artificial	EC25	5.6	Environment Canada 2007
Earthworm	*Eisenia andrei*	Reproduction	63	Sandy loam	EC25	5.4	Exova 2013
Oribatid mite	*Oppia nitens*	Reproduction	28	Loam with 2-7% OM	EC25	5.1	Princz et al. 2010
Springtail	*Folsomia fimetaria*	Reproduction	28	Sandy loam	EC25	4.7	CECOTOX 2005
Springtail	*Folsomia fimetaria*	Reproduction	28	Artificial	EC25	2.4	CECOTOX 2005

LC25	Concentration at which exposure for a specific length of time is expected to cause death in 25% of a defined experimental animal population
EC25	EC25 is a point estimate of the concentration that would cause an observable adverse effect in 25 % of the test organisms

19.3 Screening risk assessment for aquatic life

Boron can be toxic to a variety of freshwater fish, amphibians, plants, algae, and invertebrates. Boron accumulates in both aquatic and terrestrial plants, but it does not appear to be biomagnified through the food chain. No observed effect concentrations ("NOECs") for aquatic invertebrates tend to be in the range of 6-to-10 mg B/litre, while NOECs for fish in natural waters are around 1 mg/litre, although lower values have been recorded in reconstituted water (Howe 1998).

INFOTOX reviewed available published boron toxicity data for freshwater aquatic life. There is no evidence of boron biomagnification in aquatic food chains; however, boron is known to accumulate in microalgae, macrophytes, amphibians and fish (Commonwealth of Australia 2021). It is clear that the factors affecting boron toxicity to aquatic organisms are species-specific and the magnitude of the effects are variable. Table 19.3.1 presents a summary of the aquatic toxicity data published by the Commonwealth of Australia (2021). It is an extensive summary and INFOTOX did not consider it useful to elaborate on the information.

As presented in Section 9.5 of this INFOTOX report, a generic freshwater boron concentration was estimated as 0.09 mg/litre for the purpose of the health risk assessment. As indicated previously, background boron concentrations in groundwater and surface water in boron-deficient areas where fertilization is required are expected to be low and were disregarded in the health risk assessments. The toxicity values in Table 19.3.1 are all higher than the freshwater boron concentration determined by INFOTOX.

Table 19.3.1: Summary of aquatic boron toxicity data (Commonwealth of Australia 2021).

Taxonomic group (phylum)	Species	Life stage	Duration (days)	Toxicity measure (test endpoint)	Toxicity value (mg/litre)
Amphibian (Chordata)	*Anaxyrus fowleri*	Embryo	7.5	LC10 (Mortality and development)	41
	Rana pipiens	Embryo	7.5	LC10 (Mortality and development)	29
Fish (Chordata)	*Carassius auratus*	Embryo	7	LC10 (Mortality)	17
	Danio rerio	Embryo	34	NOEC (Biomass)	1.8
	Ictalurus punctatus	Embryo	9	LC10 (Mortality)	14
	Melanotaenia splendida	Embryo	12	LC10 (Mortality)	102
	Micropteris salmoides	Embryo	11	LC10 (Mortality)	6.0
	Oncorhynchus mykiss	Embryo	28	LC10 (Mortality)	6.2
	Pimephales promelas	Embryo	32	NOEC (Mortality)	11
	Cirrhinus mrigala	Juvenile	52	NOEC (Growth rate)	4
Bivalve (Mollusca)	*Lampsilis siliquoidea*	Juvenile	21	NOEC (Biomass)	10
Macrocrustacean (Arthropoda)	*Hyalella azteca*	Juvenile	42	NOEC (Reproduction)	6.6
	Daphnia magna	Neonate	14	NOEC (Reproduction)	2.4

Taxonomic group (phylum)	Species	Life stage	Duration (days)	Toxicity measure (test endpoint)	Toxicity value (mg/litre)
Microcrustacean (Arthropoda)	*Ceriodaphnia dubia*	Neonate	7	NOEC (Reproduction)	5.6
Macrophyte (Charophyta)	*Egeria densa*	Apical stem cutting	28	NOEC (Biomass)	6.1
	Lemna disperma	NR	7	EC10 (Growth)	1.4
	Potamogeton ochreatus	Apical stem cutting	30	IC10 (Shoot growth)	4.9
Green microalga (Chlorophyta)	*Pseudokirchneriella subcapitata*	NR	4	NOEC (Growth)	2.8
Diatom (Bacillariophyta)	*Cyclotella* sp.	NR	4–14	NOEC (Biomass)	10
	Navicula sp. 1	NR	4–12	IC10 (Growth)	0.6
	Navicula sp. 2	NR	4–16	NOEC (Biomass)	1.0
Blue–green alga (Cyanobacteria)	*Nostoc punctiforme* sp. 2	NR	6–26	NOEC (Growth)	10

EC10	The concentration of a substance in water or sediment that is estimated to produce a 10 % change in the response being measured
IC10	The concentration of a substance in water or sediment that is estimated to produce a 10 % inhibition of the response being measured in test organisms relative to the control response, under specified conditions
NOEC	No observed effect concentration. The highest concentration of a material used in a toxicity test that has no statistically significant adverse effect on the exposed population of test organisms as compared with the controls

INFOTOX also considered additional information from Canadian environmental quality guidelines. Canadian freshwater quality guidelines for boron are based on fish species, amphibians, invertebrates, and plant species (CCME 2009). Each data point was ranked according to sensitivity, and its centralised distribution on the species sensitivity distribution ("SSD") was determined.

Concentration SSD 5th percentile of 1.5 mg/litre was selected as the guideline value, with a lower 95 per cent confidence limit of 1.2 mg/litre, and an upper 95th per cent confidence limit of 1.7 mg/litre. Therefore, the long-term exposure Canadian Water Quality Guideline ("CWQG") for the protection of freshwater life is 1.5 mg/litre for boron (discussed in Alberta Environment and Parks 2016). This guideline is also higher than the boron concentration in surface water calculated by INFOTOX.

19.4 Honey bees

Potential impacts of boron on bees are covered in this assessment because of global concerns about declining numbers of bees and other pollinators, due to habitat loss, intensive farming practices, changes in weather conditions, and the use of agrochemicals. It is well known that the Registrar requires this issue to be adequately addressed in submissions of products for registration.

Although boron-containing fertilizers do not fall in the category of pesticides, it has been documented in the scientific literature that pesticide applications during bloom of crops are sometimes combined with foliar boron fertilizer applications.

Siede et al. (2013) conducted a study to evaluate whether foliar boron fertilizers could be hazardous for bees under real field conditions. Canola/rapeseed (*Brassica napus L.*) was selected for the study, as it is foraged intensively by honey bees (*Apis mellifera*). Pesticide applications during bloom are sometimes combined with foliar boron fertilizer applications. Six colonies of bees were transferred to a rapeseed field in bloom was treated with boron fertilizer. Six control colonies were transferred to an untreated rape field approximately 7 km away. Performance parameters of the colonies were measured. Samples of honey and beebread were collected from all colonies before and after boron fertilizer application. The contents of boron and of Al, Cd, Cr, Fe, K, Mn, Ni, P, Pb, S and Zn were measured in honey by inductively coupled plasma mass spectroscopy ("ICP-MS") and by ICP–atomic emission spectroscopy ("ICP-OES"). No significant differences were found in honey yield, number of capped brood[6], number of uncapped brood, or number of bees. Application of boron fertilizer did not affect the concentration of boron in honey or beebread. The study confirmed that the application of foliar boron fertilizers in blooming rapeseed is not hazardous for bee colonies.

In another study, Saridas et al. (2021) assessed how honey bees and boron fertilizer affect yields and marketable fruit quality of Fortuna strawberry (*Fragaria x anannassa Duch*) cultivar. The experiment was conducted in two growing tunnels. One of the tunnels was closed, not allowing any pollinators to enter. A commercial honey-bee hive (*Apismellifera L.*) was placed near the other tunnel that allowed bees to enter. Boron-containing fertilizer was applied in both tunnels.

The presence of bees increased the total fruit yield per plant considerably. The important observation in this study is that the application of boron fertilizer did not have any impacts on the honey bees.

20 Level of confidence

20.1 Philosophy in selecting exposure parameters

Whilst it is important to conduct health risk assessments on the side of caution, basing risk assessment on worst-case assumptions may have unrealistic and undesirable outcomes. The underlying philosophy of worst-case risk assessment is that if the product/formulation is safe to use in the worst-case scenario, it will also be safe for all realistically expected uses. In principle, this is a valid assumption, but it should be considered within broad realistic perspectives. The difficulty with applying the worst-case approach without professional judgement, is that risk conclusions may indicate that a product would be unsafe to use for all intended purposes, while it may be difficult, even impossible in some cases, to demonstrate this in practice. The worst-case approach may place an extreme cost burden on management of chemicals, creating minimal, if any, additional safety, or environmental benefits.

As stated in Section 1, the Registrar refers specifically to *"realistic worst-case conditions"*, which is in agreement with the broad principles of health risk assessment.

INFOTOX follows the philosophy in health risk assessment where some of the exposure parameters are kept at central tendency values, while reasonable maximum values are applied for some of the other parameters. This assures a balance between being cautious and being focused on the most severe, unrealistic, potential outcome.

[6] The term "brood" is used in beekeeping to reference the eggs, larvae, or pupae of honeybees.

20.2 Human dietary exposure to boron

As described in Section 10.1, INFOTOX used dietary exposure data for boron from the Third National Health and Nutrition Examination Survey ("NHANES III"), a nationwide probability sample in the USA of 39 695 persons aged 2 months and older (NAP 2000). It was conducted from 1988-1994 in two phases, namely, Phase 1 (1988 to 1991) and Phase 2 (1991 to 1994). The NHANES III database represents the largest source of records of dietary reference intake values of substances in food. Data for boron are presented for different sexes and age groups of the population, including pregnant females, and are available for different percentiles of the data distribution.

INFOTOX retrieved the 95th percentiles of dietary exposure data, which represent reasonable maximum exposures. Reasonable maximum exposure ("RME") refers to persons at the upper end of the exposure distribution. Following USEPA guidance (USEPA 2019b), the RME scenario assesses exposures that are higher than average but still within a realistic exposure range. RME calculations apply mean body weights.

20.3 Occupational exposure to boron

INFOTOX listed a range of studies relating to occupational exposures to boron. The references listed in Table 13.1 are covered in the review articles, but are listed in the table to illustrate the extensive list of studies that confirmed that there is extensive evidence that the developmental and reproductive effects of boron observed in test animals have not been confirmed in humans. This does not suggest that the ECHA hazard classification of boron presented in Section 3.2 is incorrect. Considering the explanation about the human health risk assessment paradigm in Section 5, the hazard classification logically should trigger a health risk assessment, as is presented in this INFOTOX report.

20.4 Toxicological parameters

In all cases, toxicological parameters were selected from reputable sources, and are referenced accordingly. Uncertainty factors are used in human non-cancer risk assessment when insufficient data are available to support the use of chemical-specific and species-specific extrapolation factors. These aspects are discussed in more detail in Section 7.1, and illustrated with toxicological data in Table 8.3.1. The methodology for establishing toxicity values for health risk assessment intends to overestimate rather than underestimate health risks.

Toxicity values for livestock, wildlife and avian species were selected from published scientific documents. Some of these references were also used by Alberta Environment and Parks (2016), and are regarded as the best information available.

20.5 Determining boron concentrations in environmental media

There are no "typical" concentrations of boron associated with fertilizers in environmental media. As discussed in Section 9.1, boron is an essential plant micronutrient, but there is a narrow range between soil deficiency and toxicity. Plant species differ considerably in terms of boron requirements, which affects the optimal fertilizer application rates. Boron that is available in soil for uptake into plants depends on the soil texture, soil chemistry, and other nutrients. INFOTOX used these basic principles as a point of departure to determine best estimates of boron in environmental

media. Key considerations were estimates of boron deficiency in soil, and levels where boron can be toxic to plants. The boron concentrations where injury to plants may occur depend on plant tolerance levels. Assessment of these effects are based on specialised analytical methods, namely, HWS boron, and saturated paste boron extractions, as described in Sections 9.2 and 9.3. As there is not a single clear cut-off concentration for plant toxicity for HWS boron, INFOTOX reviewed data and selected 2.0 mg/kg as a reasonable value to apply in further steps of the health risk assessments. As indicated in Table 9.2.6, no fertilization requirements are recommended by British Columbia (online) for HWS boron concentrations above 1.0 mg/kg. It would be unrealistic to apply a higher value than 2.0 mg/kg, at which a high incidence of injury to plants could occur.

It is also relevant to comment on the saturated paste boron, which INFOTOX selected as a proxy for boron in soil pore water. The boron concentration that is toxic to plants depends on several factors, among others, the plant type, soil texture and climate zone. Alberta Environment and Parks (2016) referred to studies suggesting that saturated paste boron concentrations <0.7 mg/litre are "*probably safe*" for sensitive plants, concentrations in the range 0.7 to 1.5 mg/litre are "*marginal*", and >1.5 mg/litre "*appear to be unsafe*". Use of a soil saturated paste boron concentration of 1.75 mg/litre is thus regarded as a conservative upper estimate to use as a proxy for soil pore water concentrations of boron at fertilized farmlands.

20.6 Human exposure to boron in drinking water, indoor house dust, and outdoor soil

INFOTOX used the boron concentration in saturated soil paste extracts as estimates of boron in soil pore water for various soil types and boron K_d values, as presented in Table 9.4.1. Selecting the highest concentration as a proxy for generic boron in soil pore water at farmlands to estimate the boron concentration in groundwater, is a reasonable, conservative approach.

INFOTOX used the HWS boron concentration as the fraction of boron in soil that is bio-accessible, as described in Section 9.6, is the best available estimate. The health risk assessment results that relied on this assumption are so low, that considerably higher bio-accessibility would still not lead to unacceptable health risks associated with incidental ingestion on indoor house dust and outdoor soil.

20.7 Exposure assessments for livestock, terrestrial wildlife, and avian species

Allometric calculations were conducted to calculate food and water intake rates for the various species.

INFOTOX applied BCFs for boron in annual crops and forage, adjusted for HWS boron of 2.0 mg/kg at farmlands. The highest concentrations in crops and forage were applied in dose calculations for representative livestock and wildlife species, which is very conservative and would have overestimated animal boron intake rates from crops and forage at farmlands.

INFOTOX selected avian species that frequent surface water. Fish, invertebrates and water plants were identified as avian foods. BCFs of boron from the water into food were taken into account, and concentrations were calculated for intake of boron from food and water. All calculations were on the conservative side and are presented with confidence.

20.8 Ecotoxicity

INFOTOX listed multiple scientific publications dealing with screening risk assessments for soil invertebrates (Table 19.2.1) and assessment of boron risks to aquatic life (Table 19.3.1). In the studies of soil invertebrates, toxic effects in the respective studies were reported at boron concentrations in saturated paste extracts. These concentrations must be compared to the boron soil saturated paste concentration of 1.75 mg/litre derived by INFOTOX in Section 9.4, as point of reference, which is a relatively high estimate. The boron concentrations at which toxic effects were observed are all higher than the INFOTOX guideline concentration, confirming insignificant risk. In the assessment of risks to aquatic life, the data in Table 19.3.1 indicate effects at concentrations higher than the estimated boron concentration of 0.09 mg/litre in surface water listed in Section 9.5. The screening assessments are based on results of multiple published studies on toxic effects of boron on soil invertebrates and aquatic receptors, and the findings are presented with confidence.

Although boron-containing fertilizers do not fall in the category of pesticides, it has been documented in the scientific literature that pesticide applications during bloom of crops are sometimes combined with foliar boron fertilizer applications. Potential impacts of boron on honey bees were investigated in well-designed studies, as described in Section 19.4.

21 Summary of conclusions

Discussions in Sections 20.1 to 20.8 above summarised some detail about the risk assessment approach that was followed by INFOTOX, and the level of confidence in the findings. As explained, INFOTOX follows the philosophy in health risk assessment where some of the exposure parameters are kept at central tendency values, while reasonable maximum values are applied for some of the other parameters. This assures a balance between being cautious and being focused on the most severe, worst-case potential outcome.

A comprehensive list of scientific literature references is provided, to illustrate that INFOTOX did not base findings on limited studies.

Overall, it is demonstrated that the INFOTOX risk assessment accommodated conservative, high-end estimates of exposure in the various studies, thus placing the risk assessments within a high margin of confidence.

Table 21.1 provides a concise summary of the studies that were conducted, and the essential findings. Detail has been presented in the main body of the report. For ease of reference, abbreviations for this section are presented in Table 21.2

Tabel 21.1: Summary of studies covered in this INFOTOX risk assessment, supporting information, and conclusions.

Study	Risk basis	Confidence	Conclusion
Human dietary	NHANES III (NAP 2000)	95th percentile data RME, conservative	Insignificant risk
Boron supplements	NHANES III (NAP 2000)	95th percentile data, RME, conservative	Insignificant risk
Drinking water	Childhood exposures	Highest exposed individuals, conservative	Insignificant risk
House dust/outdoor soil	Childhood exposures	Highest exposed individuals, conservative	Insignificant risk
Occupational exposures	Refer to 15 publications, including review articles, 1994 to 2023	High level, credible references	Insignificant evidence of risk to human developmental and reproductive effects
Livestock	Cattle, goats, horses, sheep, pigs. Boron intake from food and water	Intake of highest boron in food, conservative	Insignificant risk
Wildlife	Rats, mice, rabbits. Boron intake from food and water	Intake of highest boron in food, conservative	Insignificant risk
Avian species	Grey heron, great egret, little egret, red-billed teal. Boron intake from food and water	Intake of fish, invertebrates, and aquatic plants. Considered BCFs from boron in water, conservative	Insignificant risk
Soil invertebrates	Refer to 16 publications (Table 19.2.1). Refer to LC25 and EC25	Based on saturated paste boron concentrations, compared to INFOTOX' derived saturated paste value, reasonable estimate	Insignificant risk
Aquatic species	Refer to 22 studies, EC10, IC19, NOEC (Table 19.3.1)	Based on surface water concentration 0.09 mg/litre, reasonable estimate	Insignificant risk
Honey bees	Literature studies	High level of confidence	Application of boron fertilizer did not have any impacts on the honeybees.

Table 21.2: Abbreviations.

NHANES III	The Third National Health and Nutrition Examination Survey in the USA, Phase 1 (1988 to 1991) and Phase 2 (1991 to 1994), 39 695 people
RME	Reasonable maximum exposure
BCF	Bioconcentration factor
LC25	Concentration at which exposure for a specific length of time is expected to cause death in 25% of a defined experimental animal population
EC25	EC25 is a point estimate of the toxicant concentration that would cause an observable adverse effect in 25 percent of the test organisms
EC10	The concentration of a substance in water or sediment that is estimated to produce a 10 % change in the response being measured
IC10	The concentration of a substance in water or sediment that is estimated to produce a 10 % inhibition of the response being measured in test organisms relative to the control response, under specified conditions
NOEC	No observed effect concentration. The highest concentration of a material used in a toxicity test that has no statistically significant adverse effect on the exposed population of test organisms as compared with the controls

22 Recommendations

A comprehensive risk assessment, as summarised in Table 21.1, confirmed insignificant health risks for the CMR categories associated with boron in fertilizers.

Boron is an essential micronutrient for growth and development of healthy plants in agriculture. Since the early 1920s, the importance of boron has been recognised and it has been applied in fertilizers across the world since that time.

INFOTOX has not identified any health risks to humans, animals, or ecosystems, due to the use of boron in fertilizers. It is thus not necessary to implement precautionary measures in addition to the normal procedures that are applied in fertilization of plants at farmlands.

There is thus no scientific basis to prohibit or restrict the use of boron in fertilizers because of hazards identified in animals for boron in the CMR categories.

23 References

Alberta Environment and Parks. 2016. Soil Remediation Guidelines for Boron: Environmental and Human Health. Land Policy Branch, Policy and Planning Division. 146 pp.

Allen BC' Strong PL, Price CJ. Hubbard SA and Datson GP. 1996. Benchmark dose analysis of developmental toxicity in rats exposed to boric acid. Fund Appl Toxicol, 32:194-204.

ATSDR. 2010. Toxicological Profile for Boron. Agency for Toxic Substances and Disease Registry, US Department of Health and Human Services, Public Health Service. Atlanta, GA.

Austin OL, Clanch MH and Gill F. Online. Passeriform bird. Encyclopedia Brittanica. https://www.britannica.com/animal/passeriform.

Başaran N, Duydu Y and Bolt HM. 2012. Reproductive toxicity in boron exposed workers in Bandirma, Turkey. J Trace Elem Med Biol, 26(2-3):165-7.
PMID: 22575543 DOI: 10.1016/j.jtemb.2012.04.013.

Berger KC and Truog E. 1939. Boron determination in soils and plants. Ind Eng Chem Anal Ed, 11:540-545.

Birdfact. Online a. What Do Herons Eat? (Complete Guide).
https://birdfact.com/articles/what-do-herons-eat.

Birdfact. Online b. What Do Egrets Eat? (Full Diet, Habits and Behavior).
https://birdfact.com/articles/what-do-egrets-eat.

Bolt HM, Başaran N and Duydu Y. 2020. Effects of boron compounds on human reproduction. Archives of Toxicology, 94:717-724. https://doi.org/10.1007/s00204-020-02700-x.

Brdar-Jokanović M. 2020. Boron Toxicity and Deficiency in Agricultural Plants. Int J Mol S, 21(4):1424. Published online 2020 Feb 20. doi: 10.3390/ijms21041424.

British Columbia. Online. Boron for Field Crop. Soil Factsheet. Ministry of Agriculture.
https://www2.gov.bc.ca/assets/gov/farming-natural-resources-and-industry/agriculture-and-seafood/agricultural-land-and-environment/soil-nutrients/600-series/631012-1_using_boron_for_field_crops.pdf.

CCME. 2009. Canadian Water Quality Guidelines for the Protection of Aquatic Life. Boron. Canadian Environmental Quality Guidelines, Canadian Council of Ministers of the Environment. https://ccme.ca/en/res/boron-en-canadian-water-quality-guidelines-for-the-protection-of-aquatic-life.pdf.

CECOTOX 2005. Research in Support of the Environment Canada Collembolan Toxicity Test Method with Folsomia fimetaria for assessment of Contaminated Soils. Laboratory on Environmental Chemistry and Ecotoxicology (CECOTOX), Ecole Polytechnique federal de Laussanne (EPFL), Switzerland. Report by C Stampfli, K Becker-van Slooten, S Campiche and J Tarradellas. Cited in ALBERTA ENVIRONMENT AND PARKS 2015.

Chang BL, Robbins WA, Wei F, Xun L, Wu G, Li N and Elashoff DA. 2006. Boron workers in China: exploring work and lifestyle factors related to boron exposure. AAOHN J, 54(10):435-443. doi: 10.1177/216507990605401003.

Commonwealth of Australia. 2021. Toxicant default guideline values for aquatic ecosystem protection. Boron in freshwater. Technical brief. July 2021.

Dufour L, Sander JE, Wyatt RD, Rowland GN and Page RK. 1992. Experimental exposure of broiler chickens to boric acid to assess clinical signs and lesions of toxicosis. Avian Di, 36(4):1007-11. https://pubmed.ncbi.nlm.nih.gov/1485847/.

DEA. 2010. Framework for the Management of Contaminated Land, March 2010. Department of Environmental Affairs.

Dufour L, Sander JE, Wyatt RD, Rowland GN and Page RK. 1992. Experimental exposure of broiler chickens to boric acid to assess clinical signs and lesions of toxicosis. Avian Di, 36(4):1007-11. https://pubmed.ncbi.nlm.nih.gov/1485847/.

Duydu Y and Başaran N. 2023. Effects of boron exposure on human reproduction and development. Current Opinion in Toxicology. Volume 34, June 2023, 100403. https://doi.org/10.1016/j.cotox.2023.100403.

Duydu Y, Başaran N and Bolt HM. 2023. What can we learn from epidemiological studies on chronic boron exposure? Review Article. Critical Reviews in Toxicology. https://doi.org/10.1080/10408444.2023.2222151.

Duydu Y, Başaran N, Üstündağ A, Aydin S, Ündeğer Ü, Ataman OY, Aydos K, YDüker Y, Ickstadt K, Schulze B, Golka WK and Bolt HM. 2011. Reproductive toxicity parameters and biological monitoring in occupationally and environmentally boron-exposed persons in Bandirma, Turkey. Arch Toxicol, 85(6):589-600. doi: 10.1007/s00204-011-0692-3. Epub 2011 Mar 19. PMID: 21424392 DOI: 10.1007/s00204-011-0692-3.

DWAF. 1996. South African Water Quality Guidelines (second edition). Volume 5: Agricultural Use: Livestock Watering. Department of Water Affairs and Forestry.

ECHA. 2010. Member State Committee Draft Support Document for Identification of Boric Acid as a Substance of Very High Concern Because of its CMR Properties. Adopted on 9 June 2010 European Chemicals Agency. SVHC[7] Support Document.

ECHA. 2008: Annex XV transitional reports. Boric acid. European Chemicals Agency. http://echa.europa.eu/doc/trd_substances/boric_acid/ann_xv_trd/trd_austria_boric_acid.pdf.

EHC. 1998. Environmental Health Criteria 204. Boron. United Nations Environment Programme, International Labour Organisation, World Health Organization International Programme on Chemical Safety.

Eisler R. 1990. Boron hazards to fish, wildlife, and invertebrates: a synoptic review. US Fish Wildl. Serv. Biol Rep, 85(1.20). 32 pp. US Department of the Interior, Fish and Wildlife Service, Washington, DC 20240.

Environment Canada. 2006-2010, 2008-2010, 2010-2012. Unpublished compilation of data regarding boric acid toxicity to invertebrates in artificial soil. Biological Methods Division, Ottawa, Ontario. Cited in Alberta Environment and Parks 2016.

[7] Substance of very high concern

Environment Canada. 2007. Interlaboratory Validation of Environment Canada's New Test Methods for Measuring Survival and Reproduction of Springtails Exposed to Contaminants in Soil. Biological Methods Division, Ottawa, Ontario. Cited in Alberta Environment and Parks 2016.

Environment Canada. 2004. Inter-Laboratory Validation of Environment Canada's New Test Methods for Measuring Soil Toxicity Using Earthworms. Prepared by Juliska Princz. Biological Methods Division, Ottawa, Ontario. Cited in Alberta Environment and Parks 2016.

Exova. 2013. Data Tables and Results from 2013 Earthworm Reproduction in Sandy Loam Soil Study. Cited in Alberta Environment and Parks 2015.

FAO. 2023. Water Quality in Agriculture: Risks and risk mitigation. Edited by: Drechsel P, Zadeh SM and Salcedo FP. The Food and Agriculture Organization of the United Nations and International Water Management Institute, Rome, 2023.
https://www.fao.org/3/cc7340en/cc7340en.pdf.

Fries GF, Marrow GS and Snow PA. 1982. Soil Ingestion by Dairy Cattle. J Dairy Sci, 65:611-618.

Gupta UC, Jame YW, Campbell CA, Leyshon AJ and Nicholaichuck W. 1985. Boron toxicity and deficiency: A review. Can J Soil Sci, 65:381-409.

Hancock J and Kushlan J. 1987. The Herons Handbook. Pub Groom Helm Ltd.
Heindel JJ, Price CJ and Schwetz BA. 1994. The Developmental Toxicity of Boric Acid in Mice, Rats, and Rabbits. Environmental Health Perspectives, Volume 102, Supplement 7:107-112.

Heindel JJ, Price CJ and Schwetz BA. 1994. The Developmental Toxicity of Boric Acid in Mice, Rats, and Rabbits. Environmental Health Perspectives, Volume 102, Supplement 7:107-112.

Heindel JJ, Price CJ, Field EA, Marr MC Myers CB, Morrissey RE and Schwetz BA. 1992, Developmental toxicity of boric acid in mice and rats. Fund Appl Toxicol, 18: 266-272.

Hill Labs. Online. Technical Note: Soil Tests & Interpretation. Hill Labs.
https://www.hill-labs.co.nz/media/djdbzzhl/3196v6_technical-note-soil-tests-and-interpretation.pdf.

Hoffman DJ, Camardeses MB, Lecaptain LJ and Pendleton GW. 1990. Effects of boron on growth and physiology in mallard ducklings. Environmental Toxicology and Chemistry, Volume 9, Issue 3:335-346. First published: March 1990 https://doi.org/10.1002/etc.5620090309.

Horneck DA, Sullivan DM, Jim Owen J and John M. Hart JM. Online. Soil Test Interpretation Guide. Boron (B). Oregon State University Extension Service.
https://extension.oregonstate.edu/catalog/pub/ec1478.

Howe PD. 1998. A review of boron effects in the environment. Biol Trace Elem Res. 1998 Winter, 66(1-3):153-66. doi: 10.1007/BF02783135.

Ingraldi S. 2004. Comparison of *E.andrei* and *E. fetida* in Their Response to Contaminated Soils. University of Waterloo Work Term Report, prepared for Environment Canada. Cited in ALBERTA ENVIRONMENT AND PARKS 2015.

Institute of Medicine. 2001. Dietary Reference Intakes for Vitamin A, Vitamin K, Arsenic, Boron, Chromium, Copper, Iodine, Iron, Manganese, Molybdenum, Nickel, Silicon, Vanadium, and Zinc. Washington, DC: The National Academies Press. https://doi.org/10.17226/10026.

IPCS. 2010. WHO Human Health Risk Assessment Toolkit: Chemical Hazards. Harmonization Project Document No. 8. Published under the joint sponsorship of the World Health Organization, the International Labour Organization and the United Nations Environment Programme, and produced within the framework of the Inter-Organization Programme for the Sound Management of Chemicals.

IPCS. 1999. Principles for the Assessment of Risks to Human Health from Exposure to Chemicals. Environmental Health Criteria 210. International Programme on Chemical Safety. A cooperative agreement between UNEP, ILO, FAO, WHO, UNIDO, Unitar and OECD.

IRIS. 2022. Integrated Risk Information System (IRIS) Glossary. US Environmental Protection Agency.
https://sor.epa.gov/sor_internet/registry/termreg/searchandretrieve/glossariesandkeywordlists/search.do?details=&vocabName=IRIS%20Glossary.

IRIS. 2004. Boron and Compounds; CASRN 7440-42-8. Integrated Risak Information System, Chemical Assessment Summary. National Center for Environmental Assessment, US Environmental Protection Agency. https://iris.epa.gov/static/pdfs/0410_summary.pdf.

Janik LJ, Forrester ST, Soriano-Disla JM, Kirby JK, McLaughlin MJ and Reimann C. 2015. GEMAS Project Team, Geochemical Mapping of Agricultural Soils of Europe (GEMAS) program. GEMAS: prediction of solid-solution phase partitioning coefficients (Kd) for oxoanions and boric acid in soils using mid-infrared diffuse reflectance spectroscopy Environ Toxicol Chem, 34(2):235-46. doi: 10.1002/etc.2821. Epub 2015 Jan 8.
https://pubmed.ncbi.nlm.nih.gov/25476926/.

Karamertzanis PG, Atlason P, Nathanail AV, Provoost J, Karhu E and Rasenberg M. 2019. The impact on classifications for carcinogenicity, mutagenicity, reproductive and specific target organ toxicity after repeated exposure in the first ten years of the REACH regulation. Regulatory Toxicology and Pharmacology, 106: 303-315.

Llewellyn J. Online. Grey Heron (Ardea Cinerea).
https://ingwelala.co.za/archives/fauna-flora/grey-heron.html.

MRID 40692308. Weir RJ. 1967. 38-Week Dietary Feeding – Dogs with 20 Mule Team Borax (Sodium Tetraborate Decahydrate). Hazleton Laboratories, Inc., Falls Church,VA. No study number provided. February 28, 1967. Unpublished report.

MRID 40692310. Weir RJ and Crews LM. 1967. Two Year Dietary Feeding – Dogs. Borax (Sodium Tetraborate Decahydrate) and Addendum. Hazleton Laboratories, Inc. Falls Church, VA. Laboratory Project ID 182-104, April 10, 1967 (original study on July 8, 1966). Unpublished report.

NAP. 2000. Dietary Reference Intakes for Vitamin A, Vitamin K, Arsenic, Boron, Chromium, Copper, Iodine, Iron, Manganese, Molybdenum, Nickel, Silicon, Vanadium and Zinc. A Report of the Panel on Micronutrients, Subcommittees on Upper Reference Levels of Nutrients and of Interpretation and Uses of Dietary Reference Intakes, and the Standing Committee on the Scientific Evaluation of Dietary Reference Intakes. Food and Nutrition Board Institute of Medicine. National Academy Press, Washington, DC.

NAP. 1998. Dietary Reference Intakes: A Risk Assessment Model for Establishing Upper Intake Levels for Nutrients. Institute of Medicine (US) Food and Nutrition Board. Washington DC. National Academy of Sciences, National Academies Press.
https://www.ncbi.nlm.nih.gov/books/NBK45182/.

NRC. 1983. Risk Assessment in the Federal Government: Managing the Process. National Research Council. Committee on the Institutional Means for the Assessment of Risks to Public Health. Washington, DC: National Academy Press.

OECD. 2021. Guidance on Key Considerations for the Identification and Selection of Safer Chemical Alternative, OECD Series on Risk Management, No. 60, Environment, Health and Safety, Environment Directorate, OECD.

Oiseaux-Birds. Online. Red-billed Teal or Duck.
https://www.oiseaux-birds.com › card-red-billed-teal.

Padbhushan R and Kumar D. 2017. Fractions of soil boron: a review. The Journal of Agricultural Science, Volume 155, Issue 7. Published online by Cambridge University Press:11 April 2017.
DOI: https://doi.org/10.1017/S0021859617000181.

Personal communication. 2024. E Laubscher, Omnia Nutriology, the Agricultural Division of Omnia Holdings Limited.

Price CJ, Strong PL, Marr MC, Myers CB and Murray FJ. 1996. Developmental toxicity NOAEL and postnatal recovery in rats fed boric acid during gestation. Fund Appl Toxicol, 32:179.

Princz JI, Behan-Pelletier VM, Scroggins RP and Siciliano SD. 2010. Oribatid mites in soil toxicity testing – the use of *Oppia nitens* (C.L. Koch) as a new test species. Environmental Toxicology and Chemistry, 29(4): 971-979.
https://www.researchgate.net/publication/46159939_Oribatid_mites_in_soil_toxicity_testing_-_The_use_of_Oppia_nitens_CL_KOCH_as_a_new_test_species. Cited in Alberta Environment and Parks 2015.

Robbins WA, Xun L, Jia J, Kennedy N, Elashoff DA, Ping L. 2010. Chronic boron exposure and human semen parameters. Reprod Toxicol, 29(2):184-190.
doi: 10.1016/j.reprotox.2009.11.003.

Robbins WA, Wei F, Elashoff DA, Wu G, Xun L, Jia J. 2008. Y:X sperm ratio in boron exposed men. J Androl, 29(1):115–121. doi: 10.2164/jandrol.107.003541.

Rossi AF, Miles RD, Bootwalla SM, Wilson Hr and Eldred AR. 1993. The Effect of Feeding Two Sources of Boron on Broiler Breeder Performance. Poultry Science, 72:1931-1934.

Sample BE, Aplin MS, Efroymson RA, Suter II GW and Welsh CJE. 1997. Methods and Tools for Estimation of the Exposure of Terrestrial Wildlife to Contaminants. ORNL/TM-13391. Prepared by Oak Ridge National Laboratory, Oak Ridge, Tennessee 37831-6285. Managed by Lockheed Martin Energy Research Corporation, for the US Department of Energy, under contract DE-AC05-96OR22464.

Sample BE and Suter GW. 1994. Estimating Exposure of Terrestrial Wildlife to Contaminants. Report No ES/ER/TM- 125. Prepared by Environmental Sciences Division, Oak Ridge National Laboratory, Oak Ridge, Tennessee.

Sarıdaş MA, Karabıyık S, Eti S and Kargı SP. 2021. Boron Applications and Bee Pollinators Increase Strawberry Yields. International Journal of Fruit Science. Volume 21, Issue 1: 481-491. https://doi.org/10.1080/15538362.2021.1907010.

Sayli BS. 2003. Low frequency of fertility among workers in a borate processing facility. Biol Trace Elem Res, 93(1–3):19–30. doi: 10.1385/ BTER:93:1-3:19.

Sayli BS. 2001. Assessment of fertility and infertility in boron-exposed Turkish subpopulations. 3. Evaluation of fertility among sibs and in "borate families". Biol Trace Elem Res, 81(3):255-267.

Sayli BS. 1998. An assessment of fertility in boron-exposed Turkish subpopulations. 2. Evidence that boron has no effect on human reproduction. Biol Trace Elem Res, 66(1-3):409-422.

Sayli BS, Tuccar E, Elhan AH. 1998. An assessment of fertility in boron exposed Turkish subpopulations. Reprod Toxicol, 12(3):297-304. doi: 10.1016/s0890-6238(98)00013-6.

Siede R, Dyrba W, Augustin T, Wiegand A and Ellinghaus R. 2013. Boron fertilizers in rape – a risk for honey bees?. Journal of Applied Entomology, Volume i37, Issue 9:661-667.
First published: 15 March 2013 https://doi.org/10.1111/jen.12048.
https://onlinelibrary.wiley.com/doi/epdf/10.1111/jen.12048.

Thompson SE, Burton CA, Quinn DJ and Ng YC. 1972. Concentration Factors of Chemical Elements in Edible Aquatic Organisms. Lawrence Livermore Laboratory, University of California, Livermore, California. UCRL-50564 Rev 1.

Tuccar E, Elhan AH, Yavuz Y and Sayli BS. 1998. Comparison of infertility rates in communities from boron-rich and boron-poor territories. Biol Trace Elem Res, 66(1-3):401-407.
doi: 10.1007/BF02783151.

USEPA. 2019a. Update for Chapter 3 of the Exposure Factors Handbook Ingestion of Water and Other Select Liquids. EPA/600/R-18/259F. National Center for Environmental Assessment, Office of Research and Development, US Environmental Protection Agency, Washington, DC.

USEPA. 2019b. Guidelines for Human Exposure Assessment. EPA/100/B-19/001. Risk Assessment Forum, US Environmental Protection Agency, Washington, DC.

USEPA. 2017. Update for Chapter 5 of the Exposure Factors Handbook Soil and Dust Ingestion. EPA/600/R-17/384F. National Center for Environmental Assessment, Office of Research and Development, US Environmental Protection Agency, Washington, DC.

USEPA. 2015. Boric Acid/Sodium Salts of Boric Acid. Human Health Draft Risk Assessment for Registration Review. DP Barcode: 0418384. Office of Chemical Safety and Pollution Prevention, US Environmental Protection Agency, Washington, DC.

USEPA. 2011. Exposure Factors Handbook 2011 Edition (Final Report). EPA/600/R-09/052F, 2011. US Environmental Protection Agency, Washington, DC.

USEPA. 1996. Soil Screening Guidance: Technical Background Document. US Environmental Protection Agency. Office of Solid Waste and Emergency Response, Washington DC..

USEPA. 1993. Wildlife Exposure Factors Handbook, Volume I of II. EPA/600/R-93/187 Final. Office of Research and Development, US Environmental Protection Agency.

Weeth HJ, Speth CF and Hanks DR. 1081. Boron content of plasma and urine as indicators of boron intake in cattle. Am J Vet Res, 42(3):474-477.

Weir RJ and Fisher RS. 1972, Toxicologic studies on borax and boric acid. Toxicol Appl Pharmacol, 23:351-364.

WHO. 1998. Environmental Health Criteria 204: Boron. International Programme on Chemical Safety ("IPCS"), World Health Organization, Geneva.

Whorton MD, Haas JL, Trent L and Wong O. 1994. Reproductive effects of sodium borates on male employees: birth rate assessment. Occup Environ Med, 51(11):761–767.
doi: 10.1136/oem.51.11.761.

Wild life safari. Online. Fascinating Facts about the Great White Egret.
https://wildlifesafari.info/great_white_egret.htm.

Wolfram Research. 2016. Sample Data: Animal Weights from theWolfram Data Repository.
https://doi.org/10.24097/wolfram.43616.data.
Source metadata:
Rousseeuw PL and Leroy AM. 1987. Robust Regression and Outlier Detection
Creator: P. J. Rousseeuw and A. M. Leroy. Wiley.

Xing X, Wu G, Wei F, Liu P, Wei H, Wang C, Xu Y, Xun L, Jia J, Kennedy N, et al. 2008. Biomarkers of environmental and workplace boron exposure. J Occup Environ Hyg, 5(3):141-147. doi: 10.1080/15459620701845132.

Yazbeck C, Kloppmann W, Cottier R, Sahuquillo J, Debotte G and Huel G. 2005. Health impact evaluation of boron in drinking water: a geographical risk assessment in Northern France. Environ Geochem Health, 27(5-6):419-427. doi: 10.1007/s10653-005-1796-6.