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# Nickel in drinking-water

## Background document for development of WHO *Guidelines for drinking-water quality*

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## Preface

Access to safe drinking-water is essential to health, a basic human right and a component of effective policy for health protection. A major World Health Organization (WHO) function to support access to safe drinking-water is the responsibility "to propose ... regulations, and to make recommendations with respect to international health matters ...", including those related to the safety and management of drinking-water.

The first WHO document dealing specifically with public drinking-water quality was published in 1958 as *International standards for drinking-water*. It was revised in 1963 and 1971 under the same title. In 1984–1985, the first edition of the WHO *Guidelines for drinking-water quality* (GDWQ) was published in three volumes: Volume 1, Recommendations; Volume 2, Health criteria and other supporting information; and Volume 3, Surveillance and control of community supplies. Second editions of these volumes were published in 1993, 1996 and 1997, respectively. Addenda to Volumes 1 and 2 of the second edition were published in 1998, addressing selected chemicals. An addendum on microbiological aspects, reviewing selected microorganisms, was published in 2002. The third edition of the GDWQ was published in 2004, the first addendum to the third edition was published in 2006, and the second addendum to the third edition was published in 2008. The fourth edition was published in 2011, and the first addendum to the fourth edition was published in 2017.

The GDWQ are subject to a rolling revision process. Through this process, microbial, chemical and radiological aspects of drinking-water are subject to periodic review, and documentation relating to aspects of protection and control of drinking-water quality is accordingly prepared and updated.

Since the first edition of the GDWQ, WHO has published information on health criteria and other information to support the GDWQ, describing the approaches used in deriving guideline values, and presenting critical reviews and evaluations of the effects on human health of the substances or contaminants of potential health concern in drinking-water. In the first and second editions, these constituted Volume 2 of the GDWQ. Since publication of the third edition, they comprise a series of free-standing monographs, including this one.

For each chemical contaminant or substance considered, a background document evaluating the risks to human health from exposure to that chemical in drinking-water was prepared. The draft health criteria document was submitted to a number of scientific institutions and selected experts for peer review. The draft document was also released to the public domain for comment. Comments were carefully considered and addressed, as appropriate, taking into consideration the processes outlined in the *Policies and procedures used in updating the WHO guidelines for drinking-water quality* and the WHO *Handbook for guideline development*.

The revised draft was submitted for final evaluation at expert consultations.

During preparation of background documents and at expert consultations, careful consideration was given to information available in previous risk assessments carried out by the International Programme on Chemical Safety, in its Environmental Health Criteria monographs and Concise International Chemical Assessment Documents; the International Agency for Research on Cancer; the Joint Food and Agriculture Organization of the United Nations (FAO)/WHO Meeting on Pesticide Residues; and the Joint FAO/WHO Expert Committee on Food Additives (which evaluates contaminants such as lead, cadmium, nitrate and nitrite, in addition to food additives).

Further up-to-date information on the GDWQ and the process of their development is available on the WHO website and in the current edition of the GDWQ.

## Acknowledgements

The background document on nickel in drinking-water for the development of the WHO *Guidelines for drinking-water quality* (GDWQ) was prepared by Dr Akihiko Hirose of the National Institute of Health Sciences of Japan, under the coordination of WHO as described further below. The support of Dr Mika Takahashi, formerly of the National Institute of Health Sciences of Japan, in the preparation of this document is also gratefully acknowledged.

The work of the following experts was crucial in the development of this document and others in the second addendum to the fourth edition:

Dr M Asami, National Institute of Public Health, Japan
Dr RJ Bevan, independent consultant, United Kingdom
Mr R Carrier, Health Canada, Canada
Dr J Cotruvo, Joseph Cotruvo & Associates and NSF International WHO Collaborating Centre, United States of America
Dr D Cunliffe, South Australian Department of Health, Australia
Dr A Eckhardt, Umweltbundesamt (Federal Environment Agency), Germany
Professor JK Fawell, Cranfield University, United Kingdom
Dr A Hirose, National Institute of Health Sciences of Japan
Dr A Humpage, University of Adelaide (formerly South Australian Water Corporation), Australia
Dr P Marsden, Drinking Water Inspectorate, United Kingdom
Professor Y Matsui, Hokkaido University, Japan
Dr E Ohanian, Environmental Protection Agency, United States of America
Professor CN Ong, National University of Singapore, Singapore
Dr J Strong, formerly Environmental Protection Agency, United States of America
Dr E Testai, National Institute of Health, Italy

The draft text was discussed at the expert consultations for the second addendum to the fourth edition of the GDWQ, held on 28–30 March 2017, 13–14 July 2018 and 2 March 2021. The final version of the document takes into consideration comments from both peer reviewers and the public, including V Bhat, formerly NSF International, United States of America; J Donohue, United States Environmental Protection Agency; B Lampe, NSF International, United States of America; F Lemieux, Health Canada; M Templeton, Imperial College London, United Kingdom; M Zemlyanova, Federal Scientific Center for Medical and Preventive Health Risk Management Technologies, Russia; and K Ziegler-Skylakakis, Technical University of Munich, Germany.

The coordinator was Ms J De France, WHO. Strategic direction was provided by Mr B Gordon, WHO. Dr E Petersen, formerly of WHO, and Dr P Verger, WHO, provided liaisons with the Joint FAO/WHO Expert Committee on Food Additives and the Joint FAO/WHO Meeting on Pesticide Residues. Dr R Brown and Ms C Vickers, WHO, provided liaisons with the International Programme on Chemical Safety. Dr M Perez contributed on behalf of the WHO Radiation Programme. Dr Andina Faragher, Biotext, Australia, was responsible for the scientific editing of the document.

Many individuals from various countries contributed to the development of the GDWQ. The efforts of all who contributed to the preparation of this document are greatly appreciated.

## Acronyms and abbreviations

| | |
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| BMD | benchmark dose |
| $BMDL_{10}$ | 95% lower confidence limit on the benchmark dose for a 10% response |
| $BMDU_{10}$ | 95% upper confidence limit on the benchmark dose for a 10% response |
| bw | body weight |
| CI | confidence interval |
| CONTAM Panel | Panel on Contaminants in the Food Chain (European Food Safety Authority) |
| EFSA | European Food Safety Authority |
| FAO | Food and Agriculture Organization of the United Nations |
| GDWQ | *Guidelines for drinking-water quality* |
| GV | guideline value |
| LOAEL | lowest-observed-adverse-effect level |
| MOE | margin of exposure |
| $NiCl_2$ | nickel chloride |
| NiO | nickel oxide |
| NiS | nickel sulfide |
| $Ni_3S_2$ | nickel subsulfide |
| $NiSO_4$ | nickel sulfate |
| $NiSO_4 \cdot 6H_2O$ | nickel sulfate hexahydrate |
| NOAEL | no-observed-adverse-effect level |
| OR | odds ratio |
| SCD | systemic contact dermatitis |
| USA | United States of America |
| WHO | World Health Organization |

# Contents

## Executive summary

Nickel is a naturally occurring element. Food is the main source of nickel exposure in nonsmokers who are not exposed in occupational settings. However, drinking-water may become a significant source when nickel leaches from metal alloys that are in contact with the water. Elevated nickel in drinking-water can also result from heavy pollution or mobilization from natural deposits in rocks and soils to groundwater. Toxicity data for water-soluble nickel salts are the most relevant to assessing potential health risks from nickel exposure through drinking-water.

Human oral exposure to nickel is primarily associated with gastrointestinal and neurological symptoms after acute exposure. Exposure through skin or by inhalation may lead to nickel sensitization. Oral exposure to nickel is not known to lead to sensitization. However, individuals sensitized to nickel through skin contact and who have allergic contact dermatitis may develop eczematous flare-up reactions in the skin (systemic contact dermatitis – SCD) from a single oral exposure to nickel salts.

A health-based value of 80 µg/L for nickel was derived for chronic oral exposure based on reproductive and developmental toxicity in rats. These effects were identified as being the most sensitive human-relevant effects identified from the animal data, and some corresponding toxicological effects were suggested in recent human studies.

For the acute exposure assessment, the margin of exposure (MOE) values derived from the lowest-observed-adverse-effect level (0.3 mg/day) associated with SCD and the upper-bound acute dietary exposure (high-nickel-content food) ranged from 0.3 to 2.3 across dietary surveys, and raise a health concern for nickel-sensitized individuals. However, acute consumption of water containing nickel at the chronic health-based value of 80 µg/L would result in an MOE of approximately 16. Further, considering that SCD elicitation was associated with a bolus exposure, in contrast to the intermittent nature of drinking-water exposure, the chronic health-based value of 80 µg/L is determined to be adequately protective of SCD that may result from acute exposure.

In the current assessment, the existing guideline value (GV) of 70 µg/L is retained, as the difference between the health-based value of 80 µg/L and the existing GV of 70 µg/L is not considered significant enough to warrant a minimal relaxing of the GV. Furthermore, the existing GV is still considered to be adequately protective of human health, and is further supported by available source control measures, current treatment technologies, and measurability by analytical methods. As the major source of nickel in drinking-water is