

Trifluralin in Drinking-water

Background document for development of
WHO *Guidelines for Drinking-water Quality*

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Preface

One of the primary goals of WHO and its member states is that “all people, whatever their stage of development and their social and economic conditions, have the right to have access to an adequate supply of safe drinking water.” A major WHO function to achieve such goals is the responsibility “to propose regulations, and to make recommendations with respect to international health matters”

The first WHO document dealing specifically with public drinking-water quality was published in 1958 as International Standards for Drinking-Water. It was subsequently revised in 1963 and in 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 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 related to aspects of protection and control of public drinking-water quality is accordingly prepared/updated.

Since the first edition of the GDWQ, WHO has published information on health criteria and other supporting information to 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 examined in drinking-water.

For each chemical contaminant or substance considered, a lead institution prepared a health criteria document evaluating the risks for human health from exposure to the particular chemical in drinking-water. Institutions from Canada, Denmark, Finland, France, Germany, Italy, Japan, Netherlands, Norway, Poland, Sweden, United Kingdom and United States of America prepared the requested health criteria documents.

Under the responsibility of the coordinators for a group of chemicals considered in the guidelines, the draft health criteria documents were submitted to a number of scientific institutions and selected experts for peer review. Comments were taken into consideration by the coordinators and authors before the documents were submitted for final evaluation by the experts meetings. A “final task force” meeting reviewed the health risk assessments and public and peer review comments and, where appropriate, decided upon guideline values. During preparation of the third edition of the GDWQ, it was decided to include a public review via the world wide web in the process of development of the health criteria documents.

During the preparation of health criteria documents and at experts meetings, 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 FAO/WHO Meetings 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 internet site and in the current edition of the GDWQ.

Acknowledgements

The work of the following coordinators was crucial in the development of this background document for development of WHO *Guidelines for drinking-water quality*:

- J.K. Fawell, Water Research Centre, United Kingdom
(inorganic constituents)
- U. Lund, Water Quality Institute, Denmark
(organic constituents and pesticides)
- B. Mintz, Environmental Protection Agency, USA
(disinfectants and disinfectant by-products)

The WHO coordinators were as follows:

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Ms Marla Sheffer of Ottawa, Canada, was responsible for the scientific editing of the document.

The efforts of all who helped in the preparation and finalization of this document, including those who drafted and peer reviewed drafts, are gratefully acknowledged.

The convening of the experts meetings was made possible by the financial support afforded to WHO by the Danish International Development Agency (DANIDA), Norwegian Agency for Development Cooperation (NORAD), the United Kingdom Overseas Development Administration (ODA) and the Water Services Association in the United Kingdom, the Swedish International Development Authority (SIDA), and the following sponsoring countries: Belgium, Canada, France, Italy, Japan, Netherlands, United Kingdom of Great Britain and Northern Ireland and United States of America.

GENERAL DESCRIPTION

Identity

CAS no.: 1582-09-8

Molecular formula: C₁₃H₁₆F₃N₃O₄

Trifluralin is the common name for a,a,a-trifluoro-2,6-dinitro-*N,N*-dipropyl-*p*-toluidine.

Physicochemical properties (1)

<i>Property</i>	<i>Value</i>
Melting point	48.5–49 °C
Water solubility	<1 mg/litre at 27 °C
Vapour pressure	1.37 × 10 ⁻² Pa at 25 °C
Log octanol–water partition coefficient	4.69

Major uses

Trifluralin is a pre-emergence herbicide used for the control of annual grasses and broad-leaved weeds in beans, brassicas, cotton, groundnuts, forage legumes, orchards, ornamentals, transplanted peppers, soy beans, sugar-beet, sunflowers, tomatoes, and vineyards (1).

Environmental fate

Trifluralin has low water solubility. It is dissipated by photodecomposition, volatilization, and biodegradation (2–4). Trifluralin has a high affinity for soil and is relatively immobile (5); the half-life is 3–18 weeks, depending on soil type and geographical location (2). Its degradation in soil involves a series of oxidative dealkylation steps, the reduction of the nitro group, and oxidative cyclization (6), resulting in the formation of small quantities of several transformation products as well as significant amounts of nonextractable soil-bound compounds that reside in the fulvic and humic acid fractions of soils (7).

ANALYTICAL METHODS

Trifluralin may be extracted with dichloromethane and determined by capillary gas chromatography with a nitrogen–phosphorus detector. The method sensitivity is 0.05 µg/litre (8).

ENVIRONMENTAL LEVELS AND HUMAN EXPOSURE

Water

In the USA, trifluralin was found in 172 of 2047 surface water samples and in one of 507 groundwater samples analysed. The 85th percentile of the levels in all non-zero surface water samples was 0.54 µg/litre (9). It was not found in 229 drinking-water supplies (mainly groundwater) analysed in Italy (10).

KINETICS AND METABOLISM IN LABORATORY ANIMALS AND HUMANS

Oral doses of trifluralin were not readily absorbed by the gastrointestinal tract of the rat. About 80% of the dose was found in the faeces, the remaining appearing in the urine. Even though unchanged trifluralin was isolated from the faeces (<8% of the administered dose), the absorbed fraction was extensively metabolized. *N*-dealkylation and nitro reduction were two

of the principal metabolic pathways. The metabolic fate of trifluralin was similar in the rat and in the dog (11). Following intraperitoneal administration to rats, it was detected at higher concentrations in the fat than in the liver (12).

EFFECTS ON LABORATORY ANIMALS AND *IN VITRO* TEST SYSTEMS

Acute exposure

Oral LD₅₀s of over 10 g/kg of body weight for rats, 0.5 g/kg of body weight for mice, and over 2 g/kg of body weight for rabbits and dogs have been reported (1).

Short-term exposure

Beagle dogs were fed trifluralin at doses of 30, 150, or 750 mg/kg in the diet for 12 months. Effects at the highest doses included slightly decreased mean body weight gain, slight changes in plasma lipids, and a statistically significant increase in liver weight. A NOAEL of 30 mg/kg, equivalent to an average daily intake of 0.75 mg/kg of body weight, was derived, based on mild hepatic effects (13).

Long-term exposure

The effects of trifluralin were studied in Fischer rats at doses of 813, 3250, or 6500 mg/kg in the diet for 24 months (14); in Wistar rats at doses of 200, 800, or 3200 mg/kg in the diet for 24 and 28 months (15); in NMRI mice at doses of 50, 200, or 800 mg/kg in the diet for 104 weeks (16); and in beagle dogs at doses of 400 or 1000 mg/kg in the diet for 3 years (17). These tests were not adequate by today's standards because of methodological limitations and contamination problems.

Reproductive toxicity, embryotoxicity, and teratogenicity

Trifluralin is embryotoxic in the rat (18,19) and in the rabbit (21,22) at dose levels that are clearly maternally toxic; however, it is not teratogenic in these species.

Mutagenicity and related end-points

Studies on the mutagenicity of trifluralin show that low-purity technical trifluralin may contain nitroso contaminants and is mutagenic. High-purity trifluralin, in contrast, is not (20)

Carcinogenicity

Trifluralin containing the impurity nitrosodipropylamine was assayed for carcinogenicity in oral experiments on the rat and mouse (15,16,23,24). For each species, the first experiment was carried out with trifluralin that contained large amounts of the impurity. Carcinogenic effects on the liver, lungs, and stomach in female mice were observed, as well as equivocal indications of carcinogenicity in the rat thyroid. In the second experiment in each species, the trifluralin used contained the impurity at 0.4 mg/kg, two orders of magnitude less than in the previous studies. No carcinogenic effects were found in mice. In rats, however, there was an excess, limited to males treated with high doses, of granular cellular meningiomas (a rare benign tumour whose normal occurrence in rats is unknown). The incidence of thyroid tumours was not statistically significant and was not dose-related.

On the basis of a recent evaluation, IARC concluded that there is limited evidence in experimental animals for the carcinogenicity of technical-grade trifluralin (20).

EFFECTS ON HUMANS

In a study in the USA, the use of trifluralin was associated with an increased risk for non-Hodgkin lymphoma. In contrast, a study of ovarian cancer in Italy did not suggest an association with trifluralin exposure. In both studies, the numbers of exposed subjects were small. A larger study in the USA showed no association with leukaemia (20). IARC concluded that there is inadequate evidence in humans for the carcinogenicity of trifluralin (20).

GUIDELINE VALUE

IARC recently evaluated technical-grade trifluralin and assigned it to Group 3 (27). No evidence of carcinogenicity was found in a number of long-term toxicity/carcinogenicity studies with pure (>99%) test material. Trifluralin of high purity does not possess mutagenic properties. Technical trifluralin of low purity may contain nitroso contaminants and has been found to be mutagenic.

A NOAEL of 0.75 mg/kg of body weight per day was selected based on a 1-year feeding study in dogs (13). This species is the most sensitive for the mild hepatic effects on which the NOAEL was based. Using this NOAEL and an uncertainty factor of 100 (for inter- and intraspecies variation), a TDI of 7.5 µg/kg of body weight was derived. A guideline value of 20 µg/litre (rounded figure) is recommended, based on an allocation of 10% of the TDI to drinking-water.

Authorities should note that some impure technical grades of trifluralin could contain potent carcinogenic compounds and therefore should not be used.

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