

Endrin 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 first draft of Endrin in Drinking-water, Background document for development of WHO *Guidelines for Drinking-water Quality*, was prepared by Dr P. Toft, Canada, to whom special thanks are due.

The work of the following working group coordinators was crucial in the development of this document and others in the third edition:

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Prof. Y. Magara, Hokkaido University, Japan (*Analytical achievability*)
Mr P. Jackson, WRc-NSF, United Kingdom (*Treatment achievability*)

The contribution of peer reviewers is greatly appreciated. The draft text was posted on the world wide web for comments from the public. The revised text and the comments were discussed at the Final Task Force Meeting for the third edition of the GDWQ, held on 31 March to 4 April 2003, at which time the present version was finalized. The input of those who provided comments and of participants in the meeting is gratefully reflected in the final text.

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.

Many individuals from various countries contributed to the development of the GDWQ. The efforts of all who contributed to the preparation of this document and in particular those who provided peer or public domain review comment are greatly appreciated.

Acronyms and abbreviations used in the text

ADI	acceptable daily intake
CAS	Chemical Abstracts Service
FAO	Food and Agriculture Organization of the United Nations
JMPR	Joint FAO/WHO Meeting on Pesticide Residues
NOAEL	no-observed-adverse-effect level
NOEL	no-observed-effect level
PTDI	provisional tolerable daily intake
USA	United States of America
WHO	World Health Organization

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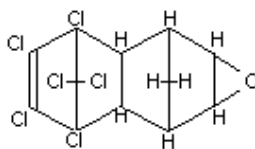
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1. GENERAL DESCRIPTION

1.1 Identity

CAS No.:	72-20-8
Molecular formula:	C ₁₂ H ₈ Cl ₆ O

The chemical name of endrin is 1,2,3,4,10,10-hexachloro-6,7-epoxy-1,4,4a,5,6,7,8,8a-octahydro-1,4-*endo,endo*-5,8-dimethanonaphthalene. Endrin is the *endo,endo* stereoisomer of dieldrin. Its structural formula is given below:



1.2 Physicochemical properties (IPCS, 1992)

Property	Value
Physical state	Crystalline solid
Melting point	226–230 °C (decomposes above 245 °C)
Vapour pressure	36×10^{-6} Pa at 25 °C
Solubility in water	Practically insoluble (0.23 mg/litre at 25 °C)
Log octanol–water partition coefficient	5.34

1.3 Major uses

Endrin is a foliar insecticide that acts against a wide range of agricultural pests at doses of 0.2–0.5 kg of active material per ha. It has a broad spectrum of control and is particularly effective against Lepidoptera. It is used mainly on cotton but also against pests of rice, sugar-cane, maize and other crops. It is also used as a rodenticide (IPCS, 1992).

1.4 Environmental fate

The mechanisms by which endrin is removed from the environment include photodecomposition and bacterial degradation. In sunlight, the ketone, δ -ketoendrin, is the main product formed; approximately 50% isomerization to the ketone took place within 7 ± 2 days with exposure to intense summer sun. Microbial degradation of endrin depends on the presence of an appropriate microbial species and suitable soil conditions; it occurs under anaerobic conditions. Biodegradation is aided by fungi and bacteria, and the major transformation product is δ -ketoendrin (IPCS, 1992).

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2. ANALYTICAL METHODS

Endrin in water is determined by extraction with hexane/ether followed by gas chromatography with electron capture detection. The detection limit is about 0.002 µg/litre (Lichtenberg et al., 1970).

3. ENVIRONMENTAL LEVELS AND HUMAN EXPOSURE

3.1 Air

A national monitoring programme for pesticides in the air of various states of the USA showed the occasional presence of endrin over agricultural areas at a mean level of 2.6 ng/m³ for positive samples (8%) and a maximum concentration of 19.2 ng/m³ (IPCS, 1992).

3.2 Water

In a programme to monitor surface water in the USA in 1976–1980, endrin was found in only 0.1% of samples, at a maximum value of 0.04 µg/litre. No endrin was found in water from 33 sites in the Upper Great Lakes in Canada (<0.01 µg/litre). In a survey of the aquatic environment in the Netherlands, including drinking-water, 1826 samples were taken at 99 sampling sites between September 1969 and 1977; traces of endrin were reported occasionally (IPCS, 1992). During 1976, endrin was found at a mean concentration of 4 ng/litre (range 1–7 ng/litre) in drinking-water in Ottawa, Canada (Williams et al., 1978).

3.3 Food

Studies on complete prepared meals in the USA, started in May 1961, have shown the occasional presence of small amounts of endrin. These measurements indicate that the total average daily intake of endrin from food decreased from 0.009 µg/kg of body weight in 1965 to 0.0005 µg/kg of body weight in 1970, with a further decrease subsequently. In total diet studies of adults in the USA, representative foods were purchased in 27 US cities in 1980–1982; the daily intake of endrin was found to be below 0.001 µg/kg of body weight in 1978, but none was detected in 1979, 1980 or 1981–1982 (IPCS, 1992).

No endrin residues were found in total diet studies carried out in the Netherlands in 1976–1978 and in similar studies carried out in the United Kingdom in 1985–1988 (IPCS, 1992).

4. KINETICS AND METABOLISM IN LABORATORY ANIMALS AND HUMANS¹

Unlike dieldrin, endrin is rapidly metabolized by animals; the storage in the fat of animals is very low compared with that of other compounds of similar chemical structure.

Formation of *anti*-12-hydroxyendrin, together with its sulfate and glucuronide conjugates, is considered to be the major route of metabolism of endrin. Four other metabolites have been reported, but their concentrations are generally lower than those of *anti*-12-hydroxyendrin and its conjugates.

The metabolism of endrin in rabbits is superficially different from that in rats. The major metabolite is still *anti*-12-hydroxyendrin, but it is conjugated with sulfate and eliminated in the urine. Some *syn*-12-hydroxyendrin was also detected as its sulfate in urine, and perhaps conjugation and elimination prevented further oxidation to 12-ketoendrin.

The plant metabolite of endrin, δ -ketoendrin, is rapidly metabolized by animals. Three metabolites were found in rabbit urine after oral administration of δ -ketoendrin. It is understood that δ -ketoendrin is unlikely to be formed under conditions of good agricultural practice and that the compound is less toxic to mammals than endrin.

5. EFFECTS ON EXPERIMENTAL ANIMALS AND IN VITRO TEST SYSTEMS²

The primary site of action of endrin is the central nervous system. This fact is evidenced by convulsions, which result from acute poisoning and from administration of repeated relatively high doses.

Long-term studies of toxicity and carcinogenicity have been performed in mice and rats. No carcinogenic effect was found, but these studies had shortcomings, including poor survival of the animals. The NOEL for toxicity in a 2-year study in rats was 1 mg/kg of diet (equivalent to about 0.05 mg/kg of body weight per day). Tumour-promoting effects were not demonstrated when endrin was tested in combination with subminimal quantities of chemicals known to be carcinogenic to animals. The data are insufficient to indicate whether endrin is a carcinogenic hazard to humans.

In a dog study in 1969, groups comprising seven male and seven female dogs were fed dietary levels of 0, 0.1, 0.5, 1.0, 2.0 or 4.0 mg of dieldrin per kg for 2 years. There were no deaths due to the treatment, nor were there any changes in body weight increase or food consumption in any group. The only clinical abnormalities were in one female and two male dogs fed 4.0 mg/kg and one female fed 2.0 mg/kg that showed evidence of, or were observed having, convulsions; the earliest incidence was

¹ This section has been summarized from FAO/WHO (1971) and IPCS (1992).

² This section has been summarized from FAO/WHO (1971) and IPCS (1992).

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in a male dog after 5 months on 4.0 mg/kg. The only changes in organ weights were occasional slight increases in liver or liver to body weight ratios in the dogs fed 2.0 and 4.0 mg/kg. After 2 years, pathological examination showed slight vacuolation of hepatic cells in the females and diffuse pigmentation in one male and all females. At 4.0 mg/kg, vacuolar degeneration and diffuse brown pigment in the hepatic cells were evident in all dogs, without any sex differentiation. In two of the dogs, which had convulsions, autopsies revealed some pathological changes in the brain. All other organs in the dogs fed 2.0 or 4.0 mg/kg and all organs in the dogs fed 1.0 mg/kg or less showed no morphological changes that were considered to be attributable to dietary endrin. There were no significant changes in the blood picture or in the chemical or physical characteristics of the urine attributable to endrin. The level of endrin causing no toxicological effects was 1 mg/kg in the diet, equivalent to 0.025 mg/kg of body weight per day.

Reproduction studies with endrin in several species revealed no influence of endrin on maturation, but fetal and postnatal mortality were increased. There is no evidence of teratogenic activity.

6. EFFECTS ON HUMANS³

Exposure of humans to a toxic dose of endrin may lead within a few hours to such signs and symptoms of intoxication as excitability and convulsions, and death may follow within 2–12 h after exposure if appropriate treatment is not administered immediately. Recovery from non-fatal poisoning is rapid and complete.

7. GUIDELINE VALUE

An ADI of 0.0002 mg/kg of body weight was established by JMPR in 1970 for endrin on the basis of the NOAEL of 0.025 mg/kg of body weight per day in the 2-year study in dogs and applying a safety factor of 100 (FAO/WHO, 1971). In 1994, JMPR converted this ADI into a PTDI with the same numerical value (FAO/WHO, 1995).

This PTDI was used as the basis for the drinking-water guideline. Intake of endrin from all sources is generally low and far below the PTDI. The proposed guideline value is therefore based on an allocation of 10% of the PTDI to drinking-water, giving a value of 0.6 µg/litre.

8. REFERENCES

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