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DDT and its Derivatives in Drinking-water

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

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.

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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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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:

Dr J. Bartram, Coordinator, Water Sanitation and Health Programme, WHO Headquarters, and formerly WHO European Centre for Environmental Health
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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

ATSDR	Agency for Toxic Substances and Disease Registry
CAS	Chemical Abstracts Service
CYP	cytochrome P-450
DDA	2,2-bis(4-chlorophenyl)ethanoic acid
DDD	dichlorodiphenyldichloroethane
DDE	dichlorodiphenyldichloroethene
DDT	*p*,*p*'-dichlorodiphenyltrichloroethane
FAO	Food and Agriculture Organization of the United Nations
GEMS	Global Environment Monitoring System
IARC	International Agency for Research on Cancer
JMPR	Joint FAO/WHO Meeting on Pesticide Residues
NOAEL	no-observed-adverse-effect level
PTDI	provisional tolerable daily intake
UNEP	United Nations Environment Programme
USA	United States of America
WHO	World Health Organization

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1. GENERAL DESCRIPTION

1.1 Identity

CAS No.:	107917-42-0
Molecular formula:	$C_{14}H_9Cl_5$

The term DDT refers to *p*,*p*'-DDT, or *p*,*p*'-dichlorodiphenyltrichloroethane. The compound's structure permits several different isomeric forms, such as *o*,*p*'-DDT. The term DDT is also applied to commercial products consisting predominantly of *p*,*p*'-DDT, but also containing smaller amounts of other compounds, including *p*,*p*'- and *o*,*p*'-DDD (dichlorodiphenyldichloroethane) and *p*,*p*'- and *o*,*p*'-DDE (dichlorodiphenyldichloroethene) (IPCS, 1989).

1.2 Physicochemical properties (IPCS, 1989)

Property	*Value*
Physical state	White, crystalline solid
Melting point	108.5–109 °C
Vapour pressure	2.53×10^{-5} Pa at 20 °C
Solubility in water	Highly insoluble (1 µg/litre)
Log octanol–water partition coefficient	7.48

1.3 Organoleptic properties

All DDT isomers are tasteless, almost odourless solids. The odour threshold for DDT in water is 0.35 mg/litre (Zoeteman, 1980).

1.4 Major uses

DDT is a non-systemic contact insecticide with a broad spectrum of activity. It was banned in several countries in the early 1970s because of ecological considerations, and many other countries have more recently restricted or banned its use except when it is needed for the protection of human health. DDT is still used in some countries for the control of vectors that transmit yellow fever, sleeping sickness, typhus, malaria and other insect-transmitted diseases.

DDT was designated as a persistent organic pollutant in 1997 by the Governing Council of the United Nations Environment Programme (UNEP, 1997).

1.5 Environmental fate

DDT and its metabolites are persistent in the environment and resistant to complete degradation by microorganisms, although photochemical degradation does occur. The persistence of DDT is substantially lower in tropical climates than in temperate ones (a few months compared with years) (IPCS, 1989).

DDT and its metabolites are readily adsorbed onto sediments and soils, which can act both as sinks and as long-term sources of exposure. Because of its strong tendency to be adsorbed onto surfaces, most DDT that enters water is and remains firmly attached to soil particles. If it does find its way into water, it is gradually lost by adsorption onto surfaces (IPCS, 1989).

The physical and chemical properties of DDT and its metabolites enable these compounds to be taken up readily by organisms from the surrounding medium and from food. In aquatic organisms, uptake from water is generally more important, whereas food is the major source for terrestrial fauna. High lipid solubility and low water solubility lead to the retention of DDT and its stable metabolites in fatty tissue. In general, organisms at higher trophic levels tend to contain more DDT-type compounds than those at lower ones. These compounds can be transported around the world in the bodies of animals, as well as in ocean and air currents (IPCS, 1989).

2. ANALYTICAL METHODS

DDT and its metabolites may be determined in water by gas chromatography with electron capture detection. The limits of detection are 60 ng/litre for *p*,*p*'-DDT, 10 ng/litre for *p*,*p*'-DDE and 2.5 ng/litre for *p*,*p*'-DDD (IARC, 1991).

3. ENVIRONMENTAL LEVELS AND HUMAN EXPOSURE

3.1 Air

When DDT is sprayed, any that fails to adhere to its target drifts away; vaporization from treated fields can be detected for more than 6 months after application. Although most of it settles in the same area, some drifts over long distances. Traces of DDT have been found in dust known to have drifted over 1000 km and in water produced by melting Antarctic snow.

With rare exceptions, concentrations of DDT in air in non-agricultural areas have been in the range <1–2.36 ng/m^3. In agricultural communities, concentrations have ranged from 1 to 22 ng/m^3. In communities with antimosquito fogging programmes, concentrations may be much higher, 8.5 µg/m^3 being the highest level recorded (IPCS, 1979).

3.2 Water

In a study of surface waters in the USA during 1964–1968, the highest level recorded for a DDT-related compound was 0.84 µg/litre. Concentrations in Germany were even lower, averaging 10 ng/litre and never going as high as 1 µg/litre. The average concentrations of total DDT in drinking-water in Czechoslovakia were 11 and 15 ng/litre in 1972 and 1973, respectively. DDT was not detected (limit 0.01 ng/litre) in tap water in a 1977 survey carried out in Ottawa, Canada (IPCS, 1979).

Within the GEMS water network, DDT and its metabolites were found in some rivers during 1979–1984. The following average concentrations were measured (Meybeck et al., 1989): India, 560 ng/litre; Italy, 3 ng/litre; Netherlands, <2 ng/litre; USA, 0.2 ng/litre; Canada and France, not detected.

3.3 Food

Daily intake of DDT from food has been measured in several countries. During 1985–1988, in Australia, Finland, Guatemala, Japan, Thailand, the United Kingdom and the USA, the reported mean daily dietary intake by the average adult was less than 2 µg (Galal-Gorchev, 1991). In Egypt, in 1988, a mean daily intake of 960 µg was reported for the average adult (Abdel-Gawaad & Shams El Dine, 1989).

Human milk may contain a higher concentration of DDT than cows' milk in the same country. The average concentration of total DDT in whole human milk in 15 countries between 1976 and 1986 ranged from 2 to 380 µg/litre (UNEP, 1988). On the assumption that a 5-kg infant consumes 0.6 litres of milk per day, the intake at the highest concentration found would amount to about 200 µg/day, or 40 µg/kg of body weight per day.

3.4 Estimated total exposure and relative contribution of drinking-water

It has been estimated that over 90% of the DDT stored in the general population is derived from food (IPCS, 1979). In 1965, intake in the USA was approximately 40 µg/day per person from food, less than 46 ng/day from water, less than 60 ng/day from urban air and less than 0.5 µg/day from air in small agricultural communities. Other investigators have also concluded that food is the major source of intake of DDT and related compounds for the general population (IPCS, 1979).

4. KINETICS AND METABOLISM IN LABORATORY ANIMALS AND HUMANS

DDT is absorbed after inhalation and ingestion, the latter being the more important route of absorption. Absorption of small doses, such as those found in food residues, is virtually complete and is facilitated by the presence of fat in food. Even in solution, DDT is poorly absorbed through the skin.

Most of the known facts concerning the distribution, storage and excretion of DDT have been demonstrated in humans as well as in laboratory animals. The compound is stored preferentially in fat, and its storage in organs and other tissues following repeated intake is proportional to their neutral fat content. However, uptake of DDT by fat is slow; therefore, much more is distributed to other tissues following a single, large dose, and much more to adipose tissue following many small doses. In spite of the affinity of DDT for adipose tissues, most of the DDT-related compounds in blood are carried by proteins, less than 1% being carried in the tiny droplets of fat normally present in the blood.

Following repeated doses, storage in adipose tissue increases rapidly at first and then more gradually until a steady state is reached. Storage is relatively less at higher dosages because excretion is relatively greater. In humans, the time necessary to reach storage equilibrium is at least 1 year. There is a gradual reduction in the amount of DDT stored in the tissues as exposure to the compound is discontinued.

Like most species, humans convert some DDT to DDE, which is stored even more avidly than the parent compound. A small amount of DDD, an intermediate in the formation of the main excretory product 2,2-bis(4-chlorophenyl)ethanoic acid (DDA), may also be found in tissues. A number of other metabolites have been detected in laboratory animals but not in humans. Technical DDT is more readily excreted and less readily stored than *p*,*p*'-DDT because it contains 15–20% of *o*,*p*'-DDT (IPCS, 1979).

5. EFFECTS ON LABORATORY ANIMALS AND IN VITRO TEST SYSTEMS[1]

Hepatic effects of DDT in rats include increased liver weights, hypertrophy, hyperplasia, induction of microsomal enzymes, including cytochrome P-450, cell necrosis, increased activity of serum liver enzymes and mitogenic effects, which might be related to a regenerative liver response to DDT. The potencies of DDT, DDE and DDD for induction of CYP2B are of the same order of magnitude. The effects on CYP2B and associated enzymes indicate that males have a lower threshold than females, in which these enzymes were induced to a greater extent.

Conflicting data were obtained with regard to some genotoxic end-points. In most studies, DDT did not induce genotoxic effects in rodent or human cell systems, nor was it mutagenic to fungi or bacteria. *p*,*p*'-DDE weakly induced chromosomal aberrations in cultured rodent cells and mutation in mammalian cells and insects, but not in bacteria. The induction of structural chromosomal aberrations in mouse spleen cells was maximal 24 h after intraperitoneal administration of DDT.

The JMPR Meeting could not reach a conclusion about the carcinogenicity of DDT in monkeys, as a 130-month study at one dose in non-human primates showed a small number of tumours at various sites. A working group convened by IARC classified the DDT complex as a non-genotoxic carcinogen in rodents and a potent promoter of liver tumours. The 1984 JMPR estimated that the lowest relevant NOAEL for carcinogenicity in rats was 6.2 mg/kg of body weight per day and concluded that "there is no significant risk of DDT producing tumours in humans." The overall evaluation of the IARC group was that "DDT is possibly carcinogenic to humans" but that "there is inadequate evidence in humans for the carcinogenicity of DDT."

The 1984 JMPR concluded that "there is no firm evidence that DDT has any reproductive or teratogenic effects." The effects of DDT on reproduction and development in humans and experimental animal have been reviewed. After treatment of rabbits with 3 mg/kg of body weight for 12 weeks, increased serum concentrations

[1] This section is taken from FAO/WHO (2001).

of DDT were found, but no adverse effects on reproductive outcome were observed. The relevance for human reproduction of slight changes in the ovulation rate, the relative proportion of uteroglobin and progesterone concentrations in rabbits is not clear. After perinatal exposure to *p*,*p*'-DDE, there was some evidence of impaired sexual development in male pups, including an increased frequency of thoracic nipple retention and a reduction in the male anogenital distance, with a NOAEL of 10 mg/kg of body weight per day. The ATSDR concluded that the DDT complex could impair reproduction and/or development in mice, rats, rabbits, dogs and avian species at doses ≥5 mg/kg of body weight per day. The lowest relevant NOAEL for developmental effects was reported to be 1 mg/kg of body weight per day in rats.

Data of limited usefulness for human risk assessment indicated changes in spontaneous behaviour and brain muscarinic receptors in mice receiving DDT by a single oral administration of a dose of 0.5 mg/kg of body weight on postnatal day 10. Similar effects were not observed when this dose was administered on other postnatal days. Three multigeneration studies in rats and mice showed no reproductive effects at doses of 1–6.5 mg/kg of body weight per day.

Quantitative measurements of the transfer of DDE from pregnant or lactating rats or rabbits to their fetuses or suckling neonates showed that the concentrations in rabbit fetuses were much higher than those in blastocysts and that, in rats, lactation is a quantitatively far more important route than transplacental transfer. The persistent DDT metabolite in animals, 3-methylsulfonyl-DDE, is a potent transplacental and transmammary adrenal toxicant in mice. Treatment of mice with a single dose of 3 mg/kg of body weight resulted in mitochondrial destruction in the adrenal zona fasciculata.

Activation of estrogen receptors and inhibition of androgen receptors may be mechanisms of the action of DDT-related compounds that lead to the observed perturbations of reproductive function. The *p*,*p*'-DDE metabolite acts as an antiandrogen. DDE binds to the androgen receptor *in vitro* and inhibits 5-dihydrotestosterone-induced transcriptional activation with a potency similar to that of the antiandrogenic drug hydroxyflutamide. The results of competitive binding assays showed that *o*,*p*'-DDT, *o*,*p*'-DDD, *o*,*p*'-DDE and *p*,*p*'-DDT bind to the human estrogen receptor but with an approximately 1000-fold weaker affinity than that of estradiol.

Numerous studies have been conducted on the effect of DDT on the immune system of laboratory animals. Because no validated study protocols were used in different species, at different doses, application periods and routes of exposure, and with evaluation of different parameters, a reliable NOAEL could not be estimated for effects on the immune system.

6. EFFECTS ON HUMANS[2]

Epidemiological studies on the association between exposure to DDT and cancer risk were reviewed for the 2000 JMPR. The association between exposure to DDT and/or DDE and breast cancer in women that was suggested in some case–control studies was not confirmed in later prospective studies. The results of studies of pancreatic cancer, multiple myeloma, non-Hodgkin lymphoma and uterine cancer did not support the hypothesis of an association with environmental exposure to the DDT complex (e.g., in food). Under circumstances of heavy, prolonged occupational exposure to technical-grade DDT, an increased risk for pancreatic cancer could not be excluded.

Pesticide applicators are exposed primarily to *p*,*p*'-DDT, whereas it is the *p*,*p*'-DDE metabolite to which the general population is exposed in the diet or drinking-water. Summaries of data on exposure and DDT concentrations in human tissues, milk and blood have shown that the mean concentrations in populations have declined in much of the world, and the declines seen in various countries correspond to restrictions on DDT use. The available data on humans do not show causal relationships for carcinogenicity in any organ system or significant adverse health effects after repeated exposure to concentrations up to 0.25 mg/kg of body weight per day.

Few data were available on reproductive effects in humans, and the few that were provided showed no correlation between exposure to DDT and stillbirth, miscarriage or premature rupture of fetal membranes. In a study of 859 children in the USA who were tested at the age of 3, 4 or 5 years, neither transplacental nor lactational exposure to DDT affected psychomotor or mental behavioural patterns or measures of school performance, even when the PTDI (see below) was exceeded.

7. GUIDELINE VALUE

IARC (1991) has concluded that there is insufficient evidence in humans and sufficient evidence in experimental animals for the carcinogenicity of DDT (Group 2B).

The newer studies and reviews provided the basis for a change by the 2000 JMPR Meeting of the PTDI established in 1984 (FAO/WHO, 1985). The JMPR Meeting (FAO/WHO, 2001) derived a PTDI of 0.01 mg/kg of body weight on the basis of the NOAEL of 1 mg/kg of body weight per day for developmental toxicity in rats and a safety factor of 100. This PTDI is used for the derivation of the guideline value.

Because infants and children may be exposed to greater amounts of chemicals in relation to their body weight and because of concern over the bioaccumulation of DDT, the guideline value was calculated on the basis of a 10-kg child drinking 1 litre of water per day. Moreover, because there can be significant exposure to DDT by routes other than water, a 1% allocation of the PTDI to drinking-water was chosen.

[2] This section is taken from FAO/WHO (2001).

This leads to a guideline value for DDT and metabolites in drinking-water of 1 μg/litre.

It should be emphasized that, as for all pesticides, the recommended guideline value for DDT in drinking-water is set at a level to protect human health; it may not be suitable for the protection of the environment or aquatic life. The benefits of DDT use in malaria and other vector control programmes outweigh any health risk from the presence of DDT in drinking-water.

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