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REGIONAL OFFICE FOR EUROPE

REVISION OF THE WHO GUIDELINES FOR DRINKING-WATER QUALITY

Report on the
Second Review Group Meeting
on Pesticides

Rennes, France
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EUR/HFA TARGET 20

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TARGET 20

WATER POLLUTION

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[a] *Targets for health for all.* Copenhagen, WHO Regional Office Europe, 1985 (European Health for All Series, No. 1).

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1. INTRODUCTION

As part of the revision of the WHO Guidelines for Drinking-Water Quality published in 1984, a First Review Group Meeting on Pesticides convened by WHO Regional Office for Europe (EURO) was held in Busto Garolfo (Milan), Italy, 25-30 June 1990. This First Review Group Meeting evaluated the following pesticides: aldicarb, aldrin/dieldrin, atrazine, bentazon, chlordane, chlortoluron, 1,2-dichloropropane, 1,3-dichloropropane, 1,3-dichloropropene, ethylene dibromide (EDB), heptachlor and heptachlor epoxide, hexachlorobenzene, isoproturon, lindane and permethrin. The rationale for deriving (or not deriving) guideline values for these pesticides can be found in the Meeting's report (EUR/ICP/CWS 027).

The Second Review Group Meeting on Pesticides was convened by EURO in Rennes, France, 2-6 September 1991 with the financial support of the French Ministry of Health, the Ecole nationale de la Santé publique hosted the meeting. The list of participants is given as Annex I.

On behalf of the Regional Director of the Regional Office for Europe, Mr Xavier Bonnefoy welcomed the participants of the Second Review Group on Pesticides to Rennes. He introduced the work of WHO on drinking-water quality guidelines, work that is being shared between WHO Headquarters and its Regional Office for Europe. He emphasized the importance of the Guidelines for Drinking-Water Quality throughout the world and of the present revision which was making good progress. Mr Bonnefoy also expressed WHO's gratitude to the Ecole nationale de santé publique for providing the scientific and administrative support in organizing the meeting. Moreover, the preparation of draft evaluation documents, on substances under consideration at this meeting, by Italy, Canada, Germany and the U.S.A. was gratefully acknowledged. He also thanked the Organics Co-ordinator, Dr U. Lund of the Water Quality Institute of Denmark who had issued the documents and prepared overviews incorporating the comments received.

Mr Antoine Montiel served as the Chairman and Dr Burin and Mr Fawell as Rapporteurs.

Professor René Seux, Chef du Département Environnement et Santé welcomed the participants on behalf of the Ecole nationale de santé publique (ENSP), Rennes. Professor Seux fully endorsed the involvement of the ENSP in this international collaboration. He emphasized the importance of reviewing the present WHO Guidelines for Drinking-Water Quality and wished the participants a successful outcome to the difficult deliberations ahead of them as well as a pleasant stay in Rennes.

2. GENERAL

Draft evaluation documents were prepared by Italy, Canada, Germany and the U.S.A. for the following pesticides considered by the Meeting: alachlor, carbofuran, 2,4-D, DDT, 1,2-dibromo-3-chloropropane (DBCP), MCPA (methylchlorophenoxy acetic acid), methoxychlor, metolachlor, molinate, pendimethalin, propanil, pyridate, simazin, trifularin and other chlorophenoxy pesticides.

Previous evaluations of these pesticides carried out by the International Agency for Research on Cancer (IARC), the Joint FAO/WHO Meeting on Pesticide Residues (JMPR) and the International Programme on Chemical Safety (IPCS) were carefully assessed prior to the derivation of guideline values. In addition, two EURO meetings, convened in 1987, evaluated a number of these pesticides (EURO Environmental Health Series 27). These evaluations were also carefully considered at the Meeting.

For most pesticides, a tolerable daily intake (TDI) was established based on the available health effects information. The TDI is expressed in μg or mg/kg of body weight. For two pesticides, DBCP and alachlor, a range of reference risk values for carcinogenity was presented.

In the derivation of guideline values, the Meeting used, unless otherwise stated, a 60 kg body weight and a daily consumption of two litres of drinking-water.

3. SUMMARY EVALUATIONS

3.1 Alachlor

Alachlor is lost from soil mainly through volatilization, photodegradation and biodegradation. Many alachlor degradation products have been identified in soil. This compound has been detected in groundwater in only a few cases, but it is found more frequently in surface water.

On the basis of available experimental data, evidence for the genotoxicity of alachlor is considered to be equivocal. However, a metabolite of alachlor has been shown to be mutagenic. Available data from two studies in rats clearly indicate that this compound is carcinogenic, causing benign and malignant tumours of the nasal turbinate, malignant stomach tumours, and benign thyroid tumours.

In view of the data on carcinogenicity, guideline values were calculated by applying the linearized multistage model, incorporating a surface area correction, to the combined data on the incidence of nasal tumours in rats. Concentrations in drinking-water relating to an excess risk of cancer of 10^{-4}, 10^{-5} and 10^{-6} are 30, 3 and 0.3 μg/l, respectively. The value at 10^{-6} is close to the limit of detection of 0.1 μg/litre.

3.2 Carbofuran

Carbofuran is a systemic acaricide, insecticide and nematocide. It can undergo photodegradation or chemical and microbial degradation. It is sufficiently mobile and persistent to leach from the soil and has been found in ground water with typical levels of 1 to 5 μg/l.

Carbofuran poisoning resembles organophosphate intoxication in its clinical manifestation. The available data on man showed that while clinical signs of acetylcholinesterase inhibition were observed at a single oral dose of 0.10 mg/kg-bw, these were absent at 0.05 mg/kg-bw. Hence, this latter level can be regarded as a NOAEL in man.

From a 1 year study in dogs a NOAEL of 0.50 mg/kg-bw/day can be derived. The NOAEL for systemic effects in dams in a rat teratology study was 0.1 mg/kg-bw/day. On the basis of the available studies this compound does not appear to be carcinogenic. Carbofuran does not have genotoxic activity.

A TDI of 1.67 µg/kg-bw can be calculated by applying an uncertainty fsctor of 30 (10 for intraspecies variation and 3 for the steep dose response curve) to the NOAEL of 0.05 mg/kg-bw in man. This TDI is supported by observations in laboratory animals giving an adequate margin of safety for the NOAEL in rat and dog.

An allocation of 10% of the TDI to water results in the proposed guideline value of 5.0 µg/l.

3.3 Chlorophenoxy Herbicides (excluding 2,4-D and MCPA)

The chlorophenoxy herbicides considered by the Working Group included dichlorprop, 2,4-DB, 2,4,5-T, silvex, mecoprop and MCPB. The half-lives for degradation in the environment of these compounds are in the order of several days. Based on limited monitoring data, these herbicides are not frequently found in drinking-water; when detected, the concentration are usually no greater than a few µg/l. These chlorophenoxy herbicides are not often found in food.

Chlorophenoxy herbicides, as a group, have been classified in Group 2B by IARC. However, based on the available data in studies in exposed populations and animals, it is not possible to assess the carcinogenic potential to humans of any specific chlorophenoxy herbicide.

The TDI for dichlorprop of 0.0364 mg/kg-bw was based on a NOAEL of 3.64 mg/kg-bw/day for renal toxicity in a two year study in rats and the incorporation of an uncertainty factor of 100 (10 for intraspecies variation and 10 for interspecies variation). With the allocation of 10% of the TDI to drinking-water, the guideline value is 109 µg/l.

The TDI of 2,4-DB of 0.03 mg/kg-bw was based on a NOAEL of 3.0 mg/kg-bw/day for effects on body and organ weights, as well as haematological parameters in a two year study in rats and the application of an uncertainty factor of 100 (10 for intraspecies variation and 10 for interspecies variation). Allocating 10% of the TDI to drinking-water the resulting guideline value for 2,4-DB i6 90 µg/l.

For 2,4,5-T, the TDI was determined to be 0.003 mg/kg-bw, based on a NOAEL of 3.0 mg/kg-bw/day for effects on body and organ weights and renal toxicity in a two year study in rats, and an uncertainty factor of 1000 (10 for intraspecies variation, 10 for interspecies variation and 10 for the suggested association between exposure to 2,4,5-T and soft tissue sarcoma and non-Hodgkin's lymphoma in epidemiological studies). Therefore, if 10% of the TDI is allocated to drinking-water, the guideline value for 2,4,5-T is 9 µg/l.

The TDI for silvex of 0.003 mg/kg-bw was based on a NOAEL of 0.9 mg/kg-bw/day for hepatic toxicity in a two year study in dogs, and the incorporation of an uncertainty factor of 300 (10 for interspecies variation, 10 for intraspecies variation and 3 for limitations in the database), resulting in a guideline value of 9 µg/l, with the allocation of 10% of the TDI to drinking-water.

The NOAEL for mecoprop was determined to be 1 mg/kg-bw/day for effects on kidney weight in one and two year studies in rats, which, when an uncertainty factor of 300 is applied (10 for intraspecies variation and 10 for interspecies variation and 3 for limitations in the data base) yields a TDI of 0.003 mg/kg-bw/day. Therefore, with the allocation of 10% of the TDI to drinking-water, the guideline value for mecoprop is 10 µg/l.

The Working Group was of the opinion that the currently available toxicological data were insufficient to be used as the basis for a guideline value for HCPB.

3.4 Chlortoluron

Chlortoluron is a pre- or early post-emergence herbicide which is slowly biodegradable and mobile in soil, and which has been detected in drinking-water at concentrations of less than 1 µg/l. There is only very limited exposure to this compound from food.

It is of low acute and chronic toxicity in animals but has been shown to cause an increase in adenomas and carcinomas of the kidney of male mice given high doses for 2 years. Chlortoluron and its metabolites show no evidence of genotoxicity.

In view of this the guideline value for chlortoluron was calculated using a TDI approach. An uncertainty factor of 1000 (100 for inter and intra species variation and 10 for evidence of carcinogenicity) was applied to the NOAEL of 11.3 mg/kg-bw in the 2 year feeding study in mice to give a TDI of 0.0113 mg/kg-bw. An allocation of 10% of the TDI to drinking-water results in the proposed guideline value of 33.9 µg/l.

3.5 DDT

The structure of DDT allows several different isomeric forms and the commercial products consist predominantly of p,p'-DDT. The use of DDT in some countries has been restricted or even prohibited, but it is still extensively used in some countries, both in agriculture and for vector control. It is a persistent insecticide, stable under most environmental conditions; both DDT and some of its metabolites are resistant to complete breakdown by soil microorganisms. In small doses, DDT and its metabolites are almost totally absorbed in humans following ingestion or inhalation and are stored in adipose tissue and milk.

IARC (in press) has concluded that there is insufficient evidence in humans and sufficient evidence in experimental animals for the carcinogenicity of DDT (Group 2B) based upon liver tumors observed in rats and mice. Moreover, JMPR concluded that the mouse is particularly sensitive to DDT because of its genetic and metabolic characteristics. In most studies, DDT did not induce genotoxic effects in rodent or human cell systems nor was it mutagenic in fungi or bacteria. DDT impaired reproduction in several species. The working group accepted the ADI of 0.02 mg/kg-bw recommended by the JMPR in 1984. This would provide for adults a 500 fold margin of safety for the NOAEL of 10 mg/kg bw/day found in a 7 year study in monkeys.

Since infants and children may be exposed to greater amounts of chemicals in relation to their body-weight and there is concern over the bio-accumulation of DDT, a 10 kg child drinking 1 litre water/day was chosen for the calculation of the guideline value. Moreover, because there is significant exposure to DDT by other routes than water, a 1% allocation of the ADI to drinking-water was chosen. This leads to a proposed guideline value for DDT and metabolites in drinking-water of 2 μg/l.

The group wished to emphasize 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.

3.6 1,2-Dibromo-3-Chloropropane (DBCP)

DBCP is a soil fumigant which is highly soluble in water. It has a taste and odour threshold in water of 10 μg/l. A limited survey found DBCP at levels of up to a few μg/l in drinking-water. DBCP was also detected in vegetables grown in treated soils, and low levels have been detected in air.

On the basis of animal data from different strains of rats and mice, DBCP was determined to be carcinogenic in both sexes by the oral, inhalation and percutaneous routes. DBCP was also determined to be a reproductive toxicant in humans and several species of laboratory animals. IARC has classified DBCP in Group 2B based upon sufficient evidence of carcinogenicity in animals. Recent epidemiological evidence suggests an increase in cancer mortality in individuals exposed to high levels of DBCP.

The linearized multistage model, incorporating a body surface area correction was applied to the data on the incidence of stomach, kidney and liver tumors in the male rat in a 104 week dietary study. The concentrations in drinking-water relating to an excess risk of cancer of 10^{-4}, 10^{-5} and 10^{-6} are 2.5 μg/l, 0.25 μg/l and 0.025 μg/l, respectively. These concentrations should be protective for the reproductive toxicity of DBCP.

The concentration associated with a cancer risk of 10^{-6} is at the present time slightly lower than the detection limit of existing analytical methods which is of the order of 0.03 μg/l.

3.7 2,4 - Dichlorophenoxyacetic Acid

2,4 - dichlorophenoxyacetic acid (2,4-D) is a chlorophenoxy herbicide which is used very extensively in the control of broadleafed weeds. The half-life for biodegradation in soil ranges from a few days to six weeks, while the half- life in water ranges from one to several weeks. Based on limited monitoring data, levels in drinking-water generally do not exceed a few μg/l. 2,4-D is rarely found in foods.

IARC has classified chlorophenoxy herbicides in Group 2B. Although in one study in humans there was a marginally significant trend in the excess risk of non-Hodgkins lymphoma with increasing duration of exposure to chlorophenoxy herbicides, it is not possible to evaluate the carcinogenic potential of 2,4-D per se on the basis of available epidemiological data. A dose-related increase in the incidence of astrocytomas of the brain was reported in a carcinogencity study in rats. However, this study was considered to be of limited value in the evaluation of carcinogenicity. Since the data on the carcinogenic potential of 2,4-D are inadequate, the guideline value is based on threshold approach for other toxic endpoints. The NOAEL for effects on the kidney in long-term studies in rats and mice was considered to be 1 mg/kg bw/day. An uncertainty factor of 100 was applied to this NOAEL (10 for intraspecies varistion and 10 for interspecies variation), resulting in a TDI of 0.01 mg/kg bw. The working group was of the opinion that use of an uncertainty factor of 100 with this NOAEL would provide a sufficient margin of safety with respect to the lowest dose which was associated with an increase in brain tumours in rats. The guideline value, based on an allocation of 10% of the TDI to drinking-water, is 30 µg/l. The Working Group was informed that carcinogenicity bioassays in rats and mice are currently being conducted, and recognized that the guideline value should be re-examined in the light of the results of these studies when available.

3.8 MCPA

MCPA is a chlorophenoxy post-emergence herbicide which is very soluble, highly mobile and can leach from the soil. It is metabolized by bacteria and can be photochemically degraded. MCPA has only limited persistence and has not been frequently detected in drinking-water.

There are only limited and inconclusive data on the genotoxicity of MCPA. IARC evaluated MCPA in 1983 and concluded that the available data on humans and experimental animals were inadequate for an evaluation of carcinogenicity. Further evaluations by IARC on chlorophenoxy herbicides in 1986 and 1987 concluded that evidence is limited in humans and inadequate in animals for the carcinogenicity of chlorophenoxy herbicides (Group 2 B). No adequate epidemiological data on exposure to MCPA alone are available.

Short-term toxicity studies are available in rats and dogs. The NOAEL was 0.15 mg/kg bw/day in a 1-year feeding study in dogs based on renal and liver toxicity observed at higher dose levels. No long-term toxicity or carcinogenicity studies in rodents were available. A TDI of 0.5 µg/kg bw was established based on the NOAEL from the 1-year study and an uncertainty factor of 300 (10 for intraspecies variation, 10 for interspecies extrapolation and 3 for the inadequacy of the data base).

An allocation of 10% of the TDI to drinking-water results in the proposed guideline value of 1.5 µg/l.

3.9 Methoxychlor

Methoxychlor is poorly soluble in water and highly immobile in most agricultural soils. Methoxychlor under normal conditions of use seems not to be of environmental concern. However, it has been detected occasionally in drinking-water. Daily intake from food and air is expected to be below 1 µg per person.

Environmental metabolites are formed preferentially under anaerobic rather than aerobic conditions and include mainly the dechlorinated and demethylated products. There is some accumulation potential of the parent compound and/or its metabolites in surface water sediments.

The genotoxic potential of methoxychlor appears to be negligible. IARC has assigned methoxychlor in 1979 to Group 3. Subsequent data suggest a carcinogenic potential of methoxychlor for liver and testis of mice. This may be caused by the hormonal activity of proestrogenic mammalian metabolites of methoxychlor and therefore have a threshold. The study, however, was inadequate because only one dose was used and because this dose (48 mg/kg bw/day) was possibly above the maximum tolerated dose.

The data base for studies on long-term, short-term and reproductive toxicity is inadequate. Although NOAELs were not established in these studies, a recent teratology study in rabbits reported a systemic NOAEL of 5 mg/kg bw/day, which is almost 10 fold lower than the LOAELS from other studies. This NOAEL was therefore selected for use in the derivation of a TDI.

The application of an uncertainty factor of 1000 (100 for inter and intraspecies differences and 10 for concern for threshold carcinogenicity and the limited data base) leads to a TDI of 5 μg/kg bw. Allocation of 10% of the TDI to drinking-water results in the proposed guideline value of 15 μg/l.

3.10 Metolachlor

Metolachlor is a herbicide which can be lost from the soil through biodegradation, photodegradation and volatilisation. It is fairly mobile and under certain conditions it can contaminate ground water but it is mostly found in surface water.

There is no evidence from available studies that metolachlor is carcinogenic in mice. In rats, an increase in liver tumours in females as well as a few nasal tumours in males have been observed.

Long-term toxicity data were available in dogs and rats. An apparent decrease in kidney weight was observed at the lowest dose level (3.5 mg/kg-bw/day) in the chronic dog study. Applying an uncertainty factor of 3000 to this LOAEL (100 for inter- and intraspecies variation, 10 due to some concern regarding carcinogenicity and 3 due to the equivocal effect observed on kidney weight at the lowest dose level) a TDI of 1.16 μg/kg-bw was derived. A 10% allocation to drinking-water results in the proposed guideline value of 3.5 μg/l.

3.11 Molinate

The available data suggest that ground water pollution by molinate is restricted to some rice-growing regions. Data on the occurence of molinate in the environment are limited but indicate that concentrations in water rarely exceed 1 μg/l. Molinate is of low persistence in water and soil with half-life of about 5 days.

Based on the limited information available, molinate does not seem to be carcinogenic to animals. Evidence suggests that impairment of the reproductive performance of the male rat represents the most sensitive indicator of molinate exposure. However, a review of epidemiological data based on the examination of workers involved in molinate production does not indicate any effect on human fertility.

The NOAEL for reproductive toxicity in the rat was found to be the equivalent of 0.2 mg/kg-bw/day and this value was chosen as a basis for calculating a TDI for molinate. Using an uncertainty factor of 100 to reflect inter- and intraspecies variation a TDI of 0.002 mg kg-bw was derived. Allocating 10% of the TDI to drinking-water results in the proposed guideline value of 6 µg/l.

3.12 Pendimethalin

Pendimethalin is a pre- emergence herbicide which is fairly immobile and persistent in soil. It is lost through photodegradation, biodegradation and volatilization. The leaching potential of pendimethalin appears to be very low but little is known about its more polar degradation products. It has been rarely found in drinking-water in the limited studies available.

On the basis of available data, pendimethalin does not appear to have significant mutagenic activity. Long-term carcinogenicity studies in mice and rats do not provide evidence of pendimethalin carcinogenicity; however, these studies have some important limitations.

In a long-term rat feeding study, evidence of slight liver toxicity was noted even at the lowest dose tested; a NOAEL for this finding was not established. The LOAEL was 5 mg/kg bw/day. Applying an uncertainty factor of 1000 (10 for intraspecies variation, 10 for interspecies extrapolation and an extra 10 for the use of a LOAEL instead of a NOAEL and for limitations in the data base), a TDI of 0.005 mg/kg-bw was calculated.

An allocation of 10% of the TDI to drinking-water results in the proposed guideline value of 15 µg/l.

3.13 Propanil

Propanil is a mobile compound with affinity for the water compartment. This herbicide, however, is not persistent, being easily transformed under natural conditions to several metabolites. Two of these metabolites, 3,4-dichloroaniline (DCA) and 3,3',4,4'-tetrachloroazobenzene (TCAB), are more toxic and more persistent than the parent compound. Although used in a number of countries, propanil has only occasionally been detected in ground water.

Propanil is considered not to be genotoxic. However, at least one of propanil's environmental metabolites (TCAB) is genotoxic. Data from a limited study in rats do not provide evidence of carcinogenicity.

Under conditions of chronic exposure, propanil is toxic to red blood cells and the liver. A TDI of 0.005 mg/kg-bw was established, based on the NOAEL of 5 mg/kg bw/day from the 2-year rat feeding study and applying an uncertainty factor of 1000 (100 for intraspecies and interspecies variation and an additional 10 for the inadequate data base on the carcinogenicity of the compound).

Based on allocation of 10% of the TDI to drinking-water, the proposed guideline value is 15 µg/l. In applying this guideline, authorities should consider the possible presence of more toxic matabolites in water.

3.14 Pyridate

Pyridate is a compound with very low water solubility and relatively low mobility. It is not persistent and is rapidly hydrolyzed, photodegraded and biodegraded. Its primary environmental metabolite (chlorohydroxyphenylpyridazine) is also not persistent but is more mobile. Under favorable conditions, the environmental half-life is of the order of a few days. This compound has been monitored in drinking-water in only a few countries and has only rarely been found.

The available evidence indicates that pyridate is not genotoxic. Pyridate has been tested in long-term feeding studies in rats and mice; no evidence of carcinogenicity was noted in either species. The NOAEL of 3.5 mg/kg-bw/day in a 2-year rat study weight is based upon increased kidney weight. An uncertainty factor of 100 (for inter and intraspecies extrapolation) was applied to this NOAEL and 10% of the resulting TDI was allocated to drinking-water, to give a guideline value of 105 µg/l.

3.15 Simazine

Simazine is fairly resistant to physical and chemical dissipation processes in the soil. Its persistance and mobility are such that it has been frequently detected in ground and surface waters at concentrations up to a few µg/l.

Simazine does not appear to be genotoxic in mammalian systems. Recent studies have shown an increase in mammary tumours in the female rat but no effects in the mouse. IARC has classified simazine in Group 3 (in press).

Based on a recent study in the rat a NOAEL of 0.52 mg/kg-bw/day has been established for carcinogenicity and long-term toxicity. By applying an uncertainty factor of 1000 (100 for intra- and inter-species variation and 10 for possible carcinogenicity in rats) a TDI of 0.5 µg/kg bw was determined. Assuming a 60 kg adult and allocating 10% of the TDI to drinking-water the proposed guideline value is 1.5 µg/l.

3.16 Trifluralin

Trifluralin has low water solubility and a high affinity for soil. However, biodegradation and photodegradation processes may give rise to polar metabolites which may contaminate drinking-water sources. Although this compound is used in many countries, relatively little data are available concerning contamination of drinking-water. Trifluralin was not detected in the small number of samples analysed.

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 number of long-term carcinogenicity/long-term toxicity studies with pure (99%) test material have not demonstrated evidence of carcinogenicity. IARC (in press) has recently evaluated technical grade trifluralin and assigned it to Group 3.

From the long-term studies available, a NOAEL of 0.75 mg/kg bw/day was selected based on a 1-year feeding study in dogs. 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, a TDI of 0.0075 mg/kg bw was derived. A guideline value of 22.5 μg/l 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 such grades of trifluralin should not be used).

4. Recommendations

1. To avoid the long-term contamination of drinking-water by pesticides, emphasis should lie on preventive measures.

2. Agricultural and industrial practices should be examined with a view to their improvement to minimize environmental contamination with pesticides which may enter drinking-water via ground and/or surface water.

3. In the evaluation of pesticides for registration purposes more attention should be paid to the potential for drinking-water contamination via ground and/or surface water. Such evaluations should take into account the pesticides themselves, possible impurities and environmental metabolites.

4. The concept of good agricultural practice should be extended to incorporate minimization of contamination of ground water and surface water. The use of pesticides should be carefully controlled in areas where such use leads to contamination of drinking-water supplies.

5. The development of guidelines for predicting and verifying environmental fate and distribution of pesticides with regard to contamination of drinking-water via ground and surface water is strongly recommended. Such guidelines should also indicate how pesticides should be managed to prevent drinking-water contamination.

6. More attention should be given to monitoring the occurence of pesticides in ground and surface water .

7. Few epidemiological data are available on occupational exposure to pesticides during production, formulation or application. This is a matter for concern, since workers may be exposed to considerably higher levels than the general population, and data gathered from this source could be used in assessing the overall health risk of these chemicals. In particular, no information is available on exposure levels, body concentration and biotransformation.

8. In view of the difficulties encountered in the evaluation of some chemicals, the need for more comprehensive investigation of systemic toxicity in oncogenicity studies is emphasized.

9. It is recommended that cognisance be taken of the breakdown products of pesticides in drinking-water, their identity and biological activity.

10. It is recommended that the use of a body suface area correction in mathematical models used for low dose risk extrapolation be critically examined

Annex 1

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