



Commission of the European Communities

agriculture

Reports of the Scientific Committee for Pesticides



Report

EUR 7581 DE, EN, FR, IT

Commission of the European Communities

agriculture

Reports of the Scientific Committee for Pesticides

Directorate-General for Agriculture

EUR 7581 DE, EN, FR, IT

Published by the
COMMISSION OF THE EUROPEAN COMMUNITIES

Directorate-General
Information Market and Innovation

Bâtiment Jean Monnet
LUXEMBOURG

LEGAL NOTICE

Neither the Commission of the European Communities nor any person acting on behalf of the Commission is responsible for the use which might be made of the following information

This publication has also been published in the following languages:

DE ISBN 92-825-2700-X

FR ISBN 92-825-2702-6

IT ISBN 92-825-2703-4

Cataloguing data be found at the end of this publication

Luxembourg: Office for Official Publications of the European Communities, 1981

© ECSC-EEC-EAEC, Brussels • Luxembourg, 1981

Printed in Belgium

ISBN 92-825-2701-8

Catalogue number: CD-NK-81-003-EN-C

CONTENTS

	<u>Page</u>
FOREWORD	v
REPORTS OF THE SCIENTIFIC COMMITTEE FOR PESTICIDES on	
- Maximum levels for certain pesticide residues in cereals and foodstuffs of animal origin	1
- The use of ethylene oxide as a fumigant of food- stuffs	11
- Maximum levels for certain pesticide residues in fruit and vegetables (Interim Report)	17
- The use of camphechlor as an insecticide	27
- The marketing and use of 2,4,5-T	43

FOREWORD

The Scientific Committee for Pesticides was set up by Commission Decision 78/436/EEC of 21 April 1978 (OJ No L 124 of 12.5.1978, p. 16) in order to provide the Commission with informed opinions on scientific and technical matters relating to the use and marketing of pesticides and to their residues, particularly in food and feedingstuffs.

The members of the Committee are independent and highly qualified in the fields of applied biology, toxicology, ecotoxicology and chemistry. The Secretariat of the Committee is provided by the Commission's Directorate-General for Agriculture.

The Committee's first series of reports, published in this volume, relate to questions put to it by the Commission on the safety in use of certain pesticides and, for a wider range of pesticides, on the maximum permitted levels of their residues in foodstuffs, in particular fruit and vegetables, cereals and products of animal origin. Questions in this connection had arisen in the course of the Commission's work on the approximation of Member States' legislation concerning pesticides.

Composition of the Scientific Committee for Pesticides

Prof. L. Broadbent, Chairman
Prof. B. Paccagnella, Vice-Chairman
Dr. M.J. Van Logten, Vice-Chairman
Dr. D.C. Abbott
Prof. G. Domenichini
Prof. R. Heitefuss
Ing. J. Henriet
Prof. O. Karlog
Dr. P. Kayser
Prof. R. Mestres
Prof. F.K. Ohnesorge
Dr. E.W. Ryan
Prof. R.C. Truhaut

Secretariat

Dr. G.H. Hudson⁽¹⁾

(1) Commission of the European Communities, Directorate-General for Agriculture

REPORT OF THE SCIENTIFIC COMMITTEE FOR PESTICIDES
ON MAXIMUM LEVELS FOR CERTAIN PESTICIDE RESIDUES
IN CEREALS AND FOODSTUFFS OF ANIMAL ORIGIN

Opinion expressed 4 October 1979

BACKGROUND AND TERMS OF REFERENCE

In the context of its work to harmonise legislation concerning pesticide residues and thereby remove barriers to trade, the Commission envisages proposing the maximum residue levels in products intended for human consumption falling within the following categories:

- (1) cereals,
- (2) foodstuffs of animal origin

contained in Annexes A and B to this report respectively.

Before submitting proposals to the Council, the Commission requested the Scientific Committee for Pesticides to give an opinion on the following questions:

- (a) Do any of the envisaged maximum residue levels contained in Annexes A and B present a risk to the health of the consumer? If so which, and what is the nature of such risk? What lower level, if any, would be toxicologically acceptable?
- (b) Are any of the envisaged maximum residue levels contained in Annexes A and B unnecessarily high, having regard to the needs of good agricultural practice? If so which, and what lower levels would be more appropriate?

OPINION OF THE COMMITTEE

The Committee examined the maximum levels contained in Annexes A and B on the basis, except where stated, of publicly available data. It is of the opinion that, save for the cases considered specifically below and for which it has made appropriate recommendations, in the light of present knowledge the levels listed do not present a hazard for public health and are consistent with the needs of good agricultural practice.

1. Ad Annex A (cereals intended for human consumption)

1.1. Camphchlor and ethylene oxide: Since the Committee is being consulted separately on the general questions of the use of camphchlor as an insecticide and of ethylene oxide as a foodstuffs fumigant, it would be more logical to examine the maximum residue levels envisaged in Annex A later and in the light of the conclusions of the wider studies.

1.2. DDT: In view of the fact that the figure applies to the sum of the levels of up to six components, each having an individual limit of determination and associated variance, it is advisable to adopt the practically applicable level of 0.05 mg/kg in place of 0.03 mg/kg, although the change is toxicologically insignificant.

1.3. Bromomethane, 1,2 dibromoethane, 1,2-dichloroethane, carbon disulphide and carbon tetrachloride:

The setting of maximum levels for residues of fumigants, particularly the so-called liquid fumigants such as those listed above, presents special difficulties and the Committee considers that these fumigants should be treated separately. The basic problem with these compounds lies in the fact that the residue levels to be found after treatment in the recommended manner are highly dependent on the relationship between the time of completing the fumigation and the time of taking the samples for analysis. The nature of the fumigant, its mode of application, and the type of foodstuff that has been treated, also affect the residue levels observed. In the case of raw cereals, which are always milled, processed and/or cooked before consumption, the parameters of interest are even more numerous. Additionally, cereals and their products may be fumigated more than once, and/or with more than one fumigant, at different stages of their journey from harvest to human consumption.

All these matters were dealt with in the Report of the 1971 FAO/WHO Joint Meeting on Pesticide Residues (1); paragraph 3.1 of the Report is particularly relevant. Thus, it is clear that a maximum level for a fumigant must be linked with a close definition of the marketing stage at which it is to apply.

Raw cereals are liable to be sampled and analysed at any stage from immediately after treatment up to milling. If sampling takes place immediately after treatment, the appropriate maximum residue levels

would need to be set above those applicable just before milling, i.e. at the highest values consistent with good fumigation practice (including free exposure to air for at least 24 hours after treatment and before sampling), provided it was established that such values resulted in toxicologically acceptable residue levels in the end-products consumed. Milling, processing and cooking all normally lead to significant reductions in the fumigant residue content. In this connection, it has been shown (2) that the residues remaining in bread and other cooked cereal products prepared from raw cereals, which had contained fumigant residues at certain known, high levels, are low or close to the limits of determination of the compounds which were studied.

In the absence of an unambiguous statement regarding the stage of marketing of raw cereals at which the levels listed in Annex A are to be applied and in view of the wording of the questions, the Committee concludes this must be understood to be at a point at which the materials are liable to be presented for direct human consumption and that for the liquid fumigants the lower levels set out in the Table below should therefore be followed. It is clear, however, that these levels are likely to be exceeded to an appreciable extent at other stages of storage, distribution and marketing, particularly as these approach the point of treatment.

The Committee is aware that further toxicological studies on these compounds are in progress and recommends an early review of these levels as the results of such studies become available.

Table

Pesticide residues	Maximum Levels in mg/kg (ppm)
4. Bromomethane (methyl bromide)	0.5
12. 1,2-dibromoethane (ethylene dibromide)	0.01*
13. 1,2-dichloroethane (ethylene dichloride)	1*
26. Carbon disulphide	0.1
27. Carbon tetrachloride	0.1

* The Committee feels that the levels proposed for 1,2-dibromo- and 1,2-dichloroethane call for special comment. There are indications

that both compounds may induce mutations (3) and recent studies (4, 5) have revealed that they are also most probably carcinogenic in both rats and mice. In the light of this information, the Committee considers that these compounds should be regarded as having potential carcinogenic properties in man and their use as food fumigants therefore discouraged. The maximum residue levels should be as low as possible and the values recommended in the Table have consequently been set at or about the current limits of determination. These levels should be reviewed in the light of developing analytical technology.

2. Ad Annex B (foodstuffs of animal origin)

2.1. Aldrin, dieldrin and heptachlor: The Committee noted that the safety of these compounds is still under discussion by toxicologists and feels it is unable to express a definitive opinion now on the maximum levels envisaged. The Committee considers it would be prudent to seek to reduce these levels as much as possible but recognises that they are presently unavoidable, due largely to past use of the products. It notes with satisfaction that the Community has already taken action (6) to phase out the few remaining agricultural uses.

2.2. DDT: The Committee considers a single significant figure of 1 mg/kg would be more realistic than 1.5 mg/kg for fat of meat.

2.3. Hexachlorobenzene (HCB):

Although HCB is seldom used as a fungicide, the existence of non-agricultural sources of this compound and its stability necessitate continued monitoring of residues in foodstuffs. On the evidence of recent monitoring data on HCB residues in products of animal origin, supplied by Member States at the request of the Committee, it is concluded that current pollution levels no longer require maximum values as high as 0.3 and 0.5 mg/kg and that a single figure of 0.1 mg/kg for all three food categories would now be justified.

2.4. α - and β -HCH: The Committee is of the opinion that separate maximum levels, rather than a combined one, are desirable and analytically feasible for these isomers. It accordingly recommends the following values for the three food categories.

α -HCH	0.5	0.2	0.1
β -HCH	0.1	0.02	0.02

2.5. Foodstuffs of low fat content: The Committee draws the Commission's attention to the analytical problems of enforcing maximum levels expressed on a fat basis in the case of foodstuffs of low fat content, particularly some milks. A solution would be to express such limits on a whole product basis.

References

1. Pesticide Residues in Food, Report of the 1971 Joint FAO/WHO Meeting, WHO Technical Report No 502, 1972; FAO Agricultural Studies No. 88, 1972, page 13
2. idem, page 14
3. Lawrence Fishbein, "Industrial mutagens and potential mutagens 1. halogenated aliphatic derivatives", Mutagen Research, 32 (1976), 267-308.
4. U.S. Department of Health, Education and Welfare, "Bioassay of 1,2-dibromoethane for possible carcinogenicity", cas no. 106-93-4. National Cancer Institute Carcinogenicity Technical Report Series no. 86 (1978).
5. U.S. Department of Health, Education and Welfare, "Bioassay of 1,2-dichloroethane for possible carcinogenicity", cas no. 107-06-2. National Cancer Institute Carcinogenicity Technical Report Series no. 55 (1978)
6. Directive 79/117/EEC, OJ No L 33 of 8.2.1979, p.36

MAXIMUM RESIDUE LEVELS ON WHICH THE OPINION OF THE SCIENTIFIC
COMMITTEE WAS SOUGHT

ANNEX A

List of products to which the maximum levels refer

Common Customs Tariff Heading No	Description of products
ex. 10.01	Wheat and meslin))
ex. 10.02	Rye))
ex. 10.03	Barley))
ex. 10.04	Oats) intended) for human
ex. 10.05	Maize) consumption)
ex. 10.06	Paddy rice))
ex. 10.07	Buckwheat, millet,) grain sorghum)

Pesticide residues	Maximum levels in mg/kg (ppm)
1. Hydrogen cyanide; cyanides expressed as hydrogen cyanide	50
2. Aldrin)) singly or combined,	0.02
3. Dieldrin) (HEOD)) expressed as) dieldrin (HEOD)	
4. Bromomethane (methyl bromide)	0.5
5. Total inorganic bromide, expressed as Br-ions	50
6. Piperonyl butoxide	20
7. Camphechlor (Toxaphene)	0.5
8. Carbaryl	1 : rice 0.5 : other cereals
9. Chlordane (sum of cis- and trans- isomers and of oxychlordane, expressed as chlordane)	0.05
10. DDT (sum of DDT-, TDE- and DDE-isomers, expressed as DDT)	0.03
11. Diazinon	0.1
12. 1,2-Dibromoethane (ethylene dibromide)	5
13. 1,2-Dichloroethane (ethylene dichloride)	10
14. Dichlorvos	2
15. Endosulfan (sum of alpha- and beta-isomers and of endosulfan sulphate, expressed as endosulfan)	0.2 : maize 0.1 : other cereals
16. Endrin (sum of endrin and delta-keto-endrin, expressed as endrin)	0.02
17. Heptachlor (sum of heptachlor and heptachlor epoxide, expressed as heptachlor epoxide)	0.02
18. Hexachlorobenzene (HCB)	0.01
19. Hexachlorocyclohexane (HCH)	
19.1. alpha-isomer	0.1
19.2. beta-isomer	0.02
19.3. gamma-isomer (lindane)	0.5

Pesticide residues	Maximum levels in mg/kg (ppm)
20. Hydrogen phosphide; phosphides expressed as hydrogen phosphide	0.1
21. Malathion (sum of malathion and malaaxon, expressed as malathion)	8
22. Methoxychlor	2
23. Ethylene oxide	0.1
24. Phosphamidon	0.1
25. Pyrethrins (sum of pyrethrins I and II, cinerins I and II, jasmolins I and II)	3
26. Carbon disulphide	0.1
27. Carbon tetrachloride	0.1
28. Trichlorfon	0.1

I. List of products to which the maximum levels refer

Common Customs Tariff Heading No	Description of products
ex. 02.01	Meat and edible offals of horses, asses, mules and hinnies, bovine animals, swine, sheep and goats, fresh, milled or frozen, except offals for the manufacture of pharmaceutical products.
02.02	Dead poultry and edible offals thereof (except liver), fresh, chilled or frozen.
02.03	Poultry liver, fresh, chilled, frozen, salted or in brine.
ex. 02.04	Other meat and edible meat offals, chilled or frozen of domestic pigeons, domestic rabbits and game.
ex. 02.05	Pig fat and poultry fat, fresh, chilled, frozen, salted, in brine, dried or smoked.
02.06	Meat and edible meat offals (except poultry liver), salted, in brine, dried or smoked.
16.01	Sausages and the like, of meat, meat offals or animal blood.
16.02	Other prepared or preserved meat of meat offal.
04.01	Milk and cream, fresh, not concentrated or sweetened.
04.02	Milk and cream, preserved, concentrated or sweetened.
04.03	Butter
04.04	Cheese and curd
04.05	Bird's eggs and eggs' yolks, fresh, dried or otherwise preserved, sweetened or not, except eggs for hatching as well as eggs and eggs yolks intended for purposes other than nutrition.

Maximum Levels

Residues of Pesticides	in mg/kg (ppm) of fat for meat, edible offals and preparations of meat listed in Annex B.I under No ex 02.01, 02.02, 02.03, ex 02.04, ex 02.05 02.06, 16.01, 16.02	in mg/kg (ppm) of fat for milk and dairy products listed in Annex B.I under No 04.01, 04.02, 04.03, 04.04	in mg/kg (ppm) of fresh eggs, without shells, for birds' eggs and eggs yolks listed in Annex B.I under No ex 04.05 (*)
1. Aldrin)singly or)combined,)expressed)as	0.2	0.15	0.1
2. Dieldrin)(HEOD))dieldrin)(HEOD)			
3. Chlordane (sum of cis- and trans-isomers and of oxychlordane, expressed as chlordane)	0.05	0.05	0.02
4. DDT (sum of DDT-, TDE- and DDE-isomers, expressed as DDT)	1.5	1	0.5
5. Endrin (sum of endrin and delta-keto-endrin, expressed as endrin)	0.02	0.02	0.02
6. Heptachlor (sum of heptachlor and heptachlor epoxide, expressed as heptachlor epoxide)	0.2	0.15	0.05
7. Hexachloro-benzene (HCB)	0.5	0.3	0.3
8. Hexachlorocyclohexane (HCH)			
8.1 alpha-isomer	} singly or combined 0.6	0.2	0.1
8.2 beta-isomer			
8.3 gamma-isomer (lindane)			
	0.7: products No 02.02 and 02.03, poultry fat and preparations of poultry meat and offals. 2: other products		

(*) For eggs and eggs yolks, dried or otherwise preserved, sweetened or not, as well as for fresh eggs yolks, the maximum level indicated refers to the weight of fresh eggs, without shell, from which these products are derived.

Report of the Scientific Committee for Pesticides on
the use of ethylene oxide as a fumigant of foodstuffs

(Opinion expressed 19 December 1979)

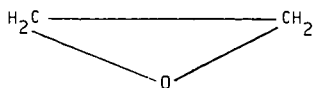
Background and terms of reference

Ethylene oxide is used in certain Member States as a fumigant of foodstuffs, particularly cereals, herbs, spices, dried vegetables and cocoa. The Commission requested the Scientific Committee for Pesticides to examine the toxicology of ethylene oxide and its conversion products in relation to its applications and to give an opinion on the following questions:

1. What are the incidence, nature and levels of its residues in foodstuffs and what will be the potential exposure of man through the diet?
2. Can the use of ethylene oxide be prejudicial to the consumer or the environment and, if so, can such risks be eliminated by selective reduction of the potential exposure of man or must a total prohibition be envisaged? If the former, by what means could exposure be reduced, having regard to the availability of satisfactory alternative treatments and their toxicological and technological consequences?

Discussion

The Committee examined the available information relating to the residues of ethylene oxide occurring in foodstuffs and to their toxicological significance. Summaries of these data are given below.



ethylene oxide

Ethylene oxide is used as a fumigant and sterilizing agent. At room temperature and normal atmospheric pressure it is a colourless gas. It has a boiling point of 10.7°C and a molecular weight of 44. It is inflammable at concentrations in air > 3%.

Ad. Question 1:

(i) Incidence of residues in foodstuffs

Ethylene oxide has only limited uses as a fumigant and hence the frequency of occurrence of its residues will be generally low. However, it has certain specialised uses, particularly on herbs and spices, and in these treated commodities the frequency of occurrence of residues will be greater. Occasional use on milk powder and some fruits and vegetables has also been indicated. The extent of use is variable from year to year and country to country.

(ii) Nature of residues in foodstuffs

Ethylene oxide is a very reactive compound and hence its residues include a number of reaction products, depending on the nature of the treated commodity, together with trace amounts of unchanged fumigant. Reaction with water gives rise to ethylene glycol and in the presence of chloride or bromide ions ethylene chlorohydrin or ethylene bromohydrin respectively may be formed; these compounds, in fact, form the major part of the residues. Reaction will also occur with food constituents containing free carboxy, hydroxy, amino or sulph-hydryl groups, etc, to yield the corresponding hydroxyethyl compounds, esters or ethers.

(iii) Levels of residues in foodstuffs

Residue levels of ethylene chlorohydrin (generally the major component of the residue) depend greatly on the conditions of fumigation, the

nature of the commodity, the amount of moisture and chloride ion present, extent of aeration, temperature, etc. Observed levels commonly range up to, or even above, 200 mg/kg, the highest levels occurring in spices such as cloves, pepper, coriander and curry powder. Similar levels of unreacted ethylene oxide have been found in treated dry cocoa powder but other commodities do not usually show these elevated residues, less than 100 mg/kg being more common. Ethylene glycol has also been found in some commodities that have been treated with ethylene oxide, usually below 100 mg/kg but flour has contained up to 2000 mg/kg.

In summary, residue levels are very variable but can range up to 5000 mg/kg under some circumstances.

(iv) Potential exposure of man through the diet

In view of limited use of ethylene oxide as a fumigant or sterilant the actual exposure of man in general to its dietary residues is low.

Only consumers of large amounts of highly spiced foodstuffs or herbs, drawn from limited sources and all of which had been treated under poor fumigation conditions with ethylene oxide are likely to receive appreciable quantities of ethylene chlorohydrin and ethylene glycol together with other as yet unidentifiable reaction products.

Ad. Question 2:

- (i) The 1968 FAO/WHO Joint Meeting on Pesticide Residues⁽¹⁾ concluded that insufficient data were available to permit an estimation of an Acceptable Daily Intake for ethylene oxide or ethylene chlorohydrin or any other possible reaction products remaining as residues. Since 1968 no new toxicological evaluation has taken place.
- (ii) The results of subacute and semi-chronic studies with several animal species suggested and/or indicated that ethylene oxide in higher concentrations may cause inter alia adverse effects on the male reproductive organs, the nervous system, the liver, kidneys and blood. However, the data available at this time with respect to these effects, are not sufficient to calculate no-effect levels after exposure to ethylene oxide. Moreover, most of the experiments carried out dealt with

exposure by inhalation. The results of these experiments are only of limited value for establishing residue limits for oral intake.

(iii) There are many data available showing very clearly the mutagenicity of ethylene oxide in a variety of test systems, including *Salmonella typhimurium*, *Escherichia coli*, *Neurospora crassa* and *Drosophila melanogaster*. Ethylene oxide has been shown to produce chromosome aberrations in plants. Chromosomal effects have also been found in mammalian in vivo systems (bone marrow metaphase test, micronucleus test and the dominant lethal test). These data indicate that ethylene oxide in both lower organisms and mammalian in vivo tests induces point mutagens and chromosomal aberrations. It belongs to a class of compounds which shows strong alkylating activity. These agents in general have a strong correlation between mutagenicity and carcinogenicity.

(iv) As various epoxides have shown an oncogenic activity in animals, ethylene oxide has to be suspected of carcinogenic properties. In a recent Swedish study⁽²⁾ three cases of leukemia were reported in workers exposed to ethylene oxide and methyl formate. According to national statistics only 0.2 cases of leukemia would have been expected. Two of the three individuals were exposed each workday to an average concentration of about 20 ppm in air. This observation may be indicative of probably carcinogenic properties of ethylene oxide.

A long-term study in which rats received food fumigated with ethylene oxide did not show positive results. However, blood was not examined and only a few organs were studied histopathologically. This study cannot be regarded therefore as adequate evidence of the absence of carcinogenic or other adverse effects.

(v) Ethylene oxide is a very reactive compound. It has been found to destroy vitamins and essential amino acids. Apart from the decrease of the nutritional value of the food, these reactions may give rise to compounds of unknown toxicity.

(vi) One of the most commonly found reaction products is ethylene chlorohydrin. The available toxicity studies of the compound are inadequate to calculate an Acceptable Daily Intake. It has been found that ethylene

chlorohydrin is mutagenic in microorganisms and in mammalian in vivo systems. These results may be indicative of a possible carcinogenic effect of ethylene chlorohydrin. However, adequate carcinogenicity studies of this compound have not been reported.

- (vii) In the case of herbs and spices, there is a particular need not to induce taint. As far as the Committee is aware, ethylene oxide is at present the only suitable chemical agent which, for this reason, can be used. Irradiation could prove to be a suitable alternative.

Opinion of the Committee

In the light of the available information the Committee is of the opinion that the potential hazards to the consumer associated with the continued use of ethylene oxide for the fumigation of staple foods, e.g. cereals, milk powder, fruits and vegetables, are such as to indicate that a total prohibition of these uses should be envisaged. In addition, the Committee agreed that the use of ethylene oxide on herbs and spices, which are minor commodities, should be kept under review, with a view to its discontinuance as and when acceptable alternative methods of treatment become available.

References

- (1) "1968 Evaluations of some pesticide residues in food"; Page 166
FAO/PL: 1968/M/9/1
WHO/FOOD ADD./69.35
- (2) JAMA, March 16 1979 - Vol. 241, No. 11, Page 1132

INTERIM
REPORT OF THE SCIENTIFIC COMMITTEE FOR PESTICIDES
ON MAXIMUM LEVELS FOR CERTAIN PESTICIDE RESIDUES
IN FRUIT AND VEGETABLES

(Opinion expressed on 1 April 1981)

BACKGROUND AND TERMS OF REFERENCE

In the context of its work to revise Annex II of Council Directive 76/895/EEC of 23 November 1976 relating to the fixing of maximum levels for pesticide residues in and on fruit and vegetables⁽¹⁾, the Commission invited the Scientific Committee for Pesticides to examine a series of draft maximum levels for certain pesticide residues in fruit and vegetables. These draft levels had been drawn up by its departments in collaboration with experts of Member States and, before submitting proposals to the Council, the Commission requested the Committee in December 1979 to give an opinion on the following questions:

- (a) Do any of the envisaged maximum residue levels present a risk to the health of the consumer? If so which, and what is the nature of such a risk? What lower level, if any, would be toxicologically acceptable?
- (b) Are any of the envisaged maximum residue levels unnecessarily high, having regard to the needs of good agricultural practice? If so which, and what lower levels would be more appropriate?

Having regard to the large number of maximum residue levels involved and the need in some cases to carry out detailed examinations of original data, the Commission invited the Committee to make an interim report on the levels it had been able to consider up to December 1980.

OPINION OF THE COMMITTEE

The Committee examined the draft maximum levels for the pesticide residues set out in the Annex to this Report on the basis, except where stated, of publicly available data.

The Committee is of the opinion that, save for the cases considered specifically below and for which it has made recommendations or comments, in the light of present knowledge the draft levels submitted to it by the Commission do not present a hazard for public health and are consistent with the needs of good agricultural practice.

For the sake of clarity, the Annex to this report sets out the draft maximum residue levels of the compounds considered by the Committee up to December 1980, amended where appropriate in accordance with its recommendations.

Aldrin, dieldrin and heptachlor:

The Committee noted that the safety of these compounds is still under discussion by toxicologists and, due to the effects on the liver in experimental animals, it is not clear if no-effect levels can be established. The Committee is unable, therefore, to express a definitive opinion now on the acceptability of the maximum levels envisaged. It notes with satisfaction that the Community has already taken action⁽²⁾ to phase out the few remaining agricultural uses.

The Committee considers it would be prudent to reduce these levels as much as possible but recognises that similar levels of residues arise unavoidably, due largely to past use of the products. In the opinion of the Committee, the envisaged levels do not represent a hazard to public health. Hence, it was not proposed to modify them.

Azinphos-ethyl:

The Committee noted that azinphos-ethyl is an organophosphorus insecticide with high acute and sub-acute toxicity, it is currently used in some countries on fruit and vegetables. In 90-day studies on rats and dogs, the no-effect levels were 0.1 mg/kg b.w./day and 0.006 mg/kg b.w./day respectively. No studies

have been reported on the effects on reproduction, potential teratogenic activity, long-term toxicity or effects on man. Due to lack of these and other data the Committee was unable fully to evaluate the toxicity of azinphos-ethyl and therefore agreed that the maximum residue level should be set at or about the lower limit of determination. The Committee recognises that this does not allow for the use of this insecticide on fruit and vegetables.

Bromophos:

The Committee proposed a maximum level of 1 mg/kg for pome fruit, leeks, radish and leaf vegetables. According to available data⁽³⁾, this maximum level satisfies the requirement of good agricultural practice and is also toxicologically acceptable.

DDT, including p,p'DDT, o,p'DDT, p,p'DDE and p,p'TDE:

The Committee agreed to recommend the following maximum levels calculated as the sum of the four compounds:

pome and stone fruit, grapes	0.5 mg/kg
other products	0.1 mg/kg

The Committee noted that the use of DDT is (apart from minor applications) prohibited within the Community. However, given that DDT is persistent in the environment and residues may still be derived from usage prior to the prohibition, the MRL of 0.5 mg/kg for grapes, pome and stone fruit is considered appropriate to accommodate the possibility of the occurrence of residues derived in this way. However it is proposed to review these levels in the near future as residues should decline as a consequence of the cessation of usage in the Community.

Dimethoate/Omethoate:

Omethoate has a high acute toxicity (28-65 mg/kg: oral, rat) compared with dimethoate (180-680 mg/kg: oral, rat). There are indications that the purer the dimethoate, the lower its toxicity. This may be due to variation in the amount of omethoate present in the technical dimethoate.

For both organophosphorus compounds, cholinesterase inhibition is the most sensitive criterion of their toxicity. Long term studies with omethoate and dimethoate on rats showed no indication of carcinogenicity of these compounds; a study in mice was also negative. In a separate study with dimethoate in rats a higher rate of tumours was observed. However the purity of the compound

was not stated, there was no dose dependency and the study was not conducted according to internationally recognised standards. There was no indication of teratogenicity of omethoate or dimethoate in maternally non-toxic doses but there are indications that at high dose levels embryotoxicity occurs.

In the past, several subacute/subchronic studies have been carried out with omethoate in rats and dogs. However in these studies brain acetylcholinesterase activity was not investigated. Recent experiments in vitro and in vivo (rats) suggest that inhibition of brain acetylcholinesterase by omethoate is more marked than inhibition of serum or RBC cholinesterase.^(4, 5, 6, 7, 8)

In long-term studies in rats with omethoate, incorporated in the diet at levels of 3 mg/kg and 10 mg/kg, a clear indication of cholinesterase inhibition was evident in brain, plasma and RBC cholinesterase. At the 1 mg/kg level there was no effect on cholinesterase activity in plasma and RBC in either sex nor on brain acetylcholinesterase of males; in females receiving 1 mg/kg omethoate in the diet, a significant, although borderline brain acetylcholinesterase inhibition⁽⁹⁾ was observed. The available data on the toxicity in man are inadequate for the purposes of providing an assessment. A study has been carried out in dogs but brain cholinesterase activity was not reported. Based on these facts the opinion of the Committee is that for omethoate a safety factor of 100 should be applied to the borderline no effect level of 1 mg/kg in the diet (= 0.05 mg/kg b.w. per day). Thus the estimate of the acceptable daily intake (ADI) for man can be set at 0.0005 mg/kg/day or 0.03 mg/man/day. This value for the ADI indicates that a maximum residue level for omethoate of approximately 0.1 mg/kg is desirable.

In the case of dimethoate several subacute / subchronic studies have been carried out. In the rat a borderline no effect level of 5 mg/kg in the diet was reported and in the dog, 10 mg/kg. Observations on humans for a period of 14 - 57 days showed a no effect level of 15 mg/man/day (= 0.2 mg/kg/day). Based on these observations, in the opinion of the Committee, a safety factor of 20 is appropriate which gives an ADI of 0.01 mg/kg/day. The value of the ADI indicates that for dimethoate a maximum residue level of approximately 1.5 mg/kg can be justified.

It was decided that separate MRL's should be set for dimethoate and omethoate in preference to the current combined level of 1.5 mg/kg.

The Committee noted that for analytical and chemical reasons it is very difficult to determine omethoate accurately at levels as low as 0.1 mg/kg. It is also noted that omethoate residues may derive from applications of dimethoate as well as from the use of omethoate itself.

Taking into account these factors the Committee proposed a MRL of 0.2 mg/kg for omethoate. It was agreed that it is preferable that MRL's should be expressed to one significant figure and the corresponding level of 1 mg/kg for dimethoate was proposed.

Fenclorphos:

The Committee noted that this product is no longer used on fruit and vegetables and recommended, particularly because of the at least theoretical presence of undesirable contaminants in preparations containing fenclorphos, that the maximum level should be reduced to at or about the lower limit of determination.

Maleic hydrazide:

The Committee reviewed the toxicology of maleic hydrazide and concluded that there is no evidence that material containing less than 0.5 mg/kg hydrazine is carcinogenic⁽¹⁰⁾. They therefore approved the level of 10 mg/kg for onions, for materials in compliance with this specification. Since usage, as far as the fruit and vegetables covered by Directive 76/895/EEC are concerned, is limited to treatment of onion haulms, the Committee agreed that the maximum level for other products should be set at or about the lower limit of determination (1 mg/kg).

-
- (1) OJ No L 340 of 9.12.1976
 - (2) Council Directive 79/117/EEC, OJ No L 33, 8.2.1979
 - (3) FAO/WHO - Evaluations of some pesticide residues in food, 1972, 1975, 1977
 - (4) FAO/WHO 1963 Evaluation of some pesticide residues in food. PL/1963/(1964) 13
 - (5) FAO/WHO 1967 Evaluation of some pesticide residues in food. PL/1967/M/11/1
 - (6) FAO/WHO 1971 Evaluation of some pesticide residues in food. AGP-(1972) 1971/M/9/1
 - (7) FAO/WHO 1975 Evaluation of some pesticide residues in food. AGP/1975/(1976)M/13
 - (8) FAO/WHO 1978 Evaluation of some pesticide residues in food. (1979) FAO Plant production and protection paper No. 15 sup.
 - (9) E. Bomhard, E. Löser und G. Kaliner. Chronische Toxikologische Untersuchungen an Ratten. Unpublished report Bayer AG Nr 8507 dated 18.7.1979
 - (10) Report of the National Institute for Public Health, Bilthoven, Report No 7/7 Tox/Path. January 1979.

Common or chemical name	Maximum Level (in mg/kg (ppm))
captafol	15 : peaches, apricots
	10 : Morello cherries
	5 : other fruit
	0.5 : onions, carrots
	10 : other vegetables
carbaryl	2 : root vegetables
	3 : other products
chlorbenside	2
chlorbenzilate	0.2 : nuts (without shells)
	2 : other products
chlordane (sum of cis- and trans-isomers)	0.05
chlorfenvinphos (sum of cis- and trans-isomers)	0.5 : bulb, tuber and root vegetables, celery, parsley
	0.05 : mushrooms, peanuts (without shells), fruit
	0.1 : other vegetables
chlormequat, expressed as chlormequat cation	3 : pome fruit
	1 : grapes
	0.05* : other products
chloroxuron	0.2
chlorpyrifos	0.5 : tomatoes, apricots, peaches, peppers, pome fruit, kale, chinese cabbage
	0.3 : citrus fruit
	0.2 : other vegetables, plums, prunes and grapes
	0.05* : other fruit
cyhexatin) sum expressed) as azocyclotin) cyhexatin	1 : citrus, pome and stone fruit, grapes, gherkins
	0.2 : berries
	0.5 : other fruiting vegetables
	0.05* : other products
DDT (sum of p,p'DDT; o,p'DDT p,p'DDE and p,p'TDE)	0.5 : pome and stone fruit, grapes
	0.1 : other products

Common or chemical name	Maximum level (in mg/kg (ppm))
di-allate) tri-allate) sum	0.1
diazinon	0.05 : nuts (without shells) 0.5 : other products
dichlofluanid	10 : lettuce, strawberries, 5 : other berries, grapes 5 : other products
dichlorprop	0.05*
dichlorvos	0.1
dicofol	2 : cucumbers, gherkins 1 : tomatoes, strawberries 3 : other fruit 0.5 : other vegetables
dimethoate	1
dinoseb	0.05*
dioxathion	3 : citrus fruit 0.2 : other products
diquat, expressed as diquat cation	0.1 : onions 0.05* : other products
endosulfan (sum of α and β endosulfan and endosulfan sulphate)	0.2 : carrots and other root 1 : other products vegetables
endrin	0.02*
fenchlorphos (sum of fenchlorphos and O,O- dimethyl O-(2,4,5- trichlorophenyl) phosphate	0.01*
fenitrothion	0.5
fentin compounds) e.g.)	
fentin acetate) sum	1 : celery
fentin chloride) expressed as fentin) hydroxide)	0.1 : other products
fentin hydroxide)	

Common or chemical name	Maximum level (in mg/kg (ppm))
heptachlor (sum of heptachlor and heptachlor epoxide)	0.05
hexachlorobenzene	0.1 : vegetables 0.005* : other products
γ-HCH (lindane)	2 : leaf vegetables 0.5 : tomatoes, stone fruit, grapes 0.2 : carrots 1 : other products
malathion (sum of malathion and malafoxon)	3 : vegetables, except root vegetables 0.5 : other products
maleic hydrazide	10 : onions 1* : other products
methidathion	2 : citrus fruit 0.5 : pome fruit 0.2 : other products
methoxychlor	10
methyl bromide (bromomethane)	0.1*
omethoate	0.2
paraquat, expressed as paraquat cation	0.05
parathion (sum of parathion and paraoxon)	1 : citrus fruit, apricots, peaches 0.5 : other products
parathion-methyl (sum of parathion-methyl and paraoxon-methyl)	0.2
phosphamidon	0.4 : citrus fruit 0.2 : other products
propoxur	3
natural pyrethrins (sum of pyrethrins I and II, cinerins I and II, jasmolins I and II)	1
TEPP	0.01*

Common or chemical name	Maximum level (in mg/kg (ppm))
thiometon (sum of thiometon, thiometon sulphoxide and thiometon sulphone)	0.5
trichlorphon	0.5
vamidothion (sum of vami- dothion and vamidothion sulphoxide)	0.5 : pome fruit 0.05 : other products
chinomethionat	0.3
folpet	20 : blueberries, currants, grapes, strawberries 15 : cherries, lettuce, rasp- berries 10 : citrus fruit, apples 5 : tomatoes 2 : other products

(*) Level set at or about the lower limit of determination

REPORT OF THE SCIENTIFIC COMMITTEE FOR PESTICIDES
ON THE USE OF CAMPHECHLOR AS AN INSECTICIDE
(Opinion expressed on 18 December 1980)

Background and terms of reference

Camphechlor (toxaphene) is used in certain Member States as an insecticide, particularly in the treatment of rape, certain forage crops, lawns, grassland and forestry plantations. The Commission requested the Scientific Committee for Pesticides to examine the composition and toxicology of camphechlor and its conversion products in relation to its applications and to give an opinion on the following questions:

1. What are currently the incidence, nature and levels of its residues in foodstuffs and the environment, and what will be the potential exposure of man?
2. Is the use, in accordance with good agricultural practice, of camphechlor prejudicial to the consumer or the environment, and, if so, can such dangers be eliminated by selective reduction of potential exposure or must a prohibition be envisaged? If the former, by what means could exposure be reduced, having regard to the availability of satisfactory alternative treatments and their toxicological and technological consequences?

Discussion

(i) Nature of camphechlor

Technical camphechlor consists predominantly of polychlorinated camphenes with 4 to 12 chlorine atoms per molecule and contains 67 to 69 per cent of chlorine. From the combined application of gas chromatography and mass spectroscopy it has been found that camphechlor is composed of at least 177 compounds of the general

formula $C_{10}H_{18-n}Cl_n$; 26 of these compounds occur in concentrations higher than 1%. Although different batches of campechlor produced by one manufacturer show reasonably consistent gas chromatographic peak patterns, much greater variation is observed between the products of different manufacturers. Such variation is to be expected because campechlor is produced by passing chlorine through a solution of technical quality camphene. It has been accepted that the addition of chlorine to the double bonds leads to 2-exo, 10-dichlorobornane; further reaction then leads to higher substituted chlorobornanes. Of these, only a few have been identified. Toxicant A comprises a mixture of 2,2,5-endo, 6-exo, 8,8,9,10-octachlorobornane and 2,2,5-endo, 6-exo, 8,9,9,10-octachlorobornane, which are present together to an extent of about 8 per cent. Toxicant B has been identified as 2,2,5-endo, 6-exo, 8,9,10-heptachlorobornane. In addition to the chlorobornanes, chlorocamphenes and other chlorotricyclenes are present.

Technical campechlor is a yellow waxy solid with a mild terpene odour. It has an empirical formula of $C_{10}H_{10}Cl_8$ and average molecular weight about 414. It melts over the range 65-90°C, has a specific gravity of about 1.6 and is readily soluble in organic solvents but very sparingly soluble in water.

(ii) Incidence of residues in foodstuffs and the environment

The latest estimate of annual world production of campechlor is about 20 million kg (4), most of which is used on cotton. Usage in the Community is relatively small and confined to rape, certain forage crops, lawns, grassland and forestry plantations. In the United States of America tolerances for raw agricultural commodities have been established at 0.1-7 mg/kg for a variety of 50 fruit, vegetable and meat products. The half life of campechlor residues on plants is reported (1,2) to be 5-13 days, depending on weathering conditions, plant type, growth rate and formulation.

Campechlor residues can be accumulated in fat of animals from ingestion or by dermal absorption. The storage level is, however, much less than that of other chlorinated hydrocarbon pesticides and an equilibrium with the exposure level is rather quickly achieved. The storage: feed ratio (concentration in fat/feed) varies from 0.3 to 0.5 in rats, sheep and cattle. Campechlor is stored in fat and transmission of residues to milk follows the same pattern. Equilibrium with input is reached within about one week and the ratio of campechlor concentration in the milk to that in the feed is about 0.01. In feeding trials, milk free from campechlor residues was produced within two weeks after cessation of feeding 10 ppm in the feed.

Under normal agricultural conditions campechlor is degraded in soil by microbial and photochemical reactions. In some cases it is reported (3) that campechlor persists for years. This can, however, be caused by a high dose which kills the micro-organisms responsible for the degradation and by incorporation with the soil, which prevents ordinary volatilization and photochemical degradation.

Residues of campechlor in water are caused by surface run off from treated fields. In surface waters of streams in western USA campechlor was not found within two years (1966-1968) among the samples collected at 20 stations. The solubility in water is low. However, campechlor has been detected in rain water at levels from 44-280 ng/L.

In the air, residues of campechlor can be found due to volatilization from crops, soil and water. These residues have been demonstrated at various locations in the USA, in relation with agricultural spraying activities. In a cotton growing area a maximum concentration of 1540 ng/m³ was found. There is also a long-range transport through the atmosphere. Air samples (fifty-six) collected over the western North Atlantic showed a mean concentration of 0.63 ng/m³.

(iii) Nature of residues in foodstuffs

There is no evidence for the existence of camphechlor metabolites as a residue in crops. Although there is an indication of a modest loss of early eluting GLC components, the residue is readily recognizable as camphechlor. No metabolites have been identified in plants. In animal fat the residue consists largely of unchanged camphechlor. However, when ^{36}Cl -camphechlor was fed to animals, 50-60% of the ^{36}Cl was quickly excreted in the urine and 30-40% in the faeces. In each case about half of the dose was excreted as chloride ion. Thus, camphechlor can undergo extensive dechlorination or dehydrochlorination or both.

(iv) Levels of residues in foodstuffs

The Joint Meeting on Pesticide Residues (FAO/WHO, 1973) has established guideline levels for a wide range of commodities. They include a level of 5 mg/kg for fat of meat of animals, 2 mg/kg for various fruits, vegetables and grains, 0.5 mg/kg for refined oils of cotton seed, rapeseed, soybean and peanut and 0.5 mg/kg for milk and milk products. However, residues of camphechlor are rarely detected in human foods.

(v) Potential exposure of man through diet or environment

In view of the limited use of camphechlor outside the cotton-growing areas, the actual exposure of man to dietary or environmental residues is low. Council Directive 76/895/EEC of 23 November 1976 relating to the fixing of maximum levels for pesticide residues in and on fruit and vegetables provides for a maximum level of 0.4 mg/kg. Since then the use of camphechlor in these crops has probably declined. International guideline levels exist as has been described in (iv). It is known that camphechlor is used outside the Community against ectoparasites on livestock. Other possible sources are air and water. Atmospheric levels of camphechlor are reported to be $<0.02 - 2 \text{ ng/m}^3$ of air, with a maximal level of 5.2 ng/m^3 . Only in cotton growing areas can higher values be found.

However, camphechlor residues have never been found in drinking water (684 samples $< 0.05 \mu\text{g/L}$). Camphechlor has not been detected in human tissues. This may be due partly to rapid elimination and partly to the relatively rare occurrence of residues in food.

In an FDA total diet study the average daily intake from food during the last 12 years was only 0.00001 mg/kg body weight.

(vi) Determination of camphechlor residues

The usual methods for determining camphechlor residues involve electron capture GLC; GC/CI/MS selected ion monitoring systems have recently been developed. Literature reports of quantification of camphechlor residues in the environment must be evaluated in the light of the methods employed. Carefully controlled studies reporting camphechlor residues in the mg/kg range are probably reliable, but reports of $\mu\text{g/kg}$ values in samples probably contaminated with other chlorinated hydrocarbons have to be considered of semi-quantitative or of qualitative value only. This consideration applies also to negative findings where a substantial camphechlor residue could be hidden in GC-baseline noise. The higher molecular weight camphechlor components tend to have lower volatilities and lower water solubilities than the lower molecular weight components. The consequence of these properties is that camphechlor residues have a relatively higher contribution from the heavier, more highly chlorinated components.

(vii) Acute and subacute toxicity

In the rat the oral and dermal LD_{50} 's are respectively 40 - 150 and 780 - 1075 mg/kg body weight. The oral LD_{50} has also been determined in many animal species with results varying generally from 25 - 200 mg/kg . Toxicity symptoms are those of chlorinated hydrocarbon pesticides. It has been shown, however, that camphechlors from different production sources have different LD_{50} 's in mice, varying from 33 - 138 mg/kg b.w.

Also various isolated components of camphechlor show a higher acute toxicity than the complete mixture. The subacute and semichronic toxicity has been determined in several animal species. The main effect found is liver enlargement, centrolobular hypertrophy of liver cells and microsomal enzyme induction in the liver. No toxic effects were observed at dietary dose levels of 25 ppm for the rat, 40 ppm for the dog and 15 ppm for the monkey. In a special experiment in which microsomal enzymes were measured it was found that 25 and 50 ppm produced marked induction of those enzymes, whilst at 5 ppm a minimal induction occurred.

(viii) Chronic toxicity and reproduction

Two chronic toxicity experiments were carried out with rats. In both the only effect was liver enlargement and microscopic changes in the liver, consisting of swelling and homogeneity of the cytoplasm and peripheral arrangement of the granules in the cytoplasm of the centrolobular hepatic cells. The highest level tested was 1500 ppm camphechlor in the diet and the no effect level was 25 ppm (FAO/WHO, 1968).

In a three generation reproduction study with rats (25 and 100 ppm in the diet) no effects were found on reproduction performance, fertility, lactation nor on viability and growth of the offspring (FAO/WHO, 1973).

In a five generation reproduction study with mice receiving 25 ppm in the diet no embryotoxic or teratogenic effects were observed. Teratogenicity was studied in an experiment in which mice and rats received oral dosages of respectively 0, 15, 25 and 35 mg/kg body weight during days 7-16 of gestation. The highest dose produced marked toxicity in the mothers. In the offspring, mice on the highest dose level showed encephaloceles, while the foetal mortality was somewhat increased at all three dose levels. In the rats small decreases in foetal body weight and ossification centres were seen, most of them in those receiving 25 mg/kg body weight. It is probable that camphechlor

in these relatively high dose levels caused an embryotoxic rather than a teratogenic response. No teratogenic response was observed when camphechlor was injected into eggs at doses up to 1.5 mg/egg.

(ix) Carcinogenicity

A number of carcinogenicity studies have been carried out (e.g. 2 in mice, 1 in rats and 1 in hamsters). In the first experiment with mice the animals of the low-dose level received a time-weighted average of 99 ppm in the diet and those of the high-dose level 198 ppm. There was a decrease in survival especially in the high-dose males. A dose related increase in the combined incidence of hepatocellular carcinomas and trabecular adenomas was observed in treated mice. High-dose males showed an incidence of 98% in the surviving animals, low-dose males of 69%, whilst in the pooled controls 8% was found. In the females 69% was found in the high-dose group, 10% in the low-dose and 0% in the pooled controls. In the matched controls this value was 0% in both sexes. Neoplastic nodules occurred in the low-dose males in 12%, whilst the matched controls showed 20%. In the females the high dose had an incidence of 12%, the low dose of 26% and in the matched controls no neoplastic nodules were present. In the second experiment with mice lower dose levels were tested. The animals received respectively 0, 7, 20 and 50 ppm in the diet for 18 months, followed by a withdrawal period of 6 months. In the males receiving 50 ppm, 18/51 animals showed hepatocellular tumours, which was significantly increased. At 20, 7 and 0 ppm these data were resp. 15/53, 10/54 and 10/53. In the female animals a slight increase was found (6/52 animals). The incidence in the groups with 20, 7 and 0 ppm were respectively 4/52, 2/53 and 2/53.

In the experiment with rats the animals of the low-dose level received 540 - 556 ppm in the diet and those of the high-dose level 1080 - 1112 ppm respectively for female and male animals. In male rats the combined incidence of follicular-cell

carcinomas and adenomas of the thyroid was 9/35 in the high-dose group, 7/41 in the low-dose, 2/44 in the pooled controls and 1/7 in the matched controls. In the females the incidence of follicular-cell adenomas was 7/42 in the high-dose group, 1/43 in the low-dose, 1/46 in the pooled controls and 0/6 in the matched controls. In both cases the incidence in the high-dose animals was significantly increased compared with the pooled controls, but not the matched controls. In addition, an increase was found in the incidence of adenomas, chromophobe adenomas or carcinomas of the pituitary high-dose females (23/39) compared with pooled controls (17/51). Two other long-term studies in rats give no indication of carcinogenicity.

In the experiment with hamsters the animals were given respectively 0, 100, 300 and 1000 ppm in the diet for 18 months (females) or 21 months (males). An increase in liver weight and liver hyperplasia were found at the highest dose levels. Only in the males were megalohepatocytes observed, with the following incidence: 0/50 (control), 3/50 (100 ppm), 3/51 (300 ppm) and 8/51 (1000 ppm). No enhanced tumour incidence was found.

(x) Mutagenicity

Mutagenicity was studied in various microorganisms, with and without activation by liver homogenate. Livers of mouse, rat, hamster and man were used for activation. With TA-98 and TA-100 bacteria (*Salmonella typhimurium*) a weak mutagenic effect was noted. Addition of S-9 preparation from rodents and human liver appeared to quench or detoxify the camphechlor activity, because no positive effect was found. With TA-1535, TA-1537 and TA-1538 and with *Saccharomyces cerevisiae* (strain D4) no mutagenic activity was found.

Camphechlor did not induce lethal mutations in mice.

(xi) Human data

No significant levels of camphechlor were found in skin fat and attached subcutaneous tissues taken from 68 newborns in 13 cities in the USA.

Eight women, working in an area (in Russia) which had been sprayed with polychlorinated camphene (not toxaphene) by aircraft, were taken to hospital. They were given cardiac drugs and 8 days later they showed an increased incidence of chromosome aberrations in lymphocyte cultures compared with an unspecified number of control individuals (13.1% versus 1.6%). It is not certain, however, that this has to be ascribed to "camphechlor".

In a survey of 199 employees who worked or had worked with camphechlor between 1949 and 1977, with exposures ranging from 6 months to 26 years (mean 5.23 years), 20 employees died, of which 1 with cancer of the colon. None of these deaths appeared to be related to exposure to camphechlor.

Application of an aerosol spray containing camphechlor to the skin of 50 human subjects daily for 30 days at a dose of 300 mg/day produced no toxic manifestations.

Fifty human volunteers who inhaled 0.0004 mg camphechlor/l aerosol for 10 minutes a day for 15 days had no subjective or objective effects. A mist containing 0,25 mg camphechlor per litre of air was inhaled by 25 humans for 30 minutes a day during 13 days. There was no evidence of local or systemic toxic manifestation.

The oral LD₅₀ for humans is estimated to be 60 mg/kg body weight.

(xii) Bioaccumulation

Bioaccumulation is found in bacteria (3000 - 5000 x) and in algae and fungi (11,000 x). This is not an active metabolic process, but a simple partitioning of the hydrophobic mixture in the lipid-like cells.

Campechlor is also bioaccumulated by fish. The bioconcentration factor in brook trout (*Salvelinus fontinalis*) is ca. 16,000, found after 140 days of exposure. Brook trout fry may have an even more pronounced tendency to accumulate campechlor than adults (14,000 - 20,000, with an extreme value of 76,000). In fathead minnow (*Pimephales Promelas*) concentration factors of 80,000 - 100,000 were found after 150 days of exposure. In practice, after the use of campechlor as a piscicide in lakes a concentration factor of ca. 10,000 was found in various fishes.

Residues determined in fish from freshwater locations in the USA showed values of 0.0 - ca. 5 mg/kg (ppm), with 12 - 25 ppm as an extreme value.

In various wild birds residues of campechlor have been reported up to 20 mg/kg (ppm); in some cases, especially in fish-eating birds, higher values were found (up to 82 mg/kg in pelicans).

(xiii) Toxicity to fish

Campechlor is extremely toxic to fish. For this reason it was used in the USA as a piscicide for many years. The LD₅₀ (96 hour) varies between 0.5 and 14 uk/l (ppb). For most species it is around 5 µg/l. When exposure is extended to longer periods very low levels of campechlor can be fatal to fish, due to bioaccumulation in a sensitive organ or tissue of the fish.

Other water organisms show a similar toxicity. The LC₅₀ (48 hour) for crustacea varies from 2.7 to 37 µg/l. Campechlor is very toxic to phytoplankton. Levels of 100 µg/l were found to cause a total inhibition of growth in 5 species of marine plankton and one of these was killed at 1 µl/l.

Chronic toxicity for fish was studied in the brook trout and fathead minnow. Brook trout were exposed to 0, 39, 68, 139, 288 and 502 ng/l (ppt) campechlor. With the two highest dose

levels growth was inhibited. During spawning 50% and 100% respectively of the 288 and 502 ng/l group died. This means that the LC_{50} (6 mo) was 0.288 $\mu\text{g/l}$, which is lower than the LC_{50} (96 hour) of 11 $\mu\text{g/l}$. The no-effect levels for reproduction and growth and survival of the young were <39 ng/l.

Camphechlor exerts a severe anatomical/developmental effect on young fish known as "broken back syndrome", which is caused by a decrease of backbone collagen. Even at 39 ng/l a decrease in collagen, but an increase in phosphorus and calcium, were found in brook trout fry after 90 days. The lowered collagen /minerals ratio is suspected to be the reason for the fragility of the fish backbones.

In a similar study with fathead minnow growth inhibition and a decrease in collagen in backbones was found at 55 ng/l (ppt), the lowest dose level tested.

(xiv) Toxicity to birds

Camphechlor shows a moderate to high toxicity in birds. The acute LD_{50} varies from 30 to 100 mg/kg b.w. In a subacute study of 4 months duration, 5, 50 and 500 ppm was given in the diet of bob-white quail. At the highest dose the birds showed significantly reduced body weights. Camphechlor also stimulated thyroid growth and iodine uptake by the thyroid as well as adrenal hypertrophy. No effect on liver weight was noted.

Attempts to correlate eggshell thickness and dietary camphechlor in Mallards and Japanese quail were inconclusive. In black ducks some indication was found that 50 ppm in the diet showed collagen and calcium changes in the backbone, similar to those seen in fish. Reproduction has been studied in hens. After dose levels of 5, 50 and 100 ppm in the diet no effects on egg production, hatchability, eggshell strength or fertilities were noted.

Camphechlor has been implicated in bird kills in some places in the USA.

(xv) Evaluation of the risk of exposure to camphechlor

- The exact composition of camphechlor is unknown and variable. It has been shown to be a complex mixture of at least 177 components. Moreover camphechlors from different production sources and even from the same source have different compositions.
- Toxicological studies have been carried out with a product of uniform reproducible composition. However, the materials in world wide agriculture do not conform to the specifications of the original products tested. This was one of the reasons why the Joint Meeting of FAO/WHO did not establish an ADI for camphechlor.
- A number of carcinogenicity and mutagenicity studies have been carried out. From two mice studies it is clear that camphechlor induces liver tumours in the mouse. In one rat study slight increase in the number of thyroid tumours was found. It is doubtful, however, whether camphechlor can be considered as a carcinogen in the rat. In two other long-term rat studies and in a study with hamsters no enhanced tumour incidence was observed. It is quite possible that the carcinogenic effect in mice livers has to be considered as a secondary effect of induction of microsomal liver enzymes and hypertrophy of centrolobular liver cells (in agreement with the same results for other chlorinated hydrocarbon insecticides). In that case a no effect level can be established for this effect. From the mutagenicity studies, however, it appeared that camphechlor has a weak mutagenic effect. Therefore a genotoxic effect (on DNA) cannot be excluded.
- The extreme complexity of the product makes residue analysis for camphechlor more difficult than for other pesticides, so residues in food and the environment may be underestimated by routine monitoring. However, there is sufficient information to say that camphechlor is slightly persistent in soil, air and water. It has been shown to accumulate through

aquatic food chains from water to plankton to fish to fish-eating birds. Very high concentration factors from water to fish have been found. Camphechlor is extremely toxic to fish. In acute toxicity tests values for LC₅₀ (96 hour) of 0.5 - 14 µg/l for fish have been found.

In long-term tests camphechlor is even more toxic. At levels of 40 ng/l reproduction can be impaired and changes in the backbone composition of young fish have been found. This causes a condition known as broken back syndrome.

Residues in water are caused by surface run-off from treated fields. Due to the extreme toxicity to fish, camphechlor may present therefore some hazards to the environment in treated areas. However, it was not detected in surface water of streams or in drinking water. It seems therefore unlikely that, outside treated areas, camphechlor shows a risk to the environment under normal conditions of use.

Opinion of the Committee

Ad. question 1

Residues of camphechlor are only very infrequently encountered in foods. Because of the very variable nature of the technical material, the nature of the residues is equally varied. Although variable gas chromatographic peak patterns are observed, any residues are readily recognisable as being due to camphechlor. The amounts of camphechlor residues occasionally observed in foods can reach a level of 1 to 5 mg per kg in fats from treated animals and up to 2 mg per kg for treated fruits or vegetables. Residues in edible oils or milk products do not exceed 0.5 mg per kg. The potential exposure of man through the diet is very low because of the infrequency of such residues actually occurring.

Ad. question 2

The use and application of camphechlor as an insecticide in the treatment of rape, certain forage crops, lawns, grassland and forestry plantations has certain disadvantages:

1. The composition of camphechlor is unknown and variable. Present specifications known to the Committee do not form an adequate basis for the definition of the composition of the product.
2. Camphechlor may present some degree of carcinogenic risk to man.
3. Due to the extreme toxicity to fish, some risk to the environment, in treated areas, cannot be excluded.

Having regard to the availability of adequate alternatives and to camphechlor's variable composition, the Committee is of the opinion that the potential hazards of camphechlor to the consumer are such that it should not be used on food, forage crops or in animal husbandry. The use of camphechlor on lawns, grassland and forestry plantations should be kept under review.

References

The data used in this summary were obtained from 7 review studies.

1. Evaluations of some pesticide residues in food FAO/WHO 1968.
2. Evaluations of some pesticide residues in food FAO/WHO 1973.
3. F Korte, J Scheuner and H Parlar

Toxaphene (camphechlor). A special report of the Commission on Terminal Residues, IUPAC

Pure and Applied Chem. 51, 1583-1601 (1979).
4. Toxaphene (polychlorinated camphenes). IARC Monographs on the evaluation of the carcinogenic risk of chemicals to humans (1979), volume 20, 327-348.
5. G A Pollock and W W Kilgore

Toxaphene. Residue Reviews, 69, 87-140 (1978).
6. W L Fitch and P M Dolinger

Toxaphene mixtures. Monograph number two. Environmental Health Evaluations of California restricted pesticides.
7. NCI. Technical background information. Report on carcinogenesis bioassay of toxaphene (March 1979).

REPORT OF THE SCIENTIFIC COMMITTEE FOR PESTICIDES
ON THE MARKETING AND USE OF 2,4,5-T

(Opinion expressed on 15 July 1981)

BACKGROUND AND TERMS OF REFERENCE

2,4,5-trichlorophenoxyacetic acid (2,4,5-T) is used in certain Member States as a herbicide, particularly in forestry, on cereals and grassland and in total weed control. Although 2,4,5-T was introduced as long ago as 1944, its safety has been questioned several times since the early 1970's following its controversial use as a defoliant during the Vietnam war. The main concern has been over contamination by the impurity 2,3,7,8-tetrachlorodibenzo-p-dioxin (TCDD), whose high toxicity has been highlighted by a number of industrial accidents during the manufacture of trichlorophenol - notably that at Seveso, Italy (1976) in which significant quantities of TCDD were released into the environment.

2,4,5-T is presently authorised for use as a plant protection product in most Member States, but not in Italy and the Netherlands. It has been the subject in recent years of numerous thorough reviews by certain national authorities (1)(2)(3). On the basis of these, Commission departments were satisfied that, when properly applied for the purpose intended, herbicides containing 2,4,5-T complying with the internationally approved specification, particularly regarding limits on TCDD-content (4), could be used without risk to human or animal health and with minimal risk to the environment.

On the other hand, the Commission is aware that there is continuing concern in some quarters, particularly following the emergency suspension of the registrations for certain uses of 2,4,5-T in the USA in February 1979 (5).

In view of the apparent divergence of views, the Commission decided to review all the available evidence to establish a scientific basis for possible Community action. To this end, it requested the Scientific Committee for Pesticides to give an opinion on the following question:

"Is the marketing and use in accordance with good agricultural practice of commercially available 2,4,5-T formulations, including their impurities, dangerous for human or animal health or prejudicial to the environment? If so, can such risks be sufficiently minimised by selective reduction of potential exposure or must a total prohibition be envisaged?"

OPINION OF THE COMMITTEE

In formulating its opinion, the Committee has taken into account all available information on the benefits and risks of 2,4,5-T usage. However, in view of the large volume of literature involved, this report cites only a representative selection of relevant scientific references.

A. 2,4,5-T Production

1. 2,4,5-T is manufactured from monochloroacetic acid and 2,4,5-trichlorophenol. The latter is produced by the alkaline hydrolysis of 1,2,4,5-tetrachlorobenzene using methanol and caustic soda at elevated pressure or ethylene glycol and caustic soda at atmospheric pressure. The hydrolysis is an exothermic reaction and unless the conditions are carefully controlled, chlorinated dioxins may be formed as byproducts. The chemistry of chlorodibenzo-p-dioxins indicates that there are 75 possible analogues ranging from mono- to octa-chlorinated species. For the tetrachloroderivatives, 22 isomers are possible, amongst them 2,3,7,8-tetrachlorodibenzo-p-dioxin (TCDD) which is the most toxic presently known. This is also the isomer most likely to be formed in the manufacture of 2,4,5-trichlorophenol. In varying amounts TCDD can therefore be present as an impurity in 2,4,5-T and its formulations.

2. Formulations available

A large number of formulations of 2,4,5-T have been approved for marketing in those Member States in which 2,4,5-T is authorised. These are principally ester or amine salt formulations containing 2,4,5-T alone or in combination with other herbicides, e.g. 2,4-D, mecoprop, MCPA, dicamba, atrazine and amitrole.

2,4,5-T is formulated widely within the Community but the sources of technical active substance seem to have been confined in recent years to producers in Austria, the Federal Republic of Germany and the USA.

3. TCDD content

All Member States in which 2,4,5-T is authorised have set a maximum permitted level of 0.1 mg TCDD per kg 2,4,5-T in the technical active substance, but recently (1980) Belgium, Germany and the UK have reduced this to 0.01 mg/kg.

The European manufacturers of the active substance now guarantee a TCDD content below 0.01 mg/kg and the Committee has been informed that the average level is about 0.002 mg/kg. USA production has been stated (6) to contain less than 0.05 mg/kg.

B. Agricultural Practice

1. Use

2,4,5-T is a selective herbicide, broad leaved plants being generally susceptible whilst grasses, coniferous trees and certain legumes are relatively resistant. This herbicide is particularly useful in controlling woody species and a few herbaceous species, e.g. Urtica dioeca and Tussilago farfara, which are relatively resistant to other herbicides. It is often used in mixtures with 2,4-D or other herbicides.

The main uses for which 2,4,5-T is authorised in Member States are the control of dicotyledonous weeds, nettles and woody vegetation in cereals (including maize), grassland, orchards, forests and non-crop land, especially rights of way such as railways, pipelines, powerlines and roads. 2,4,5-T has not been authorised for use in Italy since 1970 or in the Netherlands since 1978; it has not been commercially available in Denmark since 1979.

On the basis of information supplied by Member States, total consumption in the Community is estimated at approximately 600 tonnes of active substance (1979), of which less than 20% is used in forestry, and appears to be declining. For comparison, the amount used annually in the USA was estimated (5) at 4 200 tonnes, 28% in forestry, prior to the suspension of certain uses in 1979.

2. Rates and frequency of application

As an overall spray, application rates are generally within the range 1-5 kg/ha*. For spot treatments of individual trees or clumps of weeds, concentrations of 5-20 kg/1000 litres are applied as drenching sprays giving rates of up to 30 kg/ha.

Where 2,4,5-T or mixtures containing it are used, the frequency of application is typically as follows:

Cereal crops - 1 application per year
Rights of way - 1 application in 4 years
Grassland - 1-2 applications in 5 years
Forestry - 2-3 applications in each 50 year cycle.

3. Methods of application

In the Community the methods employed for the application of 2,4,5-T sprays include :

* expressed as acid equivalent

- (a) Tractor-mounted sprayers - mainly in cereals and grassland as well as in some non-crop situations.
- (b) Knapsack sprayers - in forestry, orchards and home gardens as well as spot treatments in various locations.
- (c) Other hand-held equipment - including ultra low volume and controlled droplet sprayers which deliver relatively concentrated oil-based sprays.
- (d) Aircraft - mainly in forestry and occasionally in other remote areas.

4. Precautions and safety intervals

The conditions of use authorised within the Community generally provide for the exclusion of livestock from treated areas immediately after treatment and avoidance of contamination of water (because of danger to fish). In the Community, aerial application is either totally prohibited or permitted only under strict conditions by authorisation of the competent authorities. Ultra-low volume spraying in general has begun to receive greater attention from regulatory authorities because of the higher concentrations involved. Special protective clothing for application may be necessary and some Member States are introducing this requirement for 2,4,5-T. Otherwise, the normal operator safety precautions for applying most liquid pesticide sprays are applied to 2,4,5-T, when using conventional ground spraying techniques.

5. Alternatives

- (a) In cereals, a large number of herbicides are available for control of herbaceous broad-leaved weeds. These include 2,4-D, MCPA and mixtures involving two or more of 2,4-D MCPA, bentazone, dicamba, dichlorprop, mecoprop, ioxynil, 2,3,6-TBA and 2,4,5-T.

The inclusion of 2,4,5-T in mixtures gives improved control of some weeds, especially species of Lamium and Galeopsis. It is also claimed that mixtures containing 2,4,5-T are more effective at low temperatures than other mixtures.

- (b) On rights of way and industrial locations woody weeds and Urtica dioeca can be controlled by a range of chemicals. However, if grass cover is desired only 2,4,5-T gives good results, with triclopyr as a possible alternative.
- (c) For control of woody weeds in grassland, triclopyr is promising but has not been widely tested. Other herbicides effective against Urtica dioeca, Ulex and Sarothamnus are not selective enough and would seriously damage grass or desirable hedge plants such as Crataegus. Glyphosate can be used effectively by careful spot treatment of clumps of weeds or by selective methods of application to tall weeds, but these methods increase application costs.
- (d) For controlling broad-leaved woody weeds in coniferous crops three alternatives to 2,4,5-T, triclopyr, glyphosate and fosamine ammonium, are available. All three give effective control of deciduous species and can be used with some selectivity in certain coniferous crops from July through to September. However, only triclopyr equals 2,4,5-T in controlling evergreens and is the most promising alternative despite some damage to Pinus.

When used early glyphosate gives control of some evergreens but causes considerable damage to conifers; it has the disadvantage of deteriorating after mixing with water. Fosamine ammonium is generally less effective than the other alternatives and causes damage to some coniferous species.

For site preparation, triclopyr, glyphosate, and ammonium sulfamate are effective for treatment of cut stumps, for tree injection and as basal bark sprays. They may also be used as overall sprays but if ground cover, such as grass, is desired neither glyphosate nor ammonium sulphamate are suitable.

The Committee wishes to stress that the alternatives are mentioned only in relation to their herbicidal activity. It has not evaluated their toxicological aspects.

C. Analytical methods for 2,4,5-T and TCDD

1. 2,4,5-T

- (a) In technical 2,4,5-T and formulations, including mixtures with other herbicides, gas-liquid chromatography and high pressure liquid chromatography methods are the most commonly used for the selective determination of 2,4,5-T.
- (b) At residue levels, various analytical procedures, depending on the nature of the materials to be analysed, have been reported. The limits of determination of the methods depend on the size of sample, the difficulty of extraction and clean-up, as well as the sensitivity and responses of the measuring equipment. They are usually of the order of some tens of micrograms per kg.

2. TCDD

The consequences of large variations in toxicity and biological activity between closely related chlorodibenzo-p-dioxin isomers and analogues make the analytical task of isomer-specific identification and quantification of TCDD both important and difficult.

- (a) TCDD determination in technical 2,4,5-T, its compounds and formulations.

Prior to 1966, thin layer and gas-liquid chromatographic methods were used to determine dioxins in 2,4,5-T. In order to increase the sensitivity and the selectivity, mass spectrometric methods (MS) were at first used successfully, but further development of combined GC-MS methods with the introduction of glass capillary columns has greatly improved the accuracy, precision, selectivity and sensitivity.

Today, these methods permit the determination more or less selectively of the TCDD isomer at concentrations of 0.001 mg/kg and are suitable for routine analysis. The methods are suitable for determining TCDD in the technical 2,4,5-T acid and esters, in their formulations and in mixtures containing other

herbicides such as 2,4-D. However, in the latter cases, additional purifications of the sample extracts by chromatography on silica gel and alumina columns are needed to eliminate interfering substances. Until now, however, no method has been standardized internationally.

(b) At residue levels

The analytical problems at residue levels are very difficult not only because methods must selectively determine TCDD but also because they must detect it at very low levels in the range of nanograms per kilogram. Moreover, the analysis of biological and environmental samples for possible TCDD contamination in the ng/kg concentration range is complicated by the presence of many interfering components ranging from naturally occurring compounds to industrial pollutants and pesticides.

Various GC-MS methods capable of detecting down to 10 picograms of TCDD are available. However, depending on their performance especially at the clean-up, separation and detection stages, they differ in specificity, some providing greater discrimination between TCDD and interfering components. Several other polychlorodibenzo-p-dioxins can be detected and confirmed.

The limits of determination of the analytical methods are variable and depend on the nature of the sample, sample size, matrix effects, performance of the apparatus and the efficiency of the clean-up procedures. It can vary from less than 0.1 ng/kg for water samples to some 10 or 20 ng/kg for beef fat and beef liver.

D. Toxicological data (7)(8)(9)(10)

1. 2,4,5-T

(a) Acute toxicity

The "pure" compound 2,4,5-T has a moderate acute oral toxicity. (LD₅₀ mouse : circa 400, rat : 500, guinea pig : circa 400 and dog : 100 mg/kg body weight (b.w.).

(b) Subacute and chronic toxicity

In a 90-day diet study with rats 100 mg 2,4,5-T/kg b.w. (TCDD content of the 2,4,5-T 1 mg/kg) induced inter alia depression of body weight, elevated serum alkaline phosphatase levels and minimal hepatocellular swelling. There were also some detectable changes in the 30 mg/kg group. The no effect level was 10 mg/kg b.w./day.

In a 13-week study with dogs in which 2,4,5-T was administered orally in capsules, the no effect level was most probably 10 mg/kg b.w./day.

Chronic toxicity data in the rat indicate a no effect level of 3 mg 2,4,5-T/kg b.w./day (TCDD content 0.05 mg/kg). At levels of 10 and 30 mg/kg b.w./day a dose related increase in mineralisation in renal papillae or pelvis were observed in females. At 30 mg/kg changes were noted in myocardium, gastric mucosa, muscles, liver and lung.

(c) Metabolism

Both in man and experimental animals 2,4,5-T is rapidly absorbed but minimally metabolised. It is excreted almost quantitatively as the acid, mainly through the kidneys (75-95%). In rats the plasma half-life is approximately three hours, but the plasma clearance rate decreases with increasing dose levels. In the dog plasma clearance is much slower, the half-life being about 80 hours. In the dog three unidentified urinary metabolites have been detected. Tissue analysis in the rat revealed that elimination is rapid, the highest concentration being found in the kidneys. Plasma elimination and excretion in human volunteers followed first-order rate processes, with a half-life of about 25 hours.

(d) Teratogenicity

Several teratogenicity studies have been carried out in rats and mice on 2,4,5-T, with TCDD levels varying from <0.02-30 mg/kg. At relatively high dose levels 2,4,5-T induced inter alia cleft palate in mice as well as kidney abnormalities and foetal mortality in both species. In mice 30 mg/kg b.w. is a no effect level (TCDD content <0.02 mg/kg). In one study with

rats cystic kidneys were observed at all doses tested (4.6-46.4 mg/kg b.w. (TCDD content 30 mg/kg)). However in another study using 1-24 mg/kg b.w. (TCDD content 0.5 mg/kg) no effects were observed.

No teratogenic effects of 2,4,5-T have been reported in rabbits, monkeys or sheep.

(e) Reproduction

At least two reproduction studies have been carried out in rats with 2,4,5-T. In one study (TCDD content < 0.5 $\mu\text{g}/\text{kg}$) neonatal survival was decreased in a dose-related manner in the groups that received 10 and 30 mg/kg b.w./day via the diet. In the group that received 3 mg/kg b.w./day no adverse effects were seen. In the other study (TCDD content approximately 0.05 mg/kg) no effects were observed at 30 mg 2,4,5-T/kg b.w., the highest level tested.

(f) Mutagenicity

Numerous studies of the mutagenicity of 2,4,5-T have been conducted with microorganisms, Drosophila and in vivo mammalian test systems. The types of tests employed measured primary DNA damage, gene mutations and chromosome effects. The results of these tests were negative or weakly positive. It cannot be ruled out that TCDD-impurities were involved in these positive results.

It can be concluded that reasonably adequate experimental data exist for 2,4,5-T and that there are insufficient indications to consider it a mutagen.

(g) Carcinogenicity

From the results of several long-term experiments in rats and mice no evidence of carcinogenic potential of 2,4,5-T was observed. In one study mice received 2,4,5-T from seven days of age for 18 months. Until weaning the compound was given by gavage (21.5 mg/kg b.w.), thereafter it was incorporated in the diet at 60 mg/kg.

In a lifespan study with rats the animals received 0, 3, 10 or 30 mg 2,4,5-T/kg b.w. Dioxins were not detected in the 2,4,5-T (analytical sensitivity below 0.4 $\mu\text{g}/\text{kg}$ for tetra-, hexa-, hepta-, and octachlorodibenzo-p-dioxins). In another study with rats at the same 2,4,5-T dose levels (TCDD content 0.05 mg/kg), there was also no evidence of 2,4,5-T-induced tumours from total incidence, altered induction time or particular tumour types.

2. 2,3,7,8-tetrachlorodibenzo-p-dioxin (TCDD)

(a) Acute toxicity

TCDD has an extremely high acute toxicity (oral LD_{50} rats : 22.5-45, guinea pigs : about 1, hamsters : 1150 and dogs : 30-300 $\mu\text{g}/\text{kg}$ b.w. Death after dosing animals with TCDD may be delayed as long as 40 days after a single dose.

(b) Subacute and chronic toxicity

TCDD and other more highly chlorinated dioxins have been identified in several commercial fats causing chick edema disease.

In a short-term study in rats TCDD was given by gavage five days a week for 13 weeks. Doses of 1 μg TCDD/kg b.w. caused inter alia some mortality, decreased body weights and liver alteration. Slight hyperplasia of bile ducts and ductular epithelium were present. These morphological alterations were less pronounced at the 0.1 $\mu\text{g}/\text{kg}$ b.w. dietary level. Rats given 0.01 $\mu\text{g}/\text{kg}$ b.w. had only a slight increase in the mean liver: body weight ratio. The no effect level was 0.001 $\mu\text{g}/\text{kg}$ b.w./day.

In a dietary study with monkeys, five out of 8 animals given 0.5 $\mu\text{g}/\text{kg}$ in the diet died within 7 to 9 months after onset of exposure. Autopsy findings included myocardium degeneration, moderate hyperkeratosis of the skin and marked biliary duct dilatation.

In a long-term dietary carcinogenicity study with rats, at the 0.1 $\mu\text{g}/\text{kg}$ b.w. treatment level there was significantly decreased body weight gain in both sexes. Liver weights were increased in males given 0.1 and 0.01 $\mu\text{g}/\text{kg}$ and in females given 0.1 $\mu\text{g}/\text{kg}$. Since the liver from females in the lowest dose test group (0.001 $\mu\text{g}/\text{kg}$ b.w./day) had an increased incidence of swollen hepatocytes, this dose level can be considered as a marginal no-effect level.

(c) Metabolism

TCDD stimulates a number of enzyme activities, notably in the liver. It is a very potent inducer of microsomal drug metabolising enzymes.

In hamsters the elimination in urine and faeces suggested a first-order process, with a half-life of about 12 days. No unmetabolized TCDD was detected in the liver or adipose tissue, indicating that the biotransformation products are readily excreted (11).

Biological half-lives have been reported of 12-21 days in rats and of about 30 days in guinea pigs. There are indications that in rats TCDD is excreted into bile in metabolized form as a water-soluble conjugate.

As yet the metabolism of TCDD is unknown, but its persistence in mammals seems to be moderate.

(d) Teratogenicity

TCDD causes a number of birth abnormalities in mice and rats, including cleft palate and kidney, skeletal and intestinal tract abnormalities. When 0.03 $\mu\text{g}/\text{kg}$ b.w. of TCDD was administered to pregnant rats, there were no terata produced ("no effect level"). Abnormalities were evident at 0.125 $\mu\text{g}/\text{kg}$ b.w. and higher. In one study embryotoxicity was also observed at this dose level.

In mice, fetotoxicity occurred at 0.3 $\mu\text{g}/\text{kg}$ b.w. Terata were observed in several strains of mice given 3 $\mu\text{g}/\text{kg}$ b.w. It produced hydronephrotic kidneys in mouse pups not exposed to TCDD in utero but nursed by dams treated with TCDD.

(e) Reproduction

In a three-generation reproduction study with rats, fertility was decreased at 0.01 $\mu\text{g}/\text{kg}$ b.w. Necropsy of pups surviving the 0.1 $\mu\text{g}/\text{kg}$ b.w. dose revealed dilated renal pelvises. No consistent adverse effects were observed in the 0.001 $\mu\text{g}/\text{kg}$ b.w. group.

(f) Mutagenicity

Direct assessment of the mutagenicity of TCDD is rather limited. TCDD appears to induce gene mutations in Salmonella and E. coli. The results from rodent dominant lethal tests and in vivo cytogenetic evaluations were predominantly negative. As the mammalian tests are relatively insensitive, TCDD must be considered, based on the positive bacterial tests, as a potential mutagenic agent.

(g) Carcinogenicity

Evidence of the carcinogenic properties of TCDD has been obtained from long-term studies in rats. In a diet study hyperplastic liver nodules were observed at 0.01 $\mu\text{g}/\text{kg}$ b.w./day and at 0.1 $\mu\text{g}/\text{kg}$ b.w./day hepatocellular carcinoma, mammary tumours and squamous cell carcinomas in the buccal cavity and lungs were noted. As these tumours were observed only at a relatively high, toxic, dose level, they may have been caused by an indirect promotor mechanism. However, in view of the mutagenic activity in bacteria, genotoxicity cannot be excluded.

3. Evaluation

Based on the no-effect level of 2,4,5-T in the rat (3 mg/kg b.w./day) and applying a high safety margin chosen because of the extreme toxicity of TCDD which may be present in minimal amounts up to 0.01 mg/kg of 2,4,5-T, a daily intake of 0.003 mg 2,4,5-T/kg b.w. by man is acceptable.

E. Residues of 2,4,5-T

1. On treated plants (10)

- (a) Grass: Immediately after application to grassland, residues of the order of 100 mg/kg of grass can be recovered for each kilogram of 2,4,5-T applied per hectare. The half-life in green tissue is 2-3 weeks and in dead tissue 3-4 weeks, the residues being present primarily as surface deposits.
- (b) Cereals: In general no residues of 2,4,5-T are detected in cereal grains after normal spraying of crops with 2,4,5-T, although levels of 10 - 15 mg/kg may occur in straw.
- (c) Forests: Residues in wild berries vary widely probably due to the shielding effect of leaves but residues as high as 100 mg/kg have been reported 3 days after spraying with 2,4,5-T at 3 kg/ha. In wild mushrooms, the highest residues detected after spraying were about 2 mg/kg.

2. In mammals

There is no evidence that 2,4,5-T accumulates in the food chain and the biological half-life in mammals ranges from 5 - 80 hours (shortest in rat).

To minimize the possibility of fruit or mushrooms containing high residues being consumed, it seems desirable that woodland areas and hedgerows to which the public have access should not be sprayed with 2,4,5-T during the ripening and harvest periods of wild fruit and mushrooms.

F. Effects on the environment

The most obvious effect of the use of any herbicide is the shift of plant communities in favour of the desired species (12). Secondary effects due to changes in the natural vegetation and in the composition of food and feedingstuffs (such as an increase in the nitrate content of plants) as a result of the use of 2,4,5-T, are not considered in this report.

1. 2,4,5-T

(a) Soil

2,4,5-T can be degraded (decarboxylated) by microorganisms and rapidly by direct sunlight. The half-life in soil has been found to be 1-2 months depending on the soil type and the activity of the microorganism (13). There is no evidence that residues are carried over from year to year, provided that 2,4,5-T is not used under extreme conditions. Even repeated application does not seem to give rise to adverse chronic effects in agricultural and forestry areas.

(b) Water

2,4,5-T has been found in surface water as a result of soil run-off after plant treatment but at very low concentrations of the order of 0.05 - 1 mg/litre. It is rapidly hydrolysed in natural surface water to trichlorophenol and then further decomposed. Most evidence indicates that microbial activity is primarily responsible for the degradation of chlorinated phenoxyacid herbicides in the aquatic environment (14). As 2,4,5-T breaks down rapidly in soil and there is no evidence of leaching, contamination of ground water is extremely unlikely provided the herbicide is used in accordance with recommendations.

(c) Wildlife

In areas treated with normal amounts of 2,4,5-T birds are not affected acutely or chronically in the egg, chick or adult stages (15). In an ecological study on a heavily treated area (16) no permanent harmful effects on wildlife were reported

and other studies (17) have shown no direct adverse effects on game animals and reindeer in 2,4,5-T treated areas. 2,4,5-T has a very low toxicity to bees (18) and only in feeding experiments using unrealistically high levels (100 - 1000 mg/kg) were severe reductions in brood development observed (19).

Although an acute numerical reduction in some cases or stimulation of growth in others has been reported for certain microorganisms (20), repeated applications of 2,4,5-T do not appear to give rise to long-term adverse effects on soil living organisms.

2,4,5-T is acutely toxic to most aquatic fauna including fish (LC_{50} (48 hrs) in the range 1 - 100 mg/litre), but serious harm to aquatic fauna has seldom been reported following normal use of 2,4,5-T. However, great care is necessary to avoid contamination of surface water by direct spraying, spillage or discharge (21).

The evidence available shows that 2,4,5-T preparations, which do not contain significant amounts of TCDD, are relatively harmless to the environment with few undesired direct effects when used in accordance with good agricultural practice.

2. TCDD

(a) Terrestrial environment

TCDD is extremely immobile even in sandy soil as it is strongly bound to soil particles. The half-life in soil is 1-3 years. Degradation by soil microorganisms is negligible but little is known of its effect on them.

Less than 0.2% of the TCDD present in soil is taken up by plants and TCDD on the surface of leaves is photodecomposed to some extent. It has been shown (22) that it is readily photodecomposed by solar and UV-light in the presence of an organic hydrogen donor in which it is soluble.

Since TCDD has a low vapour pressure, its mobility is limited to particle transport or transfer by living organisms. There is no evidence of TCDD formation in nature either photochemically or by microorganisms from 2,4,5-T or its corresponding trichlorophenol.

(b) Water

TCDD has a very low solubility in water ($< 0.2 \mu\text{g/litre}$) and there is no measurable hydrolysis or photodecomposition in natural waters. Its persistence may result in accumulation in sediments, to the particles of which it remains bound. Since it is strongly adsorbed to soil and does not leach there is little danger of ground or surface water being contaminated. For the same reasons, residues in drinking water are extremely unlikely.

(c) Wildlife

Little is known about the long-term toxicity of TCDD to terrestrial wildlife but, since it is strongly adsorbed to soil and other particles, it would only have a low degree of bioavailability.

Whilst every effort should be made to minimise the presence of TCDD in the environment because of its extreme toxicity, the Committee is satisfied that when 2,4,5-T is used according to good agricultural practice, its TCDD impurity does not give rise to undesirable ecotoxicological effects. This conclusion is supported by the fact that TCDD residues have not been found in animals, plants, soil or water in areas subject to normal annual treatment with 2,4,5-T over several years.

G. Occupational Health and Epidemiological Studies (8)(9)

1. General

A wide variety of acute and subacute health effects have been reported in workers involved in the manufacture of 2,4,5-T and/or trichlorophenol, mainly after manufacturing accidents.

It is necessary to distinguish between the effects of exposure to 2,4,5-T/trichlorophenol and those effects related to exposure to the contaminant TCDD, as it has been known since 1957 that TCDD is the agent responsible for causing occupational chloracne.

Because it is frequently seen in the absence of any other adverse effects, chloracne, a skin disease characterised by comedones, cysts, pustules and abscesses, is considered by many authors to be an early clinical manifestation of TCDD exposure and is the most consistent clinical finding. According to some authors, the appearance of chloracne is the most sensitive indicator of exposure to TCDD at a level capable of inducing clinical signs of intoxication. Liver disorders, peripheral neuritis, disorders of fat metabolism (raised cholesterol and lipid levels) and porphyria cutanea tarda are other frequently reported findings in exposed workers.

2. Occupational exposure to 2,4,5-T

- (a) The documented experience of the Dow Chemical Company shows that there were no clinical effects in 204 employees exposed for varying times to 2,4,5-T during its manufacture over a 22-year period. The exposures far exceeded any casual contact arising during the course of normal agricultural operations involving 2,4,5-T.

The individuals studied were potentially exposed to higher (unknown) levels than the current international limit for TCDD of 0.1 mg/kg. No adverse effect due to 2,4,5-T exposure was observed in any of over 50 different clinical parameters, other than occasional skin or eye irritation in a few cases where acute overexposure had occurred (23).

- (b) In workers employed in factories manufacturing chlorinated phenols, a moderately high incidence of urinary porphyria, chloracne and hirsutism has been reported. There was no correlation between the degree of the chloracne and the level of uroporphyrin in the urine (24). No increase of total

mortality or of deaths from malignant neoplasms or diseases of the circulatory system was observed in a group of workers with a high peak exposure to TCDD, who were monitored over a period of nearly thirty years (25).

- (c) In March 1980 the UK National Union of Agricultural and Allied Workers published a dossier giving brief accounts of the experiences of a number of forestry and farm workers, in which people or animals were said to have been harmed in circumstances associated with 2,4,5-T. In none of these cases, has the data been sufficient to establish a causal relationship and, despite subsequent detailed investigation by the UK authorities, no further evidence has become available that can be considered sufficient to attribute the toxic and teratogenic effects described to 2,4,5-T.

Some wives of the workers involved had miscarriages and children born with malformations. In the majority of cases, there was no known exposure of the women to 2,4,5-T and there is no conclusive evidence of association between exposure to the herbicide and birth defects in humans (26).

3. Epidemiological studies

(a) Agent Orange in Vietnam

During 1961-1970 mixtures of n-butyl esters of 2,4-D and 2,4,5-T were used as defoliants in the Vietnam War. It was estimated, based on a mean contamination of 1.68 mg TCDD/kg 2,4,5-T (range 0.1-47), that during the decade a total of 110 kg of TCDD was sprayed from the air. The major portion, 89%, was used during a four year period, 1965-1969, over about one million hectares of South Vietnam (6% of the country's total land area), equivalent to a mean of 106 mg of TCDD per hectare. With regard to claims for an increased rate of cancer, neurological disorders, birth defects and abortion in people in the sprayed area in Vietnam, it should be borne in mind that a statistical analysis of data from Vietnam is not

available, and relevant epidemiological and demographic data for that period - including hospital records - are incomplete, inadequate and insufficient.

(b) In Finland, a study was conducted on workers using 2,4,5-T and other phenoxyacetic acid herbicides in forestry and on roads and railways. Although the exposed and control groups were small, no obvious or significant differences were found between them. In another Finnish study the Institute of Occupational Health conducted a nationwide survey of the health effects of 2,4,5-T and 2,4-D. No increased mortality from cancer or from other causes was demonstrated in any workers exposed to herbicides (9).

(c) Seveso, 1976

The only accident where detectable amounts of TCDD have been released into the open environment happened in 1976 at Seveso (Italy). A few days after exposure a number of people began to complain of burning lesions. 34 cases of chloracne occurred in children under 15 years of age between 2 and 5 months after exposure. Later, dermatological screening showed 130 more cases in children distributed as follows: 19.6% of the children in Zone A (high contamination), 0.5% of those in Zone B (low contamination) and 0.7% in Zone R (minimal contamination). The frequency of chloracne in children living in a monitored area (outside A,B or R) was reported as 0.1%. From 2 to 12 months after the exposure, 23 cases of chloracne were recorded in adults over 15 years of age. No general clinical impairment was reported in these chloracne cases. In the intervening years there has been a marked improvement in the conditions of most of those affected.

According to a neurological survey, a decrease was reported to have occurred in sensory and motor conduction time in some nerves in one out of ten patients from Zone A. There was no correlation with skin effects. Clinical examination also indicated some effects on the liver which lasted for at least two years. Since an unexposed control group was not examined

in the same way at the same time, the significance of these findings is difficult to interpret. However, it is premature to say that there will be no long-term effects on the Seveso population.

4. Teratogenicity and Embryo-toxicity

Reports claiming human teratogenic effects resulting from exposure to 2,4,5-T have appeared in New Zealand and Australia where the herbicide has been implicated in the occurrence of neural tube defects (such as spina bifida). However, the conclusion drawn by the investigators was that there was no evidence to implicate 2,4,5-T as a causal factor in these defects (27).

The WHO evaluation of the effects of Agent Orange in Vietnam considered that the reports of increased birth defects in South Vietnam caused by 2,4,5-T were inconclusive owing to inadequate data (28).

Some individuals have claimed to have suffered from exposure to 2,4,5-T in the environment. One such claim involving spontaneous abortion resulted in a two-part investigation conducted by the US EPA. The second part ("Alsea II") played a prominent role in the Agency's decision to suspend certain uses of 2,4,5-T in 1979 (5). The Alsea II study has been subject to serious scientific criticism by a number of American and other bodies. These critiques find that evidence of relevant exposure to 2,4,5-T is lacking and that the rate of spontaneous abortions does not appear to be related to the use of 2,4,5-T (29).

Studies have been made on the correlation between the use of 2,4,5-T and the rates of congenital malformations in Arkansas (1948-74) and Hungary (1970-75) but there was no evidence of a relationship with 2,4,5-T exposure. However, in both studies the rate of birth defects investigated was that of the general population; no information was available to compare individual exposure to 2,4,5-T with birth defects (30).

5. Carcinogenicity

There are no epidemiological or other reports which establish a correlation between cancer and previous exposure to phenoxyacetic acids in human beings.

A recent study on a number of patients with soft tissue sarcomas and malignant lymphoma, who had apparently been exposed to chlorinated phenols or phenoxyacetic herbicides including 2,4,5-T over a period of 10 to 20 years prior to diagnosis. The investigation showed an approximately six-fold increase in the incidence of soft tissue sarcomas relative to a control group. The cases studied consisted of 21 patients still living and 31 now deceased admitted to hospital during 1970-1977. The duration of exposure varied, according to the authors, from 2 days to 49 months. The data were obtained by questionnaires and telephone interviews in 1978.

The Committee questioned the value of this study in that it seems unlikely, bearing in mind the long latency period and the time between diagnosis and the evaluations, that workers or their next of kin could recall with any accuracy the exact chemicals being used in the past or the duration of exposure to them (31).

H. Possibility of accidental formation of TCDD

Concern has been expressed about possible formation of TCDD by pyrolysis of 2,4,5-T or its formulations, or of treated crops, brushwood or forests. Investigation has shown the amounts of TCDD which would be formed under these conditions would be below the limits of detection. Obviously when storing 2,4,5-T or its formulations, the general safety precautions for chemicals must be observed (32).

I. Recommendations and conclusions

1. 2,4,5-T is a selective herbicide, which has been in continuous but limited use within the Community for more than 25 years and still remains the most effective product in nearly all its fields of use.
2. A "no observable effect" level has been demonstrated for 2,4,5-T containing 0.05 ppm TCDD in animal toxicological studies and the 1979 FAO/WHO Joint Meeting on Pesticide Residues has accordingly recommended a temporary ADI of 0.003 mg/kg body weight/day, which the Committee accepts.
3. However, in order to avoid the possibility, as far as is practicable in relation to the use of 2,4,5-T, of the occurrence of traces of TCDD in foodstuffs, the Committee is of the opinion that permitted uses of 2,4,5-T should be such as not to leave residues in food crops at harvest above the lower limit of determination of 2,4,5-T. Areas to which the public has access should not be sprayed during the ripening and harvesting periods of wild fruits and mushrooms.
4. The Committee noted that on the basis of existing manufacturing technology, an average TCDD content of about 0.002 mg/kg 2,4,5-T can be achieved and consequently considers that a guarantee level of 0.005 mg/kg should be possible. The Committee, however, is aware that no standardised method to control such a low level exists and recommends that candidate methods be collaboratively tested with a view to reducing the present guarantee of 0.01 mg/kg as soon as possible. In the meantime, this maximum level of 0.01 mg/kg, already enforced in some Member States, should be adopted by the Community.
5. There is no evidence that the proper use of 2,4,5-T preparations has in practice given rise directly to ecotoxicological effects or that 2,4,5-T and TCDD accumulate in nature when 2,4,5-T is used in accordance with good agricultural practice.

6. Whilst the Committee is satisfied that there is no particular risk to operators handling formulations containing 2,4,5-T complying with this specification, it stresses the importance, as for all pesticides, of strict observance of the appropriate precautions for use.

The Committee concludes that the marketing and proper agricultural use of 2,4,5-T, the average TCDD content of which is not more than 0.002 mg/kg (see 4 above), is not dangerous for human or animal health or prejudicial to the environment, assuming that any residues left in food crops offered or accessible to the public are not above the lower limit of determination of 2,4,5-T (presently at or below 0.05 mg/kg).

REFERENCES

- General references : "The Science of 2,4,5-T and Associated Phenoxy Herbicides", Bovey and Young, John Wiley & Sons, 1980.
- "Chlorinated Phenoxy acids and their Dioxins", C. Ramel (Ed.), Ecological Bulletins No. 27 (1978).
- (1) Bundesgesundheitsblatt (Berlin) 18. 1975, 16, 264-265.
 - (2) Mitteilungen aus der Biologischen Bundesanstalt für Land- und Forstwirtschaft, Berlin-Dahlem, Heft 181, 1978.
 - (3) "Review of the safety for use in the U.K. of the herbicide 2,4,5-T", March 1979; Ministry of Agriculture, Fisheries and Food, London.
 - (4) FAO Specifications for Pesticides, Herbicides 1977 - Not more than 0.1 mg TCDD per kg of the extractable 2,4,5-T acid content.
 - (5) U.S. Federal Register, Vol 44; No 52, 15.3.1979, p. 15874.
 - (6) "Summary of Dow's response to EPA's Risk Analysis on the use of 2,4,5-T herbicide", The Dow Chemical Company, February 1979.
 - (7) 1970 Evaluations of the 1970 Joint Meeting of the FAO Working Party of Experts on Pesticide Residues and the WHO Expert Group on Pesticide Residues, Rome, 9 - 16 November 1970. WHO Techn. Rep. Series, No. 474 (1971).
 - (8) IARC Monographs on the evaluation of the carcinogenic risk of chemicals to man.
"Some fumigants, the herbicides 2,4-D and 2,4,5-T chlorinated dibenzodioxins and miscellaneous industrial chemicals", Vol. 15, WHO-IARC, Lyon (1977) 41-102, 273-299.
 - (9) Long-term hazards of polychlorinated dibenzodioxins and polychlorinated dibenzofurans".
International Agency for Research on Cancer (1978). Internal Technical Report No. 78/001.
 - (10) Pesticide Residues in Food : 1979 Evaluations
The monographs, data and recommendations of the Joint Meeting of the FAO Panel of Experts on Pesticide Residues and the Environment and the WHO Expert Group on Pesticide Residues, Geneva, 3 - 12 December 1979, Rome (1980), 560.
 - (11) "Tissue distribution, excretion and metabolism of 2,3,7,8-tetrachlorodibenzo-p-dioxin (TCDD) in the golden Syrian Hamster".
Olson, J.R., T.A. Gasiewicz and R.A. Neal, T.A.P. 58 (1980) 75-85.
 - (12) Marker, E., "Growth regulating substances and the effect of 2,4,5-T on natural vegetation", Blyttia 32, 123-30, (1974).

- (13) Blackman, G.E., J.D. Fryer, A. Lang and N. Newton, "The effect of herbicides in South Vietnam. Part B. Persistence and disappearance of herbicides in tropical soils.", Natl. Acad. Sci. : Washington D.C., (1974).
- (14) Frank, P.A., "Herbicidal residues in aquatic environments.", Adv. Chem. Ser. no. 111, Am. Chem. Soc. E, Washington D.C. 135-48 (1972).
- (15) Kenaga, E.E., "The evaluation of the safety of 2,4,5-T to birds in areas treated for vegetation control." Residue Reviews, 59, 1-19, Ed. F.A. Gunther, (1975).
- (16) Young, A.L., C.E. Thalken and W.E. Ward, "Studies of the ecological impact of repetitive aerial applications of herbicides on the ecosystem of Test Area C-52A", Eglin Air Force Base, Florida, Final Report, May 1973 - December 1974. Air Force Armament Laboratory, Eglin AFB, Fl. Doc. No. AFATL-TR-75-142.
- (17) (a) Engdahl, B., "De klorerade fenoxyiättinsyrornas ekologiska effekter.", Statens Naturvårdsverk, PM 528, Oktober 1974.
 (b) Erne, K., "Rentiersterben - kein Herbizidunfall", Kosmos, 70, 204, (1974).
 (c) Erne, K., "Stellungnahme zum Rentiersterben in Schwedisch-Lappland.", Allgem. Forst. 29, 31, (1974).
 (d) Erne, K., "Weedkillers and Wild-life." Proceedings of XI Int. Congr. Game Biol., Stockholm 1973, 415-22, (1974).
- (18) Beran, F., and J. Neururer, "Effect of plant protection materials on the honeybee. I. Toxicity to bees.", Pflanzenschutzberichte 15, 97-147, (1955).
- (19) Morton, H.L., J.O. Moffet and R.H. Macdonald, "Toxicity of herbicides to newly emerged honeybees." Environ. Entomol. 1. 102-4, (1972).
 Morton, H.L. and J.O. Moffet, "Ovicidal and laticidal effects of certain herbicides on honeybees.", Environ. Entomol. 5, 611-14, (1972).
- (20) Stojanowicz, B.J., M.V. Kennedy and F.L. Shuman, "Edaphic aspects of the disposal of unused pesticides, pesticide wastes and pesticide containers.", J. Environ. Qual., 1, 54-62, (1972).
- (21) Kenaga, E.E., "2,4,5-T and derivatives : Toxicity and stability in the aquatic environment.", Down to Earth. 30, 19-25, (1974).
- (22) Liberti, A., D. Brocco, J. Albegrini, A. Cecinato and M. Possanzini, "Solar and UV photodecomposition of 2,3,7,8-tetrachlorodibenzo-p-dioxin in the environment.", The Science of the Total Environment, 16, 97-104, (1978).
- (23) Ott, M.G., B.B. Holder and R.D. Olson, "A mortality analysis of employees engaged in the manufacture of 2,4,5-trichlorophenoxy-acetic acid.", J. Occ. Med., 22, (1980), 47-50.
- (24) Poland, A.P., D. Smith, G. Metter and P. Possick, "A health survey of workers in 2,4-D and 2,4,5-T Plant.", Environ. Health 22 (1971), 316-327.

- (25) Zack, J.A., and R.S. Suskind, "The mortality experience of workers exposed to tetrachlorodibenzodioxin in a trichlorophenol process accident.", *J. Occ. Med.*, 22, (1980), 11-14.
- (26) "Further review of the safety for use in the U.K. of the herbicide 2,4,5-T", December 1980; Ministry of Agriculture, Fisheries and Food, London.
- (27) Smith, A.H., D.P. Matheson, D.O. Fisher and C.J. Chapman, "Preliminary Report of reproductive outcomes among pesticide applicators using 2,4,5-T.", *N.Z. Med. J.*, 93 (1981), 177-79.
- (28) World Health Organisation, (1977), EHE/EHC/77.5, "Environmental Health Criteria for tetrachlorodibenzodioxin".
- (29) (a) "Report of assessment of a field investigation of six-year spontaneous abortion rates in three Oregon areas in relation to forest 2,4,5-T spray practices.", Report by the Epidemiological Studies Program, Human Effect Monitoring Branch, Benefits and Field Studies Division, OPP, OTS, EPA, 1979.
- (b) Wagner, S.L., J.M. Witt, L.A. Norris, J.E. Higgins, A. Agresti and M. Ortiz, "A scientific critique of the EPA ALSEA II study and report.", Report of the Environmental Health Sciences Center, Oregon State University, Corvallis (1979).
- (30) (a) Nelson, C.J., J.F. Holson, H.G. Green, and D.W. Taylor, "Retrospective study of the relationship between agricultural use of 2,4,5-T and cleft palate occurrence in Arkansas.", *Teratology* 19, (1979), 377-83.
- (b) Thomas, H.F., "2,4,5-T use and congenital malformation rates in Hungary.", *The Lancet*, July 26 (1980), 214-15.
- (31) Hardell, L. and A. Sandström, "Case-control study : Soft tissue sarcomas and exposure to phenoxyacetic acids or chlorophenols.", *Br. J. Cancer*, 39 (1979), 711-17.
- (32) Stehl, R.M. et al., "Combustion of several 2,4,5-trichlorophenoxy compounds : formation of TCDD.", *Science*, 197 (1977), 1008-9.

European Communities — Commission

EUR 7581 — Reports of the Scientific Committee for Pesticides

Luxembourg: Office for Official Publications of the European Communities

1981 — VI, 69 pp. — 16.2 x 22.9 cm

Agriculture series

DE, EN, FR, IT

ISBN 92-825-2701-8

Catalogue number: CD-NK-81-003-EN-C

Price (excluding VAT) in Luxembourg

ECU 6.14 BFR 250 IRL 4.20 UKL 3.60 USD 6.70

This first series of reports of the Scientific Committee for Pesticides contains the Committee's opinions, delivered in the period up to August 1981, on the use of certain pesticides and, for a wider range of pesticides, on the maximum permitted levels of their residues in certain foodstuffs.

The opinions of the Committee relate to questions put to it by the Commission concerning ethylene oxide, camphechlor and 2,4,5-T, as well as pesticide residues in fruit and vegetables, cereals and products of animal origin.

NOTICE TO THE READER

All scientific and technical reports published by the Commission of the European Communities are announced in the monthly periodical "**euro-abstracts**". For subscription (1 year: BFR 2000) please write to the address below.

Price (excluding VAT) in Luxembourg

ECU 6.14

BFR 250

IRL 4.20

UKL 3.60

USD 6.70



OFFICE FOR OFFICIAL PUBLICATIONS
OF THE EUROPEAN COMMUNITIES

ISBN 92-825-2701-8

L-2985 Luxembourg

CDNA07581ENC